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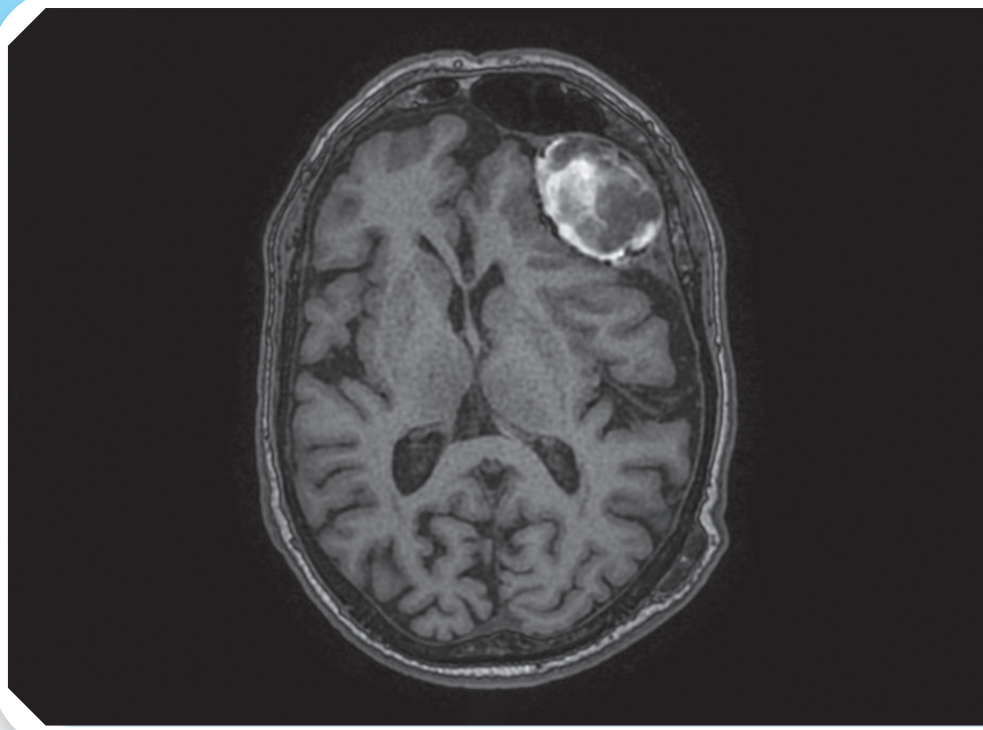

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Aneurysmal Subarachnoid Hemorrhage: Is the Time Until Intervention Related to Minor Disabilities in 6 Months?

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Abstract

Background Aneurysmal subarachnoid hemorrhages (aSAHs) account for 5% of all strokes, an appalling number when it comes to the second most common cause of death worldwide. The basis of the treatment is clinical support and either endovascular or surgical intervention. The purpose of the present study is to analyze if the time from the onset of the thunderclap headache until treatment intervention is related to the degree of disability after 6 months.

Methods In the present prospective observational study, data were collected from all patients ($n = 223$) admitted to the hospital with a diagnosis of aSAH. Patients whose data were missing or who missed the follow-up after 6 months were excluded. Then, the number of days from the thunderclap headache until the surgical intervention (Delta T) was obtained. The degree of disability was evaluated using standardized scales, Rankin Scale (RS) and Glasgow Outcome Scale (GOS), at the time of discharge as well as 6 months later. Then, the RS and GOS were correlated with Delta T.

Results An average of 6.8 days was found from the onset of symptoms to the intervention, the average age was 54 years old, 73% were women and 55% were smokers. The mean Glasgow Coma Scale on admission was 13. The mean score on the Hunt and Hess scale was 2.1. From the radiological point of view, the mean size of the aneurysm was 6 mm, and the modified Fisher Scale was 3.1. Of the total number of patients at the end of the study ($n = 78$), 50 underwent microsurgical treatment (63%). Rankin scale at discharge was 1.9 and GOS was 4.5, with no statistically significant change at 6 months. Analyzing the data distribution using linear regression, no statistically significant correlation was found between the time until treatment and

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- aneurysmal subarachnoid hemorrhage
- disability
- treatment
- outcomes

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disability using RS and GOS ($p > 0.05$). The same results were found even analyzing age subgroups (≤ 45 years old, 45 to 55 years old, 55 to 70 years old, and > 70 years old with a p-value > 0.05).

Conclusions The present study suggests that there is no linear correlation between Delta T and disability at 6 months for the population studied. However, more studies are needed to assess whether these findings may be present in other populations, especially with a shorter time from symptoms to intervention, since the greatest risk of rebleeding occurs in the first 3 days after the event.

Introduction

Aneurysmal subarachnoid hemorrhage (aSAH) accounts for 5% of all strokes,[1] which are the second most common cause of death worldwide, accounting for 11% of all deaths, as shown by the Global Burden of Disease (GBD-2017). Although decreasing in fatality,[2,3] the burden associated is high and affects economically active people, especially those < 55 years old, leading to many years lost due to disability (YLD), with variable geographic distribution ranging from 5 to 120 YLD per 100,000 (►**Figure 1**).

The cause of an aSAH is the rupture of a saccular aneurysm. Most of them are acquired and related to known risk factors such as smoking, hypertension, alcohol, and cocaine abuse.[4] Usually, the clinical presentation is characterized by a severe and sudden headache which can be described as the worst ever experienced achieving the peak within one hour (thunderclap headache), often with no other symptoms, but can include neck stiffness, focal symptoms, and loss of consciousness.[5] The standard approach to diagnosis, then, includes a head CT scan and, if negative, a lumbar puncture, achieving 98% of sensitivity, especially valuable to rule out this diagnosis.[6] Once confirmed, it is mandatory to grade the severity of SAH, which can be performed through grading systems such as that proposed by Hunt and Hess in 1968[7] complemented by the Fisher grading of vasospasm based on CT scan.[8]

The treatment aims to prevent complications such as rebleeding; thus, the repair with surgical clipping or endovascular coiling is imperative, recommended to be performed within 24 hours,[9] as a Level B of evidence, as well as clinical stabilization. Even with all efforts, disabilities are not uncommon, and their assessments help to guide the treatment and contribute to the better management of these patients. Hence, the purpose of the present study is to correlate the time from the onset of the symptoms (thunderclap headache) until the treatment (surgical or endovascular) and short and long-term disability using the Rankin Scale[10] (RS) and the Glasgow Outcome Scale (GOS)[11] aiming to evaluate if the impact of the surgical treatment is time-dependent linearly.

Methods

Study Design

The present prospective cohort collected data from all patients admitted to the tertiary care hospital (Hospital das Clínicas da FMUSP) from January 2018 to November 2019 with diagnosed aSAH either from lower complexity centers or from other hospitals of the institution. After initial stabilization, patients were selected for the microsurgical or endovascular treatment depending on imaging and clinical status, and, at discharge, were assessed using the standardized scales RS and GOS. Finally, in a 6-month outpatient consultation, patients were again assessed using the same scales evaluating long-term disability (►**Figure 2**).

Population Data

In the aforementioned period, data were collected from 223 patients. Of those, were included 79 patients in the present study ($n = 79$). A consent form and a full questionnaire were offered for patients to evaluate risk factors, such as smoking, hypertension, diabetes, and drug abuse, as well as previous events of aSAH and onset of the headache.

Exclusion Criteria

Patients with missing data about the time of onset of symptoms or RS or GOS after 6 months were excluded.

Inclusion Criteria

Patients admitted to the Hospital das Clínicas da FMUSP between January 2018 and November 2019 with diagnosed aSAH, who agreed to participate in the study, from both sexes, > 18 years old, with a known time of onset of symptoms, diagnosed aSAH and who completed the 6-month follow-up.

Ethical Standards

The present research project was approved by the Ethics and Research Committee of the Hospital das Clínicas of FMUSP. Online registration CAPPesq: 15226 approved 06/20/2016. Approved on the Brazil platform CAAE number: 61719416.6.0000.0068.

Statistical Analysis

The time from onset of symptoms (considering the thunderclap headache) and the treatment (days) was calculated and called Delta. Linear regression was used to analyze Delta and the standardized RS and GOS in two moments: at discharge and at the 6-month follow-up. Additionally, the same linear regression was used to divide the population of the study into four age subgroups (≤ 45 years old, 45 to 55 years old, 55 to 70 years old, and > 70 years old).

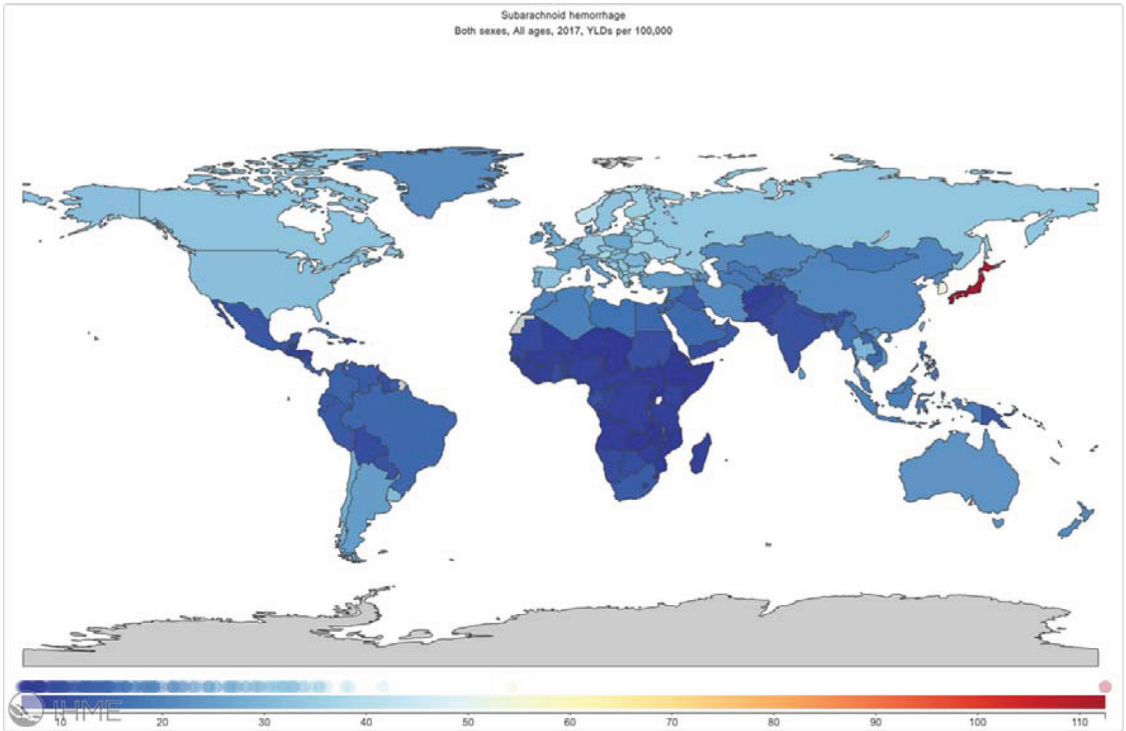

Fig. 1 Geographic distribution of the Years lost due to disability (YLD) caused by subarachnoid hemorrhage. Global Burden of Disease 2017.

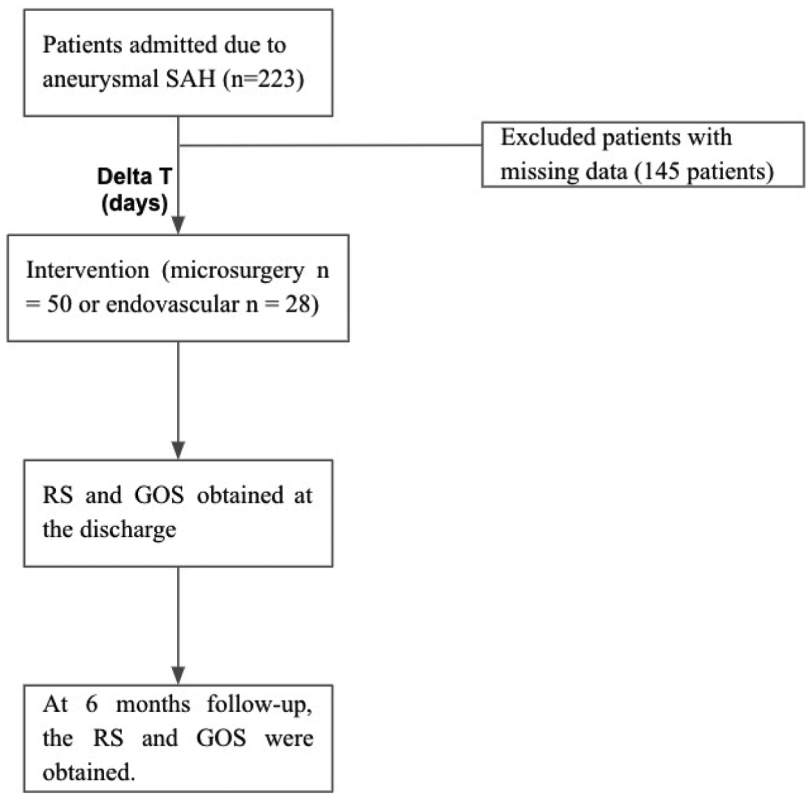

Fig. 2 Selection of patients eligible for the present study.

Results

Of the total of 223 patients included, 145 were excluded due to either missing information or loss to follow-up in 6 months, resulting in 78 patients (►**Figure 2**). The average age was 54, and 73% were women. At admission, the mean Glasgow Coma Scale was 13, and the Hunt and Hess Scale and World Federation Neurological Surgeons Grading (WFNS),

Table 1 Population characteristics of the patients

Population with aSAH (n = 78)	*n*
Epidemiology	
Age (years old)	54
Gender (female)	57 (73%)
Hypertension	53 (68%)
Diabetes	32 (41%)
Smoking	43 (55%)
Alcohol Consumption	18 (23%)
Previous aSAH	12 (15%)
Family History of aSAH (first degree)	4 (5%)
Clinical Features at Admission	
Glasgow Coma Scale (mean)	13
Hunt and Hess Score (mean)	2.1
World Federation of Neurological Surgeons	2.1
Lowered Level of Consciousness	8 (10%)
Syncope	14 (18%)
Meningeal Signs	5 (6.4%)
Motor deficits	30 (38.5%)
Radiologic Features	
Presence of Vasospasm	11 (14%)
Size of Aneurysm (mm)	6.0
More than one aneurysm	13 (16%)
Modified Fisher Grading (mean)	3.1

Abbreviation: aSAH, aneurysmal subarachnoid hemorrhage.

were both 2.1 (►**Table 1**). The average time from the onset of symptoms until intervention was 6.8 days. At discharge, the mean Rankin (RS) was 1.9 and the Glasgow Outcome Score was 4.5. At 6 months, the Rankin Score was 1.8. In the population studied, no correlation was found between the time from onset of symptoms until the treatment and better Rankin Scores, with an adjusted R-squared: 0.023 and $p = 0.09$. Using the same linear regression, but with the population stratified into four subgroups ($\leq$ 45 years old, 45 to 55 years old, 55 to 70 years old, and $>$ 70 years old) obtained similar results, with a *p*-value of 0.38, 0.92, 0.93, and 0.93, respectively.

Additionally, a subgroup analysis was performed, and the patients were divided into four groups based on their ages: $\leq$45 years old, from 45 to 55 years old, from 55 to 70 years old, and $>$ 70 years old. For each group, the same linear regression was used to investigate if there was a different outcome; however, no statistically significant difference was found. (►**Table 2**).

Using the same aforementioned strategy, other subgroup analyses were performed in a more detailed way (►**Table 3**), considering other variables possibly involved on the outcomes,[12] such as gender, days until intervention, size of the aneurysm and previous aSAH and Glasgow Coma Scale at admission, and in none of these a linear correlation between the time until intervention and the disabilities measured by the RS in the 6-month follow-up was found.

Table 2 Age-based subgroup analysis of RS after 6 months and time until intervention

Subgroup (years old)	*p-value*
$\leq$ 45	0.38
45–55	0.92
55–70	0.93
$>$ 70	0.37

Table 3 Detailed subgroup analysis of RS after 6 months and time until intervention

Subgroup	*p-value*
Gender	
Male	0.76
Female	0.57
Time until intervention	
$\leq$ 3 days	0.66
$\geq$ 4 days	0.78
Previous aSAH	
Yes	0.15
No	0.17
Size of the aneurysm	
$\leq$ 5 mm	0.84
$\geq$ 5 mm	0.81
Glasgow Coma Scale at Admission	
15	0.40
13–14	0.67
9–12	0.63
$\leq$ 8	0.27

Abbreviation: aSAH, aneurysmal subarachnoid hemorrhage.

Discussion

It is well-known that the outcomes of an aSAH are complex and depend on a myriad of variables, including characteristics of the patient (comorbidities), the size and location of the aneurysm, the extension of the bleeding,[12] and the time until the transfer to a specialized unit. Accordingly, the Cooperative Aneurysm Study has suggested that the risk of rebleeding achieves a peak during the first 24 hours after the event and subsequently decreases by 1 to 2% per day until the second week. Also, emerging data show that initial rebleeding rates can be of up to 15% in the first 24 hours, which is called ultra-early rebleeding.[13] Thus, after this critical time, the intervention may not be time-dependent for the limitations after 6 months measured by the GOS and the Rankin scales.

Conclusion

The present article suggests that there was no linear correlation between time until intervention and better outcomes using the Rankin scale or the GOS. Besides that, it is worth saying that emerging clinical therapies involving intensive care minimizing complications should be encouraged and incorporated.

Further studies are needed to understand what impacts best the life after aSAH.

Disclosure
The authors have no personal, financial, or institutional interest in any of the drugs, materials or devices described in the present article.

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

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Ten Steps for NPH Management: Advancements in Diagnosis and Treatment of Adult Hydrocephalus

Dez etapas para o manejo da NPH: avanços no diagnóstico e tratamento da hidrocefalia em adultos

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Abstract

Objectives The authors of the present study intend to describe a straightforward protocol for normal pressure hydrocephalus diagnosis and management, with the employment of a multidisciplinary team approach effort.

Methods Using a strict methodological approach for initial diagnosis, taking into consideration occupational therapy and physical therapy assessment, the authors have set out to elaborate a simple protocol for suspicion and, once diagnosed, treatment of normal pressure hydrocephalus. We have used the MoCA (Montreal Cognitive Assessment) and walking assessment that included speed, independence, and distance (SID), 10 m walk test, TUG (timed up and go) evaluation, 6-minute Walk Test, MiniBESTest, as the main factors for pre and post lumbar drainage assessment, after which, the alternatives were deliberated and followed, or not, by ventriculoperitoneal shunt insertion.

Results The authors have described a protocol, consisting of ten easy steps, which involves a multidisciplinary team, including occupational therapy and physical therapy professionals, as well as neurologists and neurosurgeons for improved and objective assessment prior to insertion of lumbar drain and, thereafter, detecting the population at most benefit for ventriculoperitoneal shunt insertion. We have described the Ten Step Approach for Normal Pressure Hydrocephalus management, including from initial clinical presentation and imaging, to pre and post lumbar drainage, for lastly deciding upon necessity for ventriculoperitoneal shunt insertion.

Conclusions A straightforward protocol for normal pressure hydrocephalus seems not only feasible, but simple to implement in most neurosurgical departments, with good accuracy of prediction of lumbar drainage assessment to shunting outcomes.

Keywords
- normal pressure hydrocephalus
- ventriculoperitoneal shunt
- idiopathic normal pressure hydrocephalus
- adult hydrocephalus

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Introduction

Normal Pressure Hydrocephalus (NPH), also known as Idiopathic Normal Pressure Hydrocephalus (iNPH), is a defective accumulation of cerebrospinal fluid (CSF) in the intracranial ventricles of the central nervous system. As the name suggests, pressure assessment varies within a normal limit range, at times with slight elevation only, although volume within intraventricular spaces seems to be significantly enlarged. Clinical presentation is commonly straightforward, with a triad at presentation being common, including gait dysfunction, sphincter control abnormalities and cognitive impairment, which has a tendency for progression if not treated.[1]

Aside from the now notorious clinical presentation, imaging findings provide substantial information into the condition. Initially, the Evans Index (EI) larger than 0.3 in brain MRI had been described as reliable measurement for ventricular dilation, however being common to other subsets of ventricular enlargement, including ex-vacuo ventriculomegaly for instance. Further measurements, thereafter, have risen as promising tools, such as the measurement of the callosal angle (50–80°), which proved to be more reliable for iNPH.[2] Although an integral part of NPH assessment, imaging by itself cannot solely predict improvement in patients after cerebrospinal fluid diversion. Albeit, assessing modifications of more objective measures may provide better understanding on potential for clinical improvement after cerebrospinal fluid diversion procedures. It is therefore necessary to evaluate objective changes in cognitive and gait after temporary cerebrospinal fluid drainage to understand which subset of this population would clinically benefit of CSF diversion intervention.[3]

Although significantly prevalent, especially in an aging population worldwide, with clinically relevant deterioration of quality of life, there is no standardization for appropriate management of NPH. Much has been previously described in medical literature in regard to diagnosis, prevalence and treatment of NPH,[4,5] however, there is no set protocol for easy to follow and lastly to replicate in everyday practice. Therefore, the authors of the present study, taking as background departmental protocol, set out to describe ten easy steps to follow for best decision-making into filling this gap of the literature.[6–8]

Methods

The authors describe an institutional protocol for idiopathic normal pressure hydrocephalus, encompassing ten steps for clear and easy-to-follow schema. The gait assessment is regularly performed by trained physical therapists (PT), experienced with gait dysfunction in various neurological conditions. For the evaluation of cognitive status, occupational therapists (OT) accustomed to assessing patients with a variety of neurological conditions. This protocol, due to its objectivity and straightforwardness, may be replicated in distinct scenarios of the neurological and neurosurgical practice.

First, a trained and experienced neurologist assesses patient upon first medical appointment, and scrutinizes his/her clinical presentation, with a thorough medical history and physical examination, focusing on a commonly described triad, which includes gait disturbance, sphincter issues (more commonly presenting with urinary incontinence) and memory deficits. For the clinical diagnosis, as previously described, it is not necessary that all of these findings be present or reported, but the presence of the common triad reinforces the probability of the clinical presentation of iNPH.

Second, appropriate imaging, including more importantly for NPH, brain MRI, with measurements of the Evans Index and of the Callosal Angle. An Evans Index greater than 0.3 and a Callosal Angle of 50 to 80° although not pathognomonic, associated with the above clinical findings, is significantly suggestive of NPH. The presence of trans ependymal transudation is not a common finding of iNPH, although its presence might be indicative of more recently decompensated hydrocephalus.[11]

Third, when the diagnosis of iNPH is suspected and before deliberating on CSF drainage (be it lumbar puncture of lumbar drain insertion), subjective questionnaires and objective assessments are done. To begin, we start with a questionnaire, which involves 11 questions (NPH Log scale – see addendum A) broadly covering physical, cognitive and sphincter domains. The same questions are interviewed to the patient and closest caretaker, separately. The scoring is done as; strongly agree, agree, unsure, disagree and strongly disagree. Thereafter, occupational, and physical therapy teams are involved for objective cognitive and physical assessments respectively. Occupational therapy is responsible of evaluating patients' cognitive status using MoCA (Montreal Cognitive Assessment). Other cognitive testes may be applicable, such as the MMSE (Mini Mental Status Exam), however, in our institution MoCA is more widely applicable for the purpose of iNPH evaluation, as is also the case in previous literature reports.[12]

Fourth, unlike on the 10-m Walk Test described below, when patient starts standing up and initiates to ambulate once the evaluator instructs in that sense, for this evaluation, TUG (Timed Up and Go), patient initiates assessment in a sitting position and is instructed to stand up and start walking. Patient is assessed for balance for standing up before ambulating, and then walk ten meters, make a 180° turn, and walk back ten meters. Patient is assessed for timing of execution, as well as imbalance that may occur more commonly during standing up from the sitting position and when turning around 180°. Above three assessments can be done; in tandem with each other. If patients can complete above test satisfactorily, patients proceed to ambulation endurance test.

Fifth, physical therapy professionals start with more objective gait evaluation with the 10-m Walk Test. The 10-m Walk Test aims to assess for gait velocity. Patients are instructed to ambulate at normal speed, and then as quickly as safely possible, being assisted all the while (from a safe distance, but which does not impact directly on the evaluation). This is

performed for two trials and averages are taken, being recorded for the number of steps and time achieved after ambulating for the monitored ten meters, recording the average speed in meters per second.

Sixth, the 6-minute Walk Test (6MWT) is employed in the sense of endurance measurement, instead of velocity, as is the case in the 10-m Walk Test. Patients are instructed to walk at his/her normal speed, as far as he or she can walk within six minutes, and the results are reported objectively in distance in meters walked.

Seventh, still with physical therapy, the Mini Balance Evaluation System Test (MiniBESTest) is performed. Patients are objectively evaluated on 14 different items, with scores rated from 0 to 2, with a maximal of 28 points, with higher scores meaning better overall balance (see addendum B). On Timed Up and Go part of the test, the recorded information previously obtained may be used in the score for documentation and comparison purposes.

Eighth, although it has been previously described lumbar puncture as a means for effective CSF drainage, with drainage of different CSF volumes, usually at least 50 mL, our institution routinely employs a lumbar drain, as it seems more effective for continuous CSF drainage and being able to drain for more prolonged periods of time and larger volumes of CSF, which may ultimately influence more significantly the post drainage assessment. A total time of drainage as minimum as 12 hours, but more commonly 24 to 48 hours is routine. Lumbar drain is inserted in sterile settings, by experienced neurosurgeons, in the operating theater and under local anesthesia. CSF is aimed to be drained from 5–10mL per hour, which is a total of 120 to 240 mL in 24 hours, a volume estimated to produce consistent changes within the central nervous system to effectively be assessed in the post lumbar drain removal reassessment.[12–14]

Ninth, after removal of lumbar drain, usually 30–60 minutes to allow patient to feel comfortable to carry out all the necessary steps, occupational and physical therapy are again involved to perform all the above-mentioned assessments, including repeating subjective questionnaire, which is re-interviewed with patient and same caregiver, at 12, 24 and 48 hours. MoCA, 10-m Walk Test, Timed Up and GO (TUG), 6-minute Walk Test (6MWT), Mini Balance Evaluation System Test (MiniBESTest) are all repeated in the same sequence previously performed. The results of reassessment are carefully described and compared with the pre-CSF drainage assessment and added to electronic medical records for documentation purposes and keeping objectivity.

Tenth, if results are significant for post CSF drainage improvement of at least 30% in comparison to pre-CSF drainage assessment, ventriculoperitoneal shunt (VPS) is indicated and performed as routine for other indications of hydrocephalus, with the use or not of neuronavigational system, depending on patients' specificities and availability. In our institution, the authors routinely use laparoscopic abdominal insertion of the distal portion of the VPS system, in order for direct visualization and possibly decreasing postoperative complications.[15] A head CT is performed on postoperative day 1 for confirmation of appropriate proximal position and to rule out any complication, and the patient is then discharged, with routine follow-up in two weeks for postoperative assessment.

Results

Upon deliberating on necessity for permanent CSF deviation procedure for NPH treatment, patient needs appropriate clinical assessment, with temporary CSF drainage and pre and post evaluation for final decision-making.[9,10] An overall improvement of 30% of symptoms after drainage, is consistent with long-term and permanent improvement of daily life activities, supporting decision for an intervention that obviously carries risks, especially in regards to infection and obstruction, with, not uncommonly, necessitating for revision surgery in the future. This ten-step flowchart, therefore, is an easy-to-follow method for decision-making of such intricate and limited comprehended condition.

The below 10-step-list is presented for an easily reproducible protocol, which may be performed in different level complexity scenarios.

1–Clinical Presentation Assessment – experience neurologists to assess for clinical presentation suggesting NPH, usually looking for the triad findings of gait instability, urinary changes, and cognitive decline.
2–Imaging – imaging showing evidence of dilatation of intracranial ventricles, with Evans Index of >0.3 and callosal angle of 50–80° is suggestive of NPH, although not conclusive (see image below - ►**Fig. 1** - showing a callosal angle at the level of anterior commissure, of a callosal angle of $\sim$65°).
3–MocA and NPH Log Questionnaire – occupational therapy professional, with experience in various neurological conditions assess patients and documents scoring based on MoCA and NPH Log Questionnaires (addendum 1), which will be used as baseline for comparison after CSF drainage.
4–TUG (Timed Up and Go) – this step precedes the other walking tests, as this will evaluate for feasibility of standing up from a sitting position before ambulating. The test has shown evidence of predictive value for balance, velocity, and endurance of gait, which carries by itself great worth for this subset of neurological patients.
5–10 m walk test – physical therapists will evaluate for gait velocity, requesting patients to initially walk in his or her normal speed and later to walk as quickly as safely possible.
6–6-Minute Walk Test – this test, performed by PT professional experienced with gait assessment in neurological patients, evaluates endurance, measuring in meters, distance walked in six minutes.
7–MiniBESTest – this more complex test, which also measures for balance, endurance, and velocity of gait, is performed after TUG, 10 m walk test and 6-minute walk test since it is more thorough and complex, demanding more of the patient, meaning that it might be halted in certain cases, needing to be repeated in a

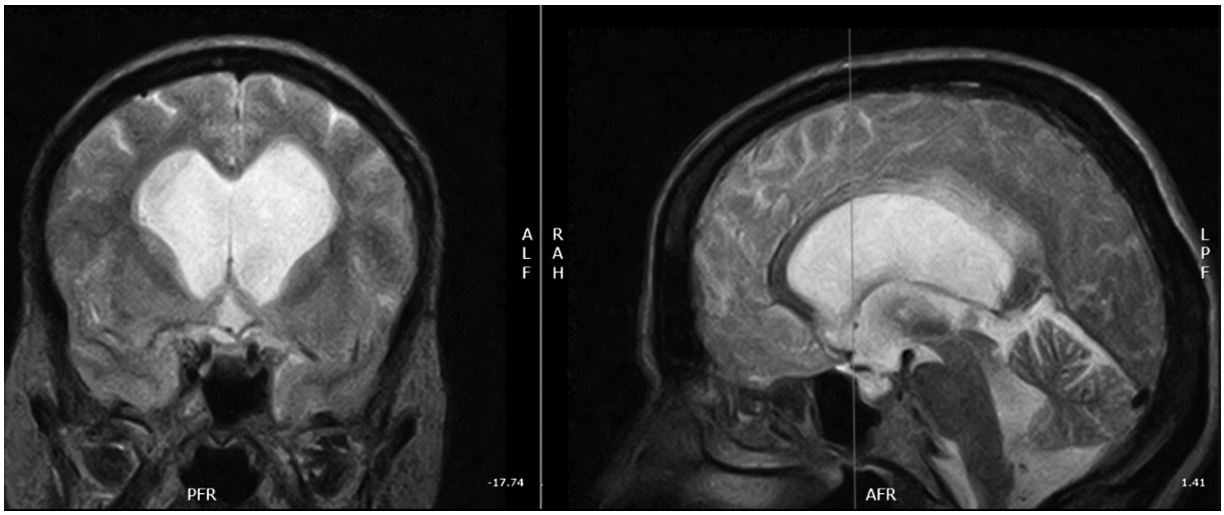

Fig. 1 Dilation of intracranial ventricular system, with an Evan's Index of > 0.3 and Callosal Angle of ~65°.

subsequent time. The score which ranges from 0 to 28, encompassing 14 questions scored 0–2, may use the TUG information to avoid repeating same tests and become too demanding for some patients.

8–Lumbar Drainage (assessment at 6–12–18–24 hours) – lumbar drainage is performed by experience neurosurgeons in operating theater setting, under sterile conditions and local anesthesia. In cases of difficult execution, due to previous lumbar surgical interventions or further anatomical nuances, the procedure may use fluoroscopy for improved outcome.

9–Post-CSF Drainage Assessment (Repeat PT and OT evaluation) – the cognitive and physical assessments are performed in the same sequence that were performed before CSF drainage, usually waiting at least 30 minutes after lumbar drain removal. The results are recorded and then compared with the pre-CSF drainage assessment. An improvement that is deemed of more than 30% is viewed as positive and decision for VPS is made, with patient's and/or family's consent.

10–Ventriculoperitoneal Shunt (yes or no) – after decision for VPS is made and consent is obtained, procedure is performed in routine surgical standards, in our department with use of laparoscopic insertion of distal part of VPS catheter and under navigation for proximal catheter. ►**Fig. 2**

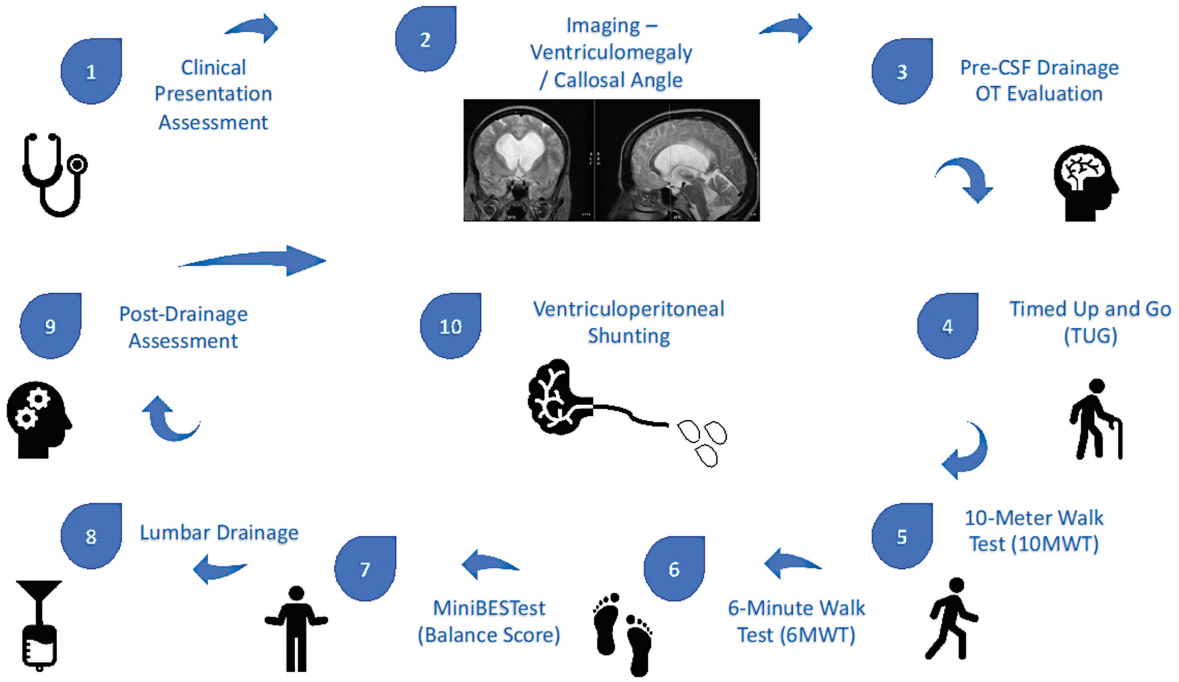

Fig. 2 10 Step for NPH Flowchart.

In our experience, the ten-step protocol has shown to be effective and reliable, for not only establishing the population at most benefit for surgical intervention with ventriculoperitoneal shun (VPS), but also, and perhaps more importantly, those that would ultimately fail any intervention, halting any deliberation of potential risk averse procedures in such patients. As previously shown, the Timed Up and Go (TUG) assessment before and after lumbar drain insertion, has been decisive in many cases, especially for cases which the initial clinical presentation might have been borderline. The objectivity of pre and post temporary CSF drainage has been shown to support decision-making with potential to reassure patient and patient's family on indication, or lack of, ventriculoperitoneal shunt insertion, significantly decreasing, therefore, procedure-related complications, as well as those attributed to not managing normal pressure hydrocephalus in a timely fashion.

Discussion

Normal Pressure Hydrocephalus (NPH) or Idiopathic Normal Pressure Hydrocephalus (iNPH) is a known entity which courses with a triad clinical presentation of gait dysfunction, sphincter issues and memory impairment. Its diagnosis and treatment have been amply discussed previously, encompassing CSF drainage and CSF diversion, respectively. In the present study, the authors present an institutional protocol for best standard of management for NPH, with an easy to follow and apply Ten-Step Protocol for NPH, which may be employed in distinct level scenarios.

Each of the ten steps makes diagnosis, using clinical findings and imaging evidence,[16] as well as cognitive assessment and gait evaluation, with velocity, endurance, and balance as its tripod basis, in two distinct phases, pre and post CSF drainage through lumbar drain,[17,18] a simple manner for managing this complex array of patients, with the best possible outcomes.

When evaluating before and after cerebrospinal fluid drainage, it is of the utmost importance to keep objectivity, as patients' and relatives' information are commonly only a subjective account of patients' status, although not to be overlooked. That is the reason that the use of established measurements tools, such as the ones here described, including MoCA, 10-m Walk Test, TUG, 6-minute Walk Test, MiniBESTest, performed before and after CSF drainage by the same professionals and utilizing same environmental infrastructure, provides a controlled surrounding to minimize any unknown bias. Also, the use of at least 30% improvement from baseline assessment, while limiting several patients whose improvement may lay below this cutoff point, brings a more clinically significant outcome after permanent CSF diversion, with little room for subjective improvement observed in other scenarios.

This descriptive narrative thoroughly details each of the ten steps, from clinical presentation assessed by a trained and experienced neurologist, with corroborating imaging in brain MRI showing specifics for probable NPH, through evaluations of occupational therapy and physical therapy professionals, before and after CSF drainage, for lastly supporting a conscious decision-making for final ventriculoperitoneal shunting, which should be the permanent treatment for the condition.[20–22]

Conclusion

Idiopathic Normal Pressure Hydrocephalus is a prevalent neurological condition, with significant influence on a large population's quality of life. Establishing an easy-to-apply protocol, such as the one herein described Ten-Step Protocol for NPH, may prove to significantly facilitate decision-making with potential great impact on this subset of neurological population.

Previous Presentations
The contents of this manuscript have not been copyrighted or published previously.

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Conflict of Interest
None.

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Addendum A

Normal Pressure Hydrocephalus (NPH) Log

Before performing the LP/Lumbar Drain and at 12, 24 and 48 hours after Lumbar Drain, the patients and caregivers were routinely asked to measure the patient's baseline performance status using questions in the LP log assessment form. The *patients and caregivers* were asked to state if they "*strongly agreed, agreed, were unsure, disagreed, or strongly disagreed*" with 11 statements describing patient's function regarding activities of daily living.

Pre LD (patient)	Pre LD (caretaker)	Questions	Post Lumbar Drainage	12 hours (Patient)	12 hours (Caretaker)	24 hours (Patient)	24 hours (Caretaker)	48 hours (Patient)	48 hours (Caretaker)
		1. I feel balanced							
		2. I feel confident walking inside and outside							
		3. I can stand up and sit down with ease.							
		4. I can walk up and down stairs and or hills with ease.							
		5. I have energy each day to complete my daily tasks.							
		6. I am easily able to make plans, problem solve, and move from one task to the next							
		7. I am easily able to pay close and continuous attention to tasks.							
		8. I have the motivation to perform daily chores, errands, and call or see my family and friends							
		9. I enjoy listening to music.							
		10. I have issues with my urinary urgency							
		11. In the past 3 months, I feel that I can process questions/commands/ requests that are made to me and react appropriately to them without delay or needing of repetition.							

Addendum B

Mini-BESTest: Balance Evaluation Systems Test

1. SIT TO STAND

Instruction: "Cross your arms across your chest. Try not to use your hands unless you must. Do not let your legs lean against the back of the chair when you stand. Please stand up now."

(2) Normal: Comes to stand without use of hands and stabilizes independently.
(1) Moderate: Comes to stand WITH use of hands on first attempt.
(0) Severe: Unable to stand up from chair without assistance OR needs several attempts with use of hands.

2. RISE TO TOES

Instruction: "Place your feet shoulder width apart. Place your hands on your hips. Try to rise as high as you can onto your toes. I will count out loud to 3 seconds. Try to hold this pose for at least 3 seconds. Look straight ahead. Rise now."

(2) Normal: Stable for 3 second with maximum height.
(1) Moderate: Heels up, but not full range (smaller than when holding hands), OR noticeable instability for 3 second
(0) Severe: < 3 second

3. STAND ON ONE LEG

_____

Instruction: "Look straight ahead. Keep your hands on your hips. Lift your leg off of the ground behind you without touching or resting your raised leg upon your other standing leg. Stay standing on one leg as long as you can. Look straight ahead. Lift now."

Left: Time in Seconds Trial 1: _____Trial 2:_____
(2) Normal: 20 second
(1) Moderate: < 20 second
(0) Severe: Unable.
To score each side separately use the trial with the longest time.
To calculate the sub-score and total score use the side [left or right] with the lowest numerical score [i.e., the worse side].
Right: *Time in Seconds Trial 1: _____Trial 2:_____* (2) Normal: 20 second
(1) Moderate: < 20 second
(0) Severe: Unable
R__E_A_C__T_IV_E__P_O__S_T_U_R__A_L_C__O_N_T__R_O_L_____-
*S__U_B__S_C_O__R_E_:_____/ _6_*

4. COMPENSATORY STEPPING CORRECTION- FORWARD

Instruction: "Stand with your feet shoulder width apart, arms at your sides. Lean forward against my hands beyond your forward limits. When I let go, do whatever is necessary, including taking a step, to avoid a fall."
(2) Normal: Recovers independently with a single, large step (second realignment step is allowed). (1) Moderate: More than one step used to recover equilibrium. (0) Severe: No step, OR would fall if not caught, OR falls spontaneously.

5. COMPENSATORY STEPPING CORRECTION- BACKWARD

Instruction: **"**Stand with your feet shoulder width apart, arms at your sides. Lean backward against my hands beyond your backward limits. When I let go, do whatever is necessary, including taking a step, to avoid a fall."
(2) Normal: Recovers independently with a single, large step.
(1) Moderate: More than one step used to recover equilibrium.
(0) Severe: No step, OR would fall if not caught, OR falls spontaneously.

6. COMPENSATORY STEPPING CORRECTION- LATERAL

Instruction: "Stand with your feet together, arms down at your sides. Lean into my hand beyond your sideways limit. When I let go, do whatever is necessary, including taking a step, to avoid a fall."

_____

Left
(2)
SENSORY ORIENTATION SUB SCORE: / 6

_____

7. STANCE (FEET TOGETHER); EYES OPEN, FIRM SURFACE
   Instruction: "Place your hands on your hips. Place your feet together until almost touching. Look straight ahead. Be as stable and still as possible, until I say stop."
   Time in seconds: _____
   (2) Normal: 30 second
   (1) Moderate: < 30 second (0) Severe: Unable.
   Normal: Recovers independently with 1 step (crossover or lateral OK). Moderate: Several steps to recover equilibrium.
   Right
   (2) Normal: Recovers independently with 1 step (crossover or lateral OK).
   (1)
   (0)
   Use the side with the lowest score to calculate sub-score and total score.
   Severe: Falls or cannot step.
   (1) Moderate: Several steps to recover equilibrium. (0) Severe: Falls or cannot step.

8. STANCE (FEET TOGETHER); EYES CLOSED, FOAM SURFACE
   Instruction: "Step onto the foam. Place your hands on your hips. Place your feet together until almost touching. Be as stable and still as possible, until I say stop. I will start timing when you close your eyes."
   Time in seconds: _____
   (2) Normal: 30 second
   (1) Moderate: < 30 second (0) Severe: Unable.

9. INCLINE- EYES CLOSED
   Instruction: "Step onto the incline ramp. Please stand on the incline ramp with your toes toward the top. Place your feet shoulder width apart and have your arms down at your sides. I will start timing when you close your eyes."
   Time in seconds: _____
   (2) Normal: Stands independently 30 second and aligns with gravity.
   (1) Moderate: Stands independently <30 second OR aligns with surface. (0) Severe: Unable.
   DYNAMIC GAIT SUB SCORE: / 10

10. CHANGE IN GAIT SPEED
    Instruction: "Begin walking at your normal speed, when I tell you 'Fast', walk as fast as you can. When I say 'slow', walk very slowly."
    (2) Normal: Significantly changes walking speed without imbalance.
    (1) Moderate: Unable to change walking speed or signs of imbalance.
    (0) Severe: Unable to achieve significant change in walking speed AND signs of imbalance.

11. WALK WITH HEAD TURNS – HORIZONTAL
    Instruction: "Begin walking at your normal speed, when I say "right," turn your head and look to the right. When I say "left" turn your head and look to the left. Try to keep yourself walking in a straight line."
    (2) Normal: performs head turns with no change in gait speed and good balance. (1) Moderate: performs head turns with reduction in gait speed.
    (0) Severe: performs head turns with imbalance.

12. WALK WITH PIVOT TURNS
    Instruction: "Begin walking at your normal speed. When I tell you to 'turn and stop', turn as quickly as you can, face the opposite direction, and stop. After the turn, your feet should be close together."
    (2) Normal: Turns with feet close FAST (< 3 steps) with good balance. (1) Moderate: Turns with feet close SLOW (>4 steps) with good balance. (0) Severe: Cannot turn with feet close at any speed without imbalance.

13. STEP OVER OBSTACLES
    Instruction: "Begin walking at your normal speed. When you get to the box, step over it, not around it and keep walking."
    (2) Normal: Able to step over box with minimal change of gait speed and with good balance. (1) Moderate: Steps over box but touches box OR displays cautious behavior by slowing gait. (0) Severe: Unable to step over box OR steps around box.

14. TIMED UP & GO WITH DUAL TASK *[3 METER WALK]*

Instruction TUG: "When I say 'Go', stand up from chair, walk at your normal speed across the tape on the floor, turn around, and come back to sit in the chair."

Instruction TUG with Dual Task: "Count backwards by threes starting at ___. When I say 'Go', stand up from chair, walk at your normal speed across the tape on the floor, turn around, and come back to sit in the chair. Continue counting backwards the entire time."

TUG: _____seconds; Dual Task TUG: _____seconds

(2) Normal: No noticeable change in sitting, standing, or walking while backward counting when compared with TUG without Dual Task.

(1) Moderate: Dual Task affects either counting OR walking (>10%) when compared with the TUG without Dual Task.

(0) Severe: Stops counting while walking OR stops walking while counting.

When scoring item 14, if subject's gait speed slows more than 10% between the TUG without and with a Dual Task the score should be decreased by a point.

TOTAL SCORE: _____/_2_8

Spinopelvic Parameters in the Clinical and Functional Outcomes of Patients Submitted to Lumbar Interbody Fusion Surgery – A Prospective Study

Parâmetros espinopélvicos nos resultados clínicos e funcionais de pacientes submetidos a fusão intersomática lombar: um estudo prospectivo

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Abstract

Objectives The relevance of spinopelvic parameters in the patients' clinical and functional outcomes has been widely studied in long spinal fusion. Yet, the importance of the spinopelvic parameters in short-segment fusion surgeries needs further investigation. We analyzed the spinopelvic parameters and surgical outcomes of patients undergoing short-segment lumbar interbody fusion.

Materials and Methods An observational, prospective study was conducted between January and June 2021. We selected 25 patients with lumbar stenosis, with or without concomitant spondylolisthesis, undergoing transforaminal lumbar interbody fusion. Variables related to the patient, diagnosis, and surgery were collected. The clinical and functional outcomes were assessed using the Visual Analogue Scale for low-back and leg pain and the Oswestry Disability Index (ODI). The surgical outcomes and spinopelvic parameters were analyzed pre- and postoperatively.

Results There was a significant clinical and functional improvement after surgery ($p < 0.001$), with a mean ODI decrease of 63.6%. The variables of obesity, concomitant spondylolisthesis, absence of osteotomy, and two-level fusion were all associated with

Keywords
- spinopelvic parameters
- Oswestry disability index
- transforaminal lumbar interbody fusion

Renata Marques and Ana Cristina Silva contributed equally to the present work.

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lower levels of improvement after surgery ($p < 0.05$). Pelvic incidence minus lumbar lordosis (PI-LL) was the only parameter that significantly changed regarding the pre- and postoperative periods ($p < 0.05$). Before surgery, PI-LL $< -10°$ correlates with less low-back pain after surgery ($r = 0.435$; $p < 0.05$). Postoperatively, no correlation was found between surgical outcomes and all the spinopelvic parameters analyzed.

Conclusions The clinical and functional outcomes significantly improved with the surgical intervention but did not correlate with the change in spinopelvic parameters. Patients with preoperative PI-LL $< -10°$ seem to benefit the most from surgery, showing greater improvement in back pain.

Resumo

Objetivos A influência dos parâmetros espinopélvicos nos resultados clínicos e funcionais dos pacientes tem sido amplamente estudada nas cirurgias de fusão espinhal que envolvem longos segmentos. Contudo, a literatura é escassa acerca da fusão de segmentos curtos. Analisamos assim os parâmetros espinopélvicos e os resultados cirúrgicos de pacientes submetidos a fusão intersomática lombar de segmentos curtos.

Materiais e Métodos Realizou-se um estudo prospectivo observacional entre janeiro e junho de 2021. Selecionaram-se 25 pacientes com estenose lombar, com ou sem espondilolistese, submetidos a fusão intersomática lombar transforaminal. Colheram-se dados relacionados com o paciente, o diagnóstico e a cirurgia. Os resultados clínicos e funcionais foram avaliados por meio da Escala Visual Analógica para dor lombar e dos membros inferiores e pela Escala de Incapacidade de Oswestry (Oswestry Disability Index, ODI, em inglês). Os resultados cirúrgicos e os parâmetros espinopélvicos foram analisadas no pré e no pós-operatório.

Resultados Verificou-se uma melhoria clínica e funcional significativa após a cirurgia ($p < 0{,}001$), com redução média do ODI de 63,6%. As variáveis obesidade, espondilolistese concomitante, ausência de osteotomia e fusão de dois níveis associaram-se a menor melhoria no pós-operatório ($p < 0{,}05$). O único parâmetro que mudou significativamente antes e após a cirurgia ($p < 0{,}05$) foi a incidência pélvica menos a lordose lombar (IP-LL). No pré-operatório, uma IP-LL $< -10°$ correlacionou-se com menos dor lombar após a cirurgia ($r = 0{,}435$; $p < 0{,}05$). No pós-operatório, não houve correlação entre os resultados clínicos e funcionais e os parâmetros espinopélvicos.

Conclusão Os resultados clínicos e funcionais melhoraram significativamente após a cirurgia, mas não se correlacionam com a mudança dos parâmetros espinopélvicos. Pacientes com IP-LL$< -10°$ no pré-operatório apresentam maior melhoria da dor lombar no pós-operatório.

Palavras-chave
- parâmetros espinopélvicos
- escala de incapacidade de Oswestry
- fusão intersomática lombar transforaminal

Introduction

The human spine is a dynamic structure, and its articulation with the pelvis and lower limbs is fundamental for the verticality of the human skeleton. Even in the presence of variations in the degree of the normal curvature, the spine enables a balanced and harmonious distribution of forces, minimizing energy expenditure.[1,2] The disruption of sagittal alignment and spinopelvic changes, by aging or various spinal pathologies (reviewed by Mehta et al.[3]), results in spinal deformity and compensation mechanisms at the pelvis and lower limbs. These changes culminate in increased muscle tension and, consequently, pain symptoms and loss of quality of life.[4,5]

In 1992, Duval-Beaupère et al.[6] characterized the pelvic parameters, drawn from long-standing lateral X-rays. The main pelvic parameter is the pelvic incidence (PI), which corresponds to the angle between the sacrum and the femoral heads.[6] The PI is geometrically related with two additional pelvic parameters, the pelvic tilt (PT) and the sacral slope (SS), according to the equation: $PI = PT + SS$. The PI is a constant pelvic parameter, and the others vary to maintain the sagittal alignment.[3,7]

Harmonization between pelvic and spinal parameters is crucial. Schwab et al.[8] described a parameter relating PI and lumbar lordosis (LL) (PI minus LL: PI-LL) that quantifies the mismatch between pelvic morphology and lumbar curvature, and PI-LL $\pm 10°$ is the threshold to achieve spinopelvic sagittal alignment.

Parameters that assess global alignment, such as the sagittal vertical axis (SVA), have also been described. This parameter corresponds to the horizontal distance between the C7 plumb line and the upper edge of the S1 vertebral body, which acquires a value < 50 mm depending on age.[5] This parameter should be used considering a temporal assessment for the same individual and not to compare different individuals.[9] Recently, Amabile et al.[10] showed that the odontoid hip axis angle (OD-HA) remains constant regardless of age, LL variations, or spinal compensatory mechanisms. This parameter hardly varies in asymptomatic patients (2° to −5°), and it is an excellent parameter for the assessment of the global sagittal alignment.[9]

It has been recognized that abnormal sagittal alignment changes after long-segment lumbar interbody fusion are related to worse clinical outcomes.[3,11] The persistence of low-back pain after lumbar interbody fusion surgery seems to be correlated with a more sacral verticalization, that is, excessive retroversion of the pelvis, with less SS and more PT, associated with a decrease in LL.[12] Also, older age, high preoperative PT, and a postoperative PI-LL $\geq 10°$ were identified as risk factors for reduced quality of life after lumbar interbody fusion surgery.[13] However, most studies are focused on long-segment fusion surgery, and few works have reported the influence of spinopelvic parameters in short-segment (one- or two-level) fusion surgeries.

The aim of the present study was to identify spinopelvic parameters that correlate with surgical outcomes in patients submitted to short-segment translumbar interbody fusion (TLIF). Therefore, we assessed spinopelvic parameters and clinical and functional outcomes through the Visual Analogue Scale (VAS) and the Oswestry Disability Index (ODI) respectively, before and after surgery. Additionally, we analyzed the relationship between patient, diagnosis, and surgery variables and the outcomes.

Methods

Study Design and Patient Selection

We conducted a prospective, observational, and descriptive study at the Neurosurgery Department of a district hospital in Portugal. All consecutive patients submitted to lumbar interbody fusion surgery from January to June 2021 were enrolled in the study.

Our cohort was selected based on the following inclusion criteria: 1) definitive diagnosis of lumbar spinal stenosis with or without concomitant spondylolisthesis, confirmed by an imaging exam; 2) full-spine lateral X-ray preoperatively (M0) and 6 months postoperatively (M6). We excluded patients with no informed consent and with a previous spine surgery or trauma to the spine, pelvis, or lower extremity.

Data Collection

Data were collected from the clinical records and interviews at M0 and M6. We used the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, IBM Corp., Armonk, NY, United States) software, version 27.0 to compile the data anonymously.

The data collected included: age; gender; height and weight to calculate the body mass index (BMI); smoking habits; comorbidities according to the American Society of Anesthesiologists (ASA) physical status classification; depression as a comorbidity; previous lumbar surgery; definitive diagnosis confirmed by an imaging exam; surgical procedure and its complications; performance of osteotomy; number and level of involved spine segments; and the postoperative length of hospital stay and its complications.

Assessment of the Clinical and Functional Outcomes

Patient outcomes were prospectively assessed at M0 and M6. Clinical data was evaluated for pain symptoms (low-back and leg pain), which was quantified through the VAS score (0–10).[14] This score is a simple and subjective tool that enables the comparison of the intensity of pain over time. Functional disability was assessed by the ODI score (0–100%), which is divided into five categories: minimal disability (0% to 20%); moderate disability (21% to 40%); severe disability (41% to 60%); crippled (61% to 80%); and bedridden patients (81% to 100%).[15] The ODI and VAS scores were analyzed at M0 and M6. Global improvement was defined by the difference in scores between M0 and M6 (M0-M6).

Radiological Measurements

The spinopelvic parameters, namely the SVA, OD-HA, PI, PT, SS, LL, and PI-LL were obtained at M0 and M6, and their variation was calculated (ΔM6-M0). The measurements were performed by the same investigator using the Sectra software (Sectra AB, Linköping, Sweden). Full spine lateral X-rays were obtained with patients in the standard standing position.[16]

Surgical Procedure

The lumbar surgeries were performed by the same senior surgeon and involved a one- or two-level fusion through open TLIF. In this procedure, an interbody spacer with a bone graft (cage) was placed via the posterolateral transforaminal route into a distracted disk space along with a pedicle screw construct. In some patients, a Smith-Petersen osteotomy (SPO) was performed to improve LL. Intraoperative radiographs were performed to assess the cage and screws positions.

Statistical Analysis

Data were analyzed using the IBM SPSS Statistics software, version 27.0. The results are expressed as the mean ± standard deviation for the continuous variables and as absolute (n) and relative frequencies (%) for the qualitative ones.

Normality distribution was assessed through the Shapiro-Wilk Test ($n < 50$), skewness, kurtosis, and visual evaluation of the histograms. If the data were normally distributed, parametric statistics were applied. Comparisons between the same variable at M0 and M6 were analyzed through the paired *t*-test (for the continuous variables) and McNemar test (for the dichotomous variables). Bivariate analysis was performed for the outcomes according to the ODI and VAS scores regarding patient characteristics, diagnosis, surgery

variables, and spinopelvic parameters. To test for homogeneity of the variances, the Levene test was performed, and the mean differences between outcomes and variables were obtained using the independent-samples *t*-test (for the dichotomous variables) or one-way analysis of variance (ANOVA, for the nominal variables) with Bonferroni (homogeneity of variance) as the post-hoc test. The effect size was calculated using Cohen D (d) or Eta-squared (η^2) respectively.

The association between spinopelvic parameters and the outcomes according to the ODI and VAS scores was evaluated with the Pearson correlation (for the continuous variables) and the Bissel correlation (for the dichotomous variables).

Statistical significance was defined as $p < 0.05$, with a confidence interval of 95% (95%CI).

Results

The study design chart is shown in ►**Fig. 1**.

Demographic and Surgical Descriptive Analysis

The mean age of the sample was of 55 ± 9.4 (range: 32 to 69) years. At the time of the surgery, most patients were non-smokers ($n = 21$; 84%) and 52% ($n = 13$) were obese (BMI ≥ 30 Kg/m^2), presenting a mean BMI of 28.8 ± 4.9 Kg/m^2 (range: 20.7 Kg/m^2 to 42 Kg/m^2). In terms of comorbidities, 80% of the patients were ASA 2, and 7 patients (28%) presented with depression (►**Table 1**).

We included patients with a definite diagnosis of spinal stenosis with or without spondylolisthesis. Foraminal stenosis was identified in 72% of the patients ($n = 18$), followed by both foraminal and central stenosis ($n = 4$; 16%) and central stenosis ($n = 3$; 12%). About 17 patients (68%) also presented spondylolisthesis grades 1 or 2 (►**Table 2**).

All patients underwent open TLIF surgery with a lordotic cage to preserve the disc height, and in 9 patients (36%), an SPO was performed. L4-L5 and L5-S1 were the segments most often intervened ($n = 22$; 88%), and the fusion involving two levels was only performed in 3 patients (12%). The only documented surgical complication was durotomy ($n = 3$; 12%). No cage migration or screw malposition was detected after surgery. The postoperative period developed with no serious complications, and only 1 patient presented with a self-limiting episode of fever with no need for antibiotics (►**Table 3**).

Analysis of the Spinopelvic Parameters

The detailed spinopelvic parameters measurements at M0 and M6 are presented in ►**Supplementary Table S1** (online only). In some cases, the M0 and/or M6 X-ray presented artifacts that prevented a correct analysis of the SVA in 4 patients ($n = 21$) and of the OD-HA in 3 patients ($n = 22$).

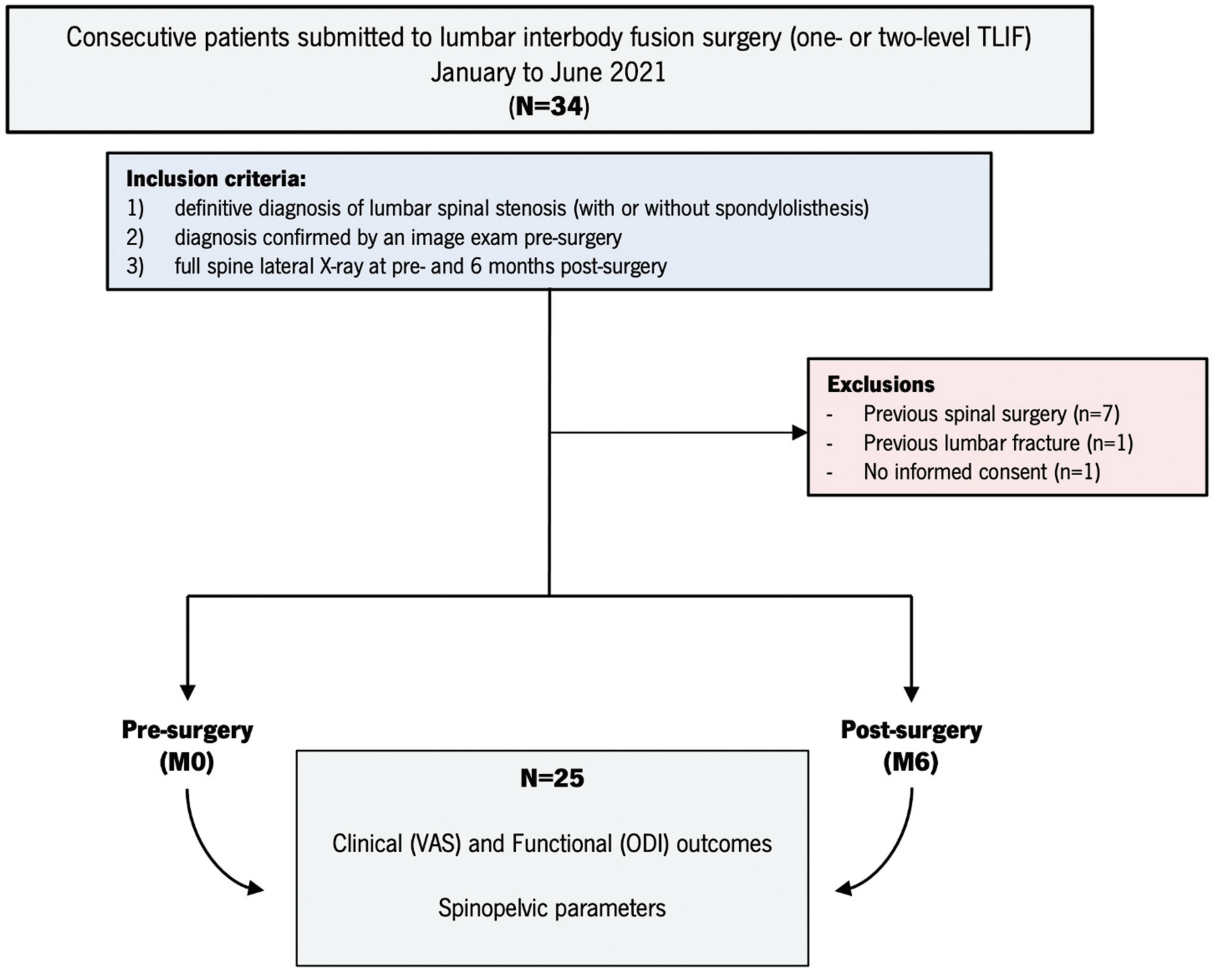

Fig. 1 Flowchart of the study design.

Table 1 Descriptive analysis of the demographic data of the study sample

Demographic data		Value
Age (years)		55.0 ± 9.4 (range: 32 to 69)
Gender	Female	10 (40%)
	Male	15 (60%)
BMI (Kg/m^2)		28.8 ± 4.9 (range: 20.7 to 42)
	Normal	5 (20%)
	Overweight	7 (28%)
	Obesity I, II or III	13 (52%)
Smokers		4 (16%)
ASA classification	1	3 (12%)
	2	20 (80%)
	3	2 (8%)
Depression		7 (28%)

Abbreviations: ASA, American Society of Anesthesiologists physical status classification; BMI, Body Mass Index.
Note: The continuous variables are presented as mean ± standard deviation (range) and the qualitative variables, as absolute (n) and relative (%) frequencies.

Table 2 Descriptive analysis of the diagnoses of the patients

Diagnosis		n (%)
Stenosis	Central	3 (12%)
	Foraminal	18 (72%)
	Central and foraminal	4 (16%)
Spondylolisthesis		17 (68%)
Type	Degenerative	8 (32%)
	Isthmic lysis	9 (36%)
Grade	1	9 (36%)
	2	8 (2%)

Table 3 Descriptive analysis of surgical intervention

		n (%)
Osteotomy	Smith-Petersen	9 (36%)
Fusion levels	1	22 (88%)
	2	3 (12%)
Levels	L4-L5	11 (44%)
	L5-S1	11(44%)
	L3-L4-L5	1 (4%)
	L4-L5-S1	2 (8%)
Surgical complications	Incidental durotomy	3 (12%)
Medical complications	Fever	1 (4%)
Postoperative length of hospital stay (days)		4 [3, 4]*
Cage migration		0 (0%)
Screw malposition		0 (0%)

Note: *Continuous variables that do not follow a normal distribution are presented as median [first, third quantiles].

The mean OD-HA increased after surgery to 1.0° ± 2.6°, but this was not statistically significant ($p = 0.093$). There was no change in the mean SVA (4.1 ± 28.9 mm; $p = 0.527$) or PT (−0.1° ± 5.1°; $p = 0.928$) (►**Table 4**) after the intervention.

Most patients ($n = 20$) experienced an increase in LL after surgery, with a mean of 1.9° ± 5.7°, which was not statistically significant ($p = 0.101$) (►**Supplementary Table S2** (online only)). The PI-LL was the only parameter that revealed a statistically significant result in the comparison between M0 and M6, showing a decrease of −2.4° ± 5.7° ($p = 0.045$) (►**Table 4**).

Interestingly, the analysis of the spinopelvic parameters in M0 and M6 for the subgroup of patients with stenosis and spondylolisthesis ($n = 17$), showed a statistical significance for PI-LL mismatch (−4.1 ± 5.7, $p = 0.009$). Moreover, the LL and OD-HA showed a higher mean increase after surgery (3.2° ± 4.9° and 1.4° ± 2.3° respectively), with statistical significance ($p = 0.017$ and $p = 0.036$ respectively) (►**Supplementary Table S2**) (online only).

Analysis of the Clinical and Functional Outcomes

The detailed M0 and M6 clinical and functional outcomes are also demonstrated in ►**Supplementary Table S1** (online only). The mean percentual ODI improvement between M0 and M6 was of 63.6% ± 32.1%, which corresponds to a mean score improvement of 35.6 ± 18.1 ($p < 0.001$) (►**Table 5**). Most patients (64%) presented an M6 ODI of 0% to 20%, which corresponds to minimal disability (►**Fig. 2c**). Moreover, low-back and leg pain showed a statistically significant improvement after surgery ($p < 0.001$). At baseline (M0) the VAS scores for low-back and leg pain were similar, of 7.4 ± 1.8 and 7.8 ± 2.1 respectively. The back pain among 28% of patients completely disappeared, and 24% of the patients presented residual pain (VAS score of 1 or 2) (►**Fig. 2a**). Leg pain showed a more prominent improvement, and was completely absent in 68% the of patients (►**Fig. 2b**).

There were no significant differences in the clinical and functional outcomes in terms of gender (male/female), age (cut-off of 55 years), ASA score, or the presence of depression ($p > 0.05$). Regarding BMI, obese patients (BMI ≥ 30 Kg/m^2) had higher postoperative ODI scores than non-obese patients (27.5 ± 20.5 versus 13.3 ± 10.2 respectively; $p = 0.041$) (►**Table 6**). The smoking status was not analyzed because almost all patients who were smokers at the time of surgery underwent smoking cessation postoperatively.

Patients with both central and foraminal stenosis displayed a higher mean M6 ODI score when compared with patients with only central or foraminal stenosis (40.8 ± 17.2 versus 16.7 ± 15.9 and 18.0 ± 13.1 respectively; $p = 0.037$) (►**Table 6**). No differences were observed regarding back or leg pain. Patients with stenosis and concomitant spondylolisthesis, when compared with patients without

Table 4 Preoperative (M0) and postoperative (M6) spinopelvic parameters

Spinopelvic parameter	N	Mean ± standard deviation (range)	Paired *t*-test
SVA (mm)			
M0	21	−9.7 ± 30.4 (−78.0 to 47.5)	$p = 0.527$
M6		−5.6 ± 22.1 (−41.0 to 40.0)	
ΔM6-M0		4.1 ± 28.9 (−63.5 to 62.0)	
OD-HA (degrees)			
M0	22	−4.2 ± 3.3 (−11.0 to 1.1)	$p = 0.093$
M6		−3.3 ± 2.0 (−6.6 to 0.3)	
ΔM6-M0		1.0 ± 2.6 (−3.0 to 7.2)	
PT (degrees)			
M0	25	17.1 ± 7.9 (1.0 to 33.0)	$p = 0.928$
M6		17.2 ± 6.3 (4.5 to 27.2)	
ΔM6-M0		−0.1 ± 5.1 (−9.2 to 10.0)	
PI-LL (degrees)			
M0	25	−5.6 ± 7.2 (−16.3 to 6.0)	**$p = 0.045$** (t = −2.120; d = −0.424*)
M6		−8.1 ± 7.0 (−20.0 to 3.7)	
ΔM6-M0		−2.4 ± 5.7 (−18.0 to 16.5)	

Abbreviations: ΔM6-M0, variation between the preoperative (M0) and postoperative (M6) periods; OD-HA, odontoid hip axis angle; PI-LL, pelvic incidence minus lumbar lordosis; PT, pelvic tilt; SVA, sagittal vertical axis. Note: *The effect size measure for *t*-tests was calculated using the Cohen's D.

spondylolisthesis, showed higher levels of leg pain at M6 (2.1 ± 2.8 versus 0.0 ± 0.0 respectively; $p = 0.008$), resulting in a lower global improvement in leg pain (5.6 ± 3.3 versus 8.1 ± 1.6 respectively; $p = 0.021$).

Patients submitted to two-level fusion presented higher ODI scores at M6 than those submitted to one-level fusion, which was statistically significant (43.3 ± 25.3 versus 17.6 ± 14.5 respectively; $p = 0.014$) (►**Table 6**). Individuals submitted to osteotomy had lower levels of leg pain at M6 compared to those who were not (0.1 ± 0.3 versus 2.1 ± 2.8 respectively; $p = 0.014$), which reflected in a higher global improvement in leg pain (8.4 ± 1.5 versus 5.3 ± 3.2 respectively; $p = 0.003$).

The Relationship between Spinopelvic Parameters and Clinical Outcomes

Considering all the patients, the PI-LL was the only spinopelvic parameter that significantly changed between M0 and M6. Thus, we performed a bivariate analysis regarding this parameter and the clinical and functional outcomes (►**Table 7**). For this, we divided the patients in two subgroups considering the normal range for PI-LL mismatch (that is, ± 10°): patients with PI-LL ± 10° and those who fall outside this range (PI-LL > 10° or < −10°). In our population, all the patients out of the normal range had PI-LL < −10°. Our analysis revealed that patients with PI-LL < −10° at M0 had a higher clinical improvement in the VAS score for low-back pain after surgery than patients with a PI-LL ± 10° (6.8 ± 2.1 *versus* 3.6 ± 3.2 respectively; $p = 0.030$). No differences were observed between patients with PI-LL < −10° or PI-LL ± 10° at M0 and M6 for the ODI or VAS scores for leg pain.

Table 5 Analysis of the clinical and functional outcomes

	Mean ± standard deviation (range)	*t*-test		
		p-value	Independent-samples *t*-Test	Effect size[a]
VAS – low-back pain				
M0	7.4 ± 1.8 (1 to 10)	< **0.001**	t = 6.678	d = 1.336
M6	3.1 ± 3.0 (0 to 9)			
Improvement	4.4 ± 3.3 (−1 to 9)			
VAS – leg pain				
M0	7.8 ± 2.1 (1 to 10)	< **0.001**	t = 10.398	d = 2.080
M6	1.4 ± 2.5 (0 to 8)			
Improvement	6.4 ± 3.1 (1 to 10)			
ODI				
M0	56.3 ± 13.7 (34.0 to 82.0)	< **0.001**	t = 9.849	d = 1.970
M6	20.7 ± 17.6 (0 to 70)			
Improvement	35.6 ± 18.1 (−22 to 62)			
% Improvement	63,6% ± 32.1% (−50% to 100%)			

Abbreviations: M0, preoperative period; M6, six months postoperatively; ODI, Oswestry Disability Index; VAS, Visual Analogue Scale.
Note: [a]The effect size measure was calculated using the Cohen D.

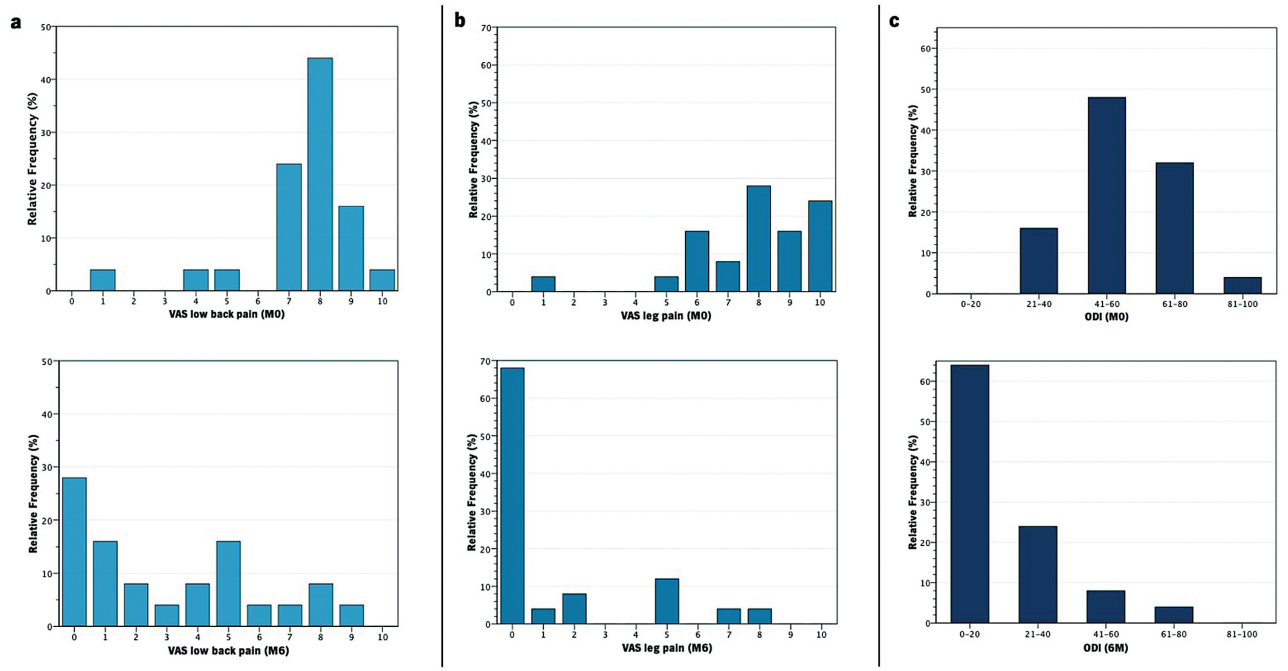

Fig. 2 Graphical representation of the preoperative (M0) and postoperative (M6) clinical and functional outcomes: a) VAS low-back pain; b) VAS leg pain; and c) ODI.

A correlation analysis was performed to assess the relative influence of the PI-LL on the clinical and functional outcomes before and after surgery, as well as on the overall improvement (►**Table 8**). There was a statistically significant moderate correlation between preoperative PI-LL $< -10°$ and improvement in low-back pain ($r_b = 0.435$; $p = 0.030$). No correlation was found regarding the clinical and functional outcomes and other radiological parameters at M0 and M6.

Discussion

In the present study, most patients benefited from surgical intervention, with a mean improvement in ODI scores of 63.6%. They also reported absence of or decrease in pain after surgery. The positive effect of TLIF surgery in pain control and improvement in quality of life is also supported by other studies.[17]

Regarding variables related to patient characteristics, only BMI ≥ 30 Kg/m^2 influenced the functional outcome, as obese patients had higher degree of disability at M6. Obesity has been linked with low-back pain and to worse quality of life and surgical outcomes after lumbar fusion surgery.[18] However, some studies have reported an absence of correlation;[19] thus, the specific effect of obesity on patient outcomes is still unclear. Recently, Duan et al.[20] reported that BMI can be a risk factor for adjacent segment pathology (ASP) after TLIF in patients who present changes in spinopelvic parameters, mainly PI-LL $> 10°$.

Patients who, in addition to spinal stenosis, also had spondylolisthesis, had lower levels of improvement in leg pain after surgery in comparison with patients without spondylolisthesis. However, no differences were verified regarding ODI scores or back pain. This discrepancy can be due to the short postoperative follow-up. Försth et al.[21] concluded that the clinical outcomes in two years of follow-up in patients who had lumbar spinal stenosis, with or without concomitant degenerative spondylolisthesis, were not better than those of patients only submitted to decompression surgery. Better surgical outcomes have been reported for one-level fusion than two-level fusion,[22] which is similar to our results.

Previous studies[8,23,24] have highlighted the influence of spinopelvic parameters, mainly PT and PI-LL, in postoperative residual symptoms. Preoperative loss of LL, assessed by PI-LL $> 10°$, strongly correlates with disability and loss of quality of life in patients with spinal deformities.[25,26] Accordingly, postoperative PI-LL $< 10°$ seems to be the ideal value for spinopelvic alignment that correlates with reduced pain and disability.[8,27,28] Traditionally, PI-LL $< 10°$ is considered a parameter that needs special attention on the part of surgeons in the planning of corrective surgeries involving long-segment fusions to acquire a suitable LL that achieves a good spinopelvic alignment. However, recent reports[19] revealed that, for some patients and pathologies, higher PI-LL values might be required to reach better outcomes. For example, PI-LL between 10° and 20° seems to be adequate in long-segment fusions in patients with scoliosis.[29] A higher PT, decrease in LL, and PI-LL $> 10°$ have also been associated with postoperative pain in short-segment fusion surgeries.[12,23,30] In our cohort, we observed a significant PI-LL decrease, a trend in LL increase, and no changes in PT when we measured these parameters at M0 and at M6 (►**Table 4** and ►**Supplementary Table S2**) (online only). At M0, most individuals had PI-LL $\pm 10°$, and the ones who did

Table 6 Bivariate analysis regarding the clinical (VAS) and functional (ODI) outcomes and patient characteristics, diagnosis, and surgery aspects

	ODI			VAS low-back pain			VAS leg pain		
	M0	M6	Imp.	M0	M6	Imp.	M0	M6	Imp.
Patient characteristics									
Gender (M/F)	*	*	*	*	*	*	*	*	*
Age ($\geq$ 55 years)	*	*	*	*	*	*	*	*	*
BMI ($\geq$ 30 Kgm^2)	*	$p = 0.041$ (t = 2.204; d = 0.860)	*	*	*	*	*	*	*
ASA score	*	*	*	*	*	*	*	*	*
Depression (no/yes)	*	*	*	*	*	*	*	*	*
Diagnosis									
Stenosis (F/C/CF)		$p = 0.037$ (F = 3.827)							
Spondylolisthesis (no/yes)	*	*	*	*	*	*	*	$p = 0.008$ (t = −3.038; d = −0.883)	$p = 0.021$ (t = 2.489; d =0.847)
- Degenerative/Isthmic	*	*	*	*	*	*	*	*	*
- Grade (½)	*	*	*	*	*	*	*	*	*
Surgery									
Levels (½)	*	$p = 0.014$ (t = −2.657; d = −1.635)	*	*	*	*	*	*	*
Osteotomy	*	*	*	*	*	*	*	$p = 0.014$ (t = 2.772; d = 0.865)	$p = 0.003$ (t = −3.300; d = −1.140)
Surgical complications									
- Incidental durotomy (no/yes)	*	*	*	*	*	*	*	*	*
Medical complications									
- Fever (no/yes)	*	*	*	*	*	*	*	*	*

Abbreviations: ASA, American Society of Anesthesiologists physical status classification; BMI, Body Mass Index; C, central; CF, central and foraminal; F, female; F, foraminal; Imp., improvement; M, male; M0, preoperative period; M6, six months postoperatively; ODI, Oswestry Disability Index; VAS, Visual Analogue Scale.
Notes: The homogeneity in the variances was assessed by Levene test. t, test statistics for independent-samples *t*-test; F, test statistics for one-way analyss of variance; d, Cohen D; η^2, Eta-squared. *p-value > 0.05.

Table 7 Bivariate analysis regarding PI-LL and the clinical (VAS) and functional (ODI) outcomes

PI-LL ($\pm 10°$ versus $< -10°$)	ODI			VAS low-back pain			VAS leg pain		
	M0	M6	Δ	M0	M6	Δ	M0	M6	Δ
M0	*	*	*	*	*	$p = 0.030$ (t = 2.314; d = 1.084)	*	*	*
M6	*	*	*	*	*	*	*	*	*

Abbreviations: M0, preoperative period; M6, six months postoperatively; ODI, Oswestry Disability Index; PI-LL, pelvic incidence minus lumbar lordosis; VAS, Visual Analogue Scale.
Notes: The homogeneity in the variances was assessed by the Levene test. t: test statistics for independent-samples *t*-test; d, Cohen D. *p-value > 0.05.

not meet this criterium had PI-LL $< -10°$. At M6, a decrease in patients with PI-LL $\pm 10°$ and an increase in patients with PI-LL $< -10°$ were verified in relation with the LL increase. No patients with PI-LL $> 10°$ were identified in the pre- and postoperative assessments.

Aoki et al.[23] were the first to report that postoperative PI-LL $> 10°$ was associated with residual postoperative low-back and leg pain (assessed by the VAS score) in patients who underwent short-segment TLIF. No significant differences regarding disability, assessed by the ODI, were

Table 8 Correlation of the PI-LL with clinical (VAS) and functional (ODI) outcomes

	ODI			VAS low back pain			VAS leg pain		
	M0	M6	Imp.	M0	M6	Imp.	M0	M6	Imp.
PI-LL $< -10°$									
M0	0.087	−0.223	0.283	0.176	−0.371	**0.435***	0.136	−0.285	0.320
M6	0.208	−0.015	0.172	0.032	−0.165	0.167	0.233	−0.026	0.177
PI-LL (degrees)									
M0	−0.087	0.084	−0.148	−0.259	0.158	−0.288	−0.103	0.329	−0.333
M6	−0.184	0.033	−0.172	−0.253	0.220	−0.341	−0.262	0.141	−0.288
ΔM6-M0	−0.108	−0.068	−0.016	0.029	0.061	−0.039	−0.179	−0.250	0.080

Abbreviations: Imp., improvement; M0, preoperative period; M6, six months postoperatively; ODI, Oswestry Disability Index; PI-LL, pelvic incidence minus lumbar lordosis; VAS, Visual Analogue Scale.
Notes: The values on the table correspond to correlation coefficients (r). $^{*}p < 0.05$.

observed between patients with PI-LL $\leq 10°$ and PI-LL $> 10°$, and no correlation was found between PI-LL and the ODI score postoeratively.[23] Recently, Divi et al.[31] concluded that, in a cohort of 306 patients with lumbar degenerative disease submitted to one- or two-level lumbar fusion and a mean follow-up of 13 months, the surgery outcomes (ODI and VAS scores for back and leg pain) were similar in patients with PI-LL$\leq$ 10° and $> 10°$. In the present study, we evaluated the association of PI-LL $\pm 10°$ and PI-LL $< -10°$ with the surgical outcomes. As reported by other authors,[23,31] no correlation was found between PI-LL and the postoperative outcomes (►**Table 8**). The results of the present study showed that the improvement in pain and disability does not seem to be related to the change in spinopelvic parameters after surgery. Similar results were obtained in patients with a low grade of spondylolisthesis undergoing TLIF.[32]

We also analyzed the correlation between preoperative spinopelvic parameters and the outcomes (►**Table 8**). Interestingly, our results suggest that PI-LL $< -10°$ may be a predictor for a greater postoperative improvement in leg pain, bringing forth the notion that these patients might be good candidates for TLIF.

The short postoperative follow-up is one of the limitations of the present study. First, we were unable to document the rate of fusion. Second, it is important to analyze if any variable is related to the occurrence of ASP. Some studies[25,33,34] have reported that preoperative global sagittal misalignment and lower LL and PI-LL $> 10°$ pre- and postoperatively resulted in increased load on adjacent segments, predisposing to ASP, which can be analyzed after longer follow-ups. Nevertheless, the observation that preoperative PI-LL $< -10°$ is associated with higher improvement in surgical outcome lead us to believe that our results are reliable and provide a new point of view in the field of short-segment interbody lumbar fusion for the treatment of patients with lumbar spinal stenosis.

The present study shows that, in patients with spinal stenosis with or without concomitant spondylolisthesis, PI-LL$< -10°$ can be a predictor of low back pain improvement after TLIF surgery. Moreover, the global surgery improvement seems to be unrelated to the change in spinopelvic parameters change after surgery. We found that patients with BMI $> 30 Kg/m^2$, concomitant spondylolisthesis, absence of osteotomy, and two-level fusion TLIF had lower levels of improvement in surgical outcomes, but no correlation with spinopelvic parameters was observed.

The results of the present study highlight the importance of preoperative planning, first, due to the relevance of spinal sagittal alignment parameters even in short-segment interbody fusion, and second, to identify patients that can benefit more from short-segment lumbar fusion to treat stenosis with or without spondylolisthesis.

Data Availability

The authors declare that all relevant data supporting the findings of the present study are either provided in the Article and Supplementary files or available from the authors upon request.

Funding

The authors declare they have not received funding pertaining to the present study.

Conflict of Interests

The authors have no conflict of interests to declare.

Ethical Standards

The present study was approved by the appropriate local ethics committee. Informed consent, after the description of all the procedures and goals of this research protocol, was obtained before any data collection.

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Surgical Outcome of Microvascular Decompression for Hemifacial Spasm: Symptom Control and Quality of Life

Resultado Cirúrgico da Descompressão Microvascular no Espasmo Hemifacial: Controle de Sintomas e Qualidade de Vida

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Abstract

Introduction Hemifacial spasm (HFS) is characterized by a segmental myoclonus of the face muscles innervated by the ipsilateral facial nerve. The accepted pathophysiology of HFS suggests that it is a disease process of the nerve root entry zone associated with any neuro-vascular conflict.

Aim Review the surgical results and outcome regarding spasm control, post-operative quality of life and morbidity of microvascular decompression (MVD) for HFS from a Brazilian neurosurgical team.

Method An observational investigation was conducted with data collection from patients with hemifacial spasm treated with MVD from January 2000 to December 2015 in two different centers in the West of São Paulo State, Brazil.

Results A total of 152 patients underwent MVD for the treatment of HFS, ninety-eight (64.5%) female. Eighty-seven (57.2%) patients presented right-side spasms. The most common offending vessel was the posterior inferior cerebellar artery (PICA) with 78 (51.3%) patients. According to clinical presentation, an amount of 144 (94.7%) patients presented total control of symptoms after 36 months of follow-up. Regarding quality of life, a total of 125 (82.2%) patients referred normal quality of life after MVD for HFS and 121 (96.8%) from then were able to return to work or previous occupation. Permanent facial paresis / palsy was observed in 6 (3.6%) patients. There was no surgical mortality.

Conclusion MVD for the treatment of HFS is a safe and efficacious surgical procedure to control spasm. Neurosurgeons experience, adequate patient selection and good anatomical knowledge are fundamental to success of the treatment.

Keywords
- hemifacial spasm
- microvascular decompression

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Resumo

Introdução O espasmo hemifacial (EHF) é caracterizado por mioclonia segmentar dos músculos da face inervados pelo nervo facial ipsilateral. A fisiopatologia aceita da EHF sugere que é um processo da doença da zona de entrada da raiz nervosa associada a conflito neuro-vascular.

Objetivo Revisar os resultados e desfechos cirúrgicos em relação ao controle de espasmo, a qualidade de vida pós-operatória e a morbidade da descompressão microvascular (DMV) para EHF de uma equipe de neurocirurgia brasileira.

Método Realizada investigação observacional com coleta de dados de pacientes com espasmo hemifacial tratados com DMV entre janeiro de 2000 a dezembro de 2015, em dois diferentes centros do Oeste do Estado de São Paulo, Brasil.

Resultados Um total de 152 pacientes foram submetidos a DMV, noventa e oito (64,5%) do sexo feminino. Oitenta e sete (57,2%) pacientes apresentavam espasmos no lado direito. O conflito mais comum foi com a artéria cerebelar inferior posterior (PICA) em 78 (51,3%) pacientes. Um total de 144 (94,7%) pacientes apresentou controle total dos sintomas após 36 meses de acompanhamento. Em relação à qualidade de vida, 125 (82,2%) pacientes referiram qualidade de vida normal após a MVD para HFS e 121 (96,8%) puderam retornar ao trabalho/ocupação anterior. Paresia/paralisia facial permanentes foram observadas em 6 (3,6%) pacientes. Não houve mortalidade cirúrgica.

Conclusão DMV para o tratamento da EHF é um procedimento cirúrgico seguro e eficaz para o controle do espasmo. A experiência dos neurocirurgiões, a seleção adequada dos pacientes e o bom conhecimento anatômico são fundamentais para o sucesso do tratamento.

Palavras-chave

- espasmo hemifacial
- descompressão microvascular

Introduction

Hemifacial spasm (HFS) is characterized by a segmental myoclonus of the face muscles innervated by the ipsilateral facial nerve (1–3), usually starting around the eyes before progressing inferiorly to the cheek, mouth, and neck (4–6). Its prevalence is 9.8 per 100,000 persons with an average age of onset of 40–50 years (7–10). The accepted pathophysiology of HFS suggests that it is a disease process of the nerve root entry zone of the facial nerve (11–13) and the most frequently involved vascular structures are veins, vertebro-basilar artery, anterior inferior cerebellar artery (AICA) and/or posterior inferior cerebellar artery (PICA) (2, 13–15). Clinical examination and imaging modalities such as electromyography (EMG) and magnetic resonance imaging (MRI) are useful to differentiate HFS from other facial movement disorders and for intraoperative planning (16–18). Botulinum toxin A is the standard medical management for HFS, which provides low-risk but limited symptomatic relief (19–21). Microvascular decompression (MVD) is a surgical therapeutic option that provides lasting symptomatic relief by reducing compression of the facial nerve root (22–25).

The aim of the present investigation is to review the surgical results and outcome regarding spasm control, post-operative quality of life and complications of MVD for HFS from a Brazilian neurosurgical team.

Method

Study Delineation

An observational investigation was conducted with data collection from patients with hemifacial spasm treated with MVD from January 2000 to December 2015 in two different centers in the West of São Paulo State, Brazil. Clinical data were obtained retrospectively from the patient records and files. For all patients with the diagnosis of hemifacial spasm and radiological evidence of neurovascular conflict on magnetic resonance image (MRI), the following data were collected: gender, age at surgery, side of pain, type of the conflict, type and number of medications used.

Pre-Surgical Evaluation

Brain MRI was obtained from all patients with HFS accordingly with a specific protocol using a 1.5 Tesla Scanner, Philips, at the Department of Neuroradiology in our institution. All MRIs were analyzed by an experienced neuroradiologist that confirmed the visual radiological diagnosis of neurovascular conflict. High-resolution MRIs were performed to view the cerebellopontine angle anatomy of the patients and to exclude the presence of any organic/expansive lesion.

Surgical Technique

The surgical approach was similar for all patients and neurosurgeons experienced in MVD surgery for HFS performed all

procedures. The surgery was done under general anesthesia with a flexible spiral tracheal tube to allow flexion of the neck while securing the airways. All patients were placed in the lateral position with the head supported with a three-pin Mayfield head fixation. A 3- to 4-cm curvilinear incision was made obliquely inside the hairline at the upper retromastoid area. A 1.5- to 2-cm diameter keyhole bone opening or small craniectomy or craniotomy was performed using a 4- and 4-mm extra-coarse power Diamond drill system. The keyhole was located at the inner corner of the transverse sinus and the sigmoid sinus. Before dural opening, precise hemostasis was accomplished with bone wax, Surgicel, and cautery. The mastoid air cells were sealed with bone wax. The dura was opened in an inverted-T fashion and small dural flaps were stitched to make a maximal dural opening (5 to 10 mm). The cerebrospinal fluid (CSF) was gradually aspirated and, under the operating microscope, infratentorial lateral supracerebellar dissection was advanced to expose the petrosal vein (one to three bridging veins). Sufficient arachnoid dissection around the petrosal veins and caudally was performed to carefully expose the facial nerve and any offending vessels around the neural structures from proximal to distal. Any compressing arterial loops or venous contact were carefully dissected and mobilized off the nerve root. A nonabsorbable material was interposed between the offending vessel and the entry zone of the facial nerve. Cerebellar retraction was judiciously used when necessary. Meticulous hemostasis and clean-up of the operating field was often achieved. Watertight dural closure with or without fascial graft was done and cranioplasty completed whenever possible. Cutaneous layers were closed as routinely.

Outcome Assessment and Follow-Up

Three years follow-up investigation was performed in all patients included in the present study. The patients were clinically reassessed at 12, 24 and 36 months after surgery regarding the subjective improvement of pre-operative facial spasm. They were included in four different groups according to percentage of amelioration of spasm, respecting to the following descriptions: (I) total relief (>90% control of spasm) and patient satisfied with operation; (II) partial relief (75–90% control of spasm) and patient satisfied with operation; (III) incomplete relief (50–75% control of spasm) and patient not satisfied with operation; (IV) failure or poor control (<50% control of spasm) and patient not satisfied with operation. A questionnaire on quality of life was also applied to each patient regarding daily activities, including driving, reading (journal and/or books, PC/Cellphones/Tablets), watching TV, depressive feelings, other people avoidance, return to previous work functions and physical activities. Quality of life was graded as follow: (I) normal quality of life and no disability; (II) mild disability and no impairment; (III) moderate disability and functional impairment; and (IV) severe disability.

Ethical Statement

The ethical committee of our institution analyzed the project and approved the performance of our investigations. All patients have given their informed consent for participation in the research study. This study complied with the Declarations of Helsinki and Nuremberg. Informed consent for surgery was acquired from all patients.

Statistical Analysis

The data collected from all patients were organized in tables. The data are expressed as the means $\pm$ the standard deviation (SD) for parametric variables and as the median values for nonparametric variables. A normal distribution to sample collected data was assumed. HFS improvement rate was assessed using Kaplan-Meier curves and Montel-Cox chi-square test. The statistical analyses and review of the numerical results obtained in the present investigation were performed by a mathematical team and p-value < 0.05 was considered statistically significant.

Results

In the present study, we operated on 152 consecutive patients. ►**Table 1** shows the clinical characteristics of patients with HFS. ►**Table 2** reveals the main causes of HFS regarding offending vessels. ►**Table 3** reports the efficacy of MVD for HFS according to spasm control. ►**Table 4** shows the outcome of surgery in respect of patient's quality of life. Patients with severe disability presented high grade facial palsy and reported that nerve paralysis was directly affecting their quality of life. ►**Table 5** shows the relation of quality of life after MVD for HFS and depressive feelings, physical activities and return to work or previous occupation. ►**Table 6** reveals the main complications of operated patients. There was no surgical mortality.

Discussion

Hemifacial spasm (HFS) is a movement disorder of the muscles innervated by the facial nerve (cranial nerve VII)

Table 1 Characteristics of patients with HFS

Characteristics	(%)
Age (years)	52.1 $\pm$ 10.8
Gender	
Female	98 (64.5)
Male	54 (35.5)
Spasm side	
Right	87 (57.2)
Left	65 (42.8)
Duration (years)	6.8 $\pm$ 4.7
Risk factors	
Diabetes	11 (7.2)
Hypertension	42 (27.6)
Alcohol use	17 (11.2)
Smoking	21 (13.8)
Total	152/100

Table 2 Causes of HFS: offending vessels

Offending Vessels	n/%
PICA	78/51.3
AICA	42/27.6
VBA	16/10.5
AICA + PICA	12/7.9
PICA + Vein	4/2.6
Total	152/100

Abbreviations: PICA, posterior inferior cerebellar artery; AICA, anterior inferior cerebellar artery; VBA, vertebral/basilar artery.

(1–3). This movement disorder triggers involuntary short or longer contractions of the facial muscles and usually causes serious psychosocial problems, once affected persons often suffer immensely and tend to increasingly withdraw socially (10). Microvascular decompression (MVD) is a surgical therapeutic option that provides lasting symptomatic relief, and the pioneers of the technique were James Gardner and Peter Jannetta, who proved that reducing compression of the facial nerve root eliminates involuntary movements (26). In our investigation, all patients presented symptoms of HFS associated with at least evidence of neuro-vascular conflict with the corresponding facial nerve.

Female patients are usually more affected with a sex ration of 0.6 (male/female) and left side is the most involved (10, 27–29). HFS is more common in the elderly and is extremely rare in the adolescent (27–29). According to Liu et al. (27), the disease affects patients between the fourth and fifth decades of life and usually presents a mean duration of six years in all operated patients. Additionally, it is also believed that some individuals present risk factors for higher rates of surgical failure or recurrence due to stronger compression of the nerve, such as arterial hypertension, diabetes, and morbid obesity (30, 31). In the present study, most patients were female, were in the fifth decade of life and presented more frequently right sided

Table 3 Outcome of MVD for HFS: Spasm control (n/%)

		12 months	24 months	36 months
I	Total (>90% control)$^{+}$	136/89.5	141/92.8	144/94.7
II	Partial (75%-90% control)$^{+}$	11/7.2	9/5.9	6/3.9
III	Incomplete (50%-75% control)$^{\times}$	4/2.6*	2/1.3	2/1.3
IV	Failure/Poor control (<50% control)$^{\times}$	1/0.6$^{\#}$	0	0
Total		152/100		

$^{+}$: Patient satisfied with operation.
$^{\times}$: Patient not satisfied with operation.
$^{\#}$: Patient was re-operated.
*: Patients were complementarily treated with Botulinum toxin A.

Table 4 Outcome of MVD for HFS: Quality of life (n/%)

		12 months	24 months	36 months
I	Normal	111/73.0	121/79.6	125/82.2
II	Mild disability	27/17.8	21/13.8	19/12.5
III	Moderate disability	11/7.2	8/5.3	6/3.9
IV	Severe disability	3/1.9	2/1.3	2/1.3
Total		152/100		

Table 5 Quality of life after MVD for HFS (n/%) (36 months)

		Depressive feelings	Physical activities	Return to work	Total (36m)
I	Normal	8/6.6	118/77.6	121/96.8	125
II	Mild disability	5/26.3	15/78.9	16/94.7	19
III	Moderate disability	3/50	2/33.3	4/66.7	6
IV	Severe disability	2/100	0/0	0/0	2
Total					152

Table 6 Complications of MVD for HFS

Temporary Complications		Permanent Complications	
	n/%		n/%
Facial paresis/palsy	18/11.8	Facial paresis/palsy	6/3.6
Vertigo/ Nystagmus	13/8.5	Hearing decrease	9/5.9
CSF leakage	4/2.6	Deafness	3/1.97
Wound infection	7/4.6	Mortality	0/0
Total	42/27.6	Total	18/11.8

symptoms with mean duration of 6.8 years before surgery. We also observed that cerebrovascular and atherosclerotic risk factor, such as diabetes type 2, arterial hypertension, alcohol use and smoking, were noted in 7.2–27.6% of patients, but none were statistically associated with recurrence or failure in our investigation.

Primary HFS is associated with neuro-vascular conflicts in the facial nerve, especially its root exit zone (REZ) (1, 2, 7). Negative surgical exploration of the cerebellopontine angle is extremely rare and is verified in only 0% - 2% of cases (32). Miller et al. (33) reviewing 22 papers published from 2000 to 2010 confirmed as source of conflicting vessel the anterior inferior cerebellar artery (AICA) in 37% cases, the posterior inferior cerebellar artery (PICA) in 30% and multiple vascular contacts including vertebro-basilar-artery (VBA) and veins in 23%. Mercier et al. (32) studying 2489 cases from the literature and 340 from their own series reported as the most frequently encountered conflicting vessel the PICA (in 47.2% of the patients on average) followed by the AICA (45.9%), but ranges with these arteries were large between different publications. In our investigation, we found as the most common offending vessel the PICA in 51.3% of cases followed by AICA in 27.6%. Megadolicho vertebral/basilar artery or multiple conflicting vessels, i.e., AICA-PICA or PICA-vein, were found in 10.5%, 7.9% and 2.6% of cases, respectively. We found no case with veins as the only offender vessel.

In many series investigating surgical effectiveness of MVD for HFS, spasm control was observed in 65% - 100% of operated patients (33–35). Miller et al. (33), in 2012, reported complete resolution of spasm in 91.1% of the patients, notably delayed in 11.2%. Sindou et al. (35) affirmed that percentage of patients with total relief ranged between 85% and 90% and spasm control was obtained after a certain delay in as many as in $33\% \pm 8\%$ of the patients in many series. Relief remained permanent in all but 1–2% of the long-term followed patients, when effect of MVD was considered achieved (33–35). In the present study, total control of HFS was observed in 144 (94.7%) patients, with 8 (5%) cases presenting delayed improvement during follow of 36 months. One (0.6%) patient showed recurrence of HFS after one year of follow up and was reoperated and evolved with satisfactory result. Our patients with incomplete outcome (50–75% control) and not satisfied with operation after 12 months of follow up (4 cases / 2.6%) were referred to complementarily treatment with Botulinum toxin A. All these four patients with incomplete results presented complex conflicts with megadolicho vertebral/basilar artery coincidentally.

HFS is a movement disturbance that affects profoundly quality of life. It can be disabling and cause visual disfigurement for the patients and normally withdraw individuals from social and working life (28, 36, 37). According to Cheng et al (36), patients with severe HFS symptoms or a higher educational level were at higher risk of worse quality of life. MVD for HFS significantly improves quality of life and ameliorate physical and mental health aspects of patients (28, 36, 37). In our investigation, we observed during follow up progressive raise of patient's quality of life for 36 months. At the end of the study, most of patients referred normal (82.2%) or mild disability (12.5%) in life activities, social interactions, and psychological satisfaction after operation. We also observed that depressive feelings seem more frequent in patients presenting worst disability while physical activity and return to working life more common in patients normal life of mild disability. Kim et al (38) affirmed that HFS patients seem to gain benefits from MVD not only for their facial disfigurement but also for social anxiety symptoms that may be associated with mental health improvements in their quality of life. This looks also true in the present investigation.

MVD for HFS is a functional procedure and should be associated with low rates of clinical and surgical complications. Besides hearing complications, facial palsy (FP) is the most frequent neurological deficit observed after MVD surgery for HFS (33, 35). Immediate FP has occurred as a transient event in 2.7–22.5% and was permanent in 0–8% of the patients according to series (35). Miller et al. (33) reported the average percentage of transient FP in 9.5% and of permanent in 0.9% of cases. Regarding hearing deficits, the reported occurrence is of 1.9–20% of cases (35). Miller et al. (33) showed a permanent loss of hearing function in 2.3%. Episodes of vertigo with nystagmus and some gait imbalances are not infrequent and, according to Sindou et al (35) happened in 5.4% in their series, and remained permanent and to some degree disabling in 1.4%. Cerebrospinal fluid (CSF) leakage is a complication indirectly related with surgeon's experience. Beginning authors experience CSF leakage in ~2.5–10% according to series, 4.7% on average (35), while surgeons with stabilized learning curves present an incidence ranging between 1–2% (35). We present our surgical complications in ►**Table 6**. Mortality is a very seldom complication with less than 0.1% of cases in the literature (33, 35). There was no surgical mortality in the present study.

There are several methodological aspects in the present findings, which should be interpreted in the context of several limitations. First, this study is a non-randomized investigation performed in a highly selected population of a tertiary center. Second, these findings cannot be generalized once some patients lost their follow up due to the continental dimension from Brazil. On the other hand, the present study described the surgical outcomes of a relatively large number of patients that underwent surgery due to HFS for an extended follow-up duration.

Conclusion

MVD for the treatment of HFS is a safe and efficacious surgical procedure to control spasm. Neurosurgeons experience, adequate patient selection and good anatomical knowledge are fundamental to success of the treatment.

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External Validation of a Clinical Nomogram for Predicting Intracranial Hematoma Following Head Computed Tomography in Pediatric Traumatic Brain Injury

Validação externa de um nomograma clínico para previsão de hematoma intracraniano após tomografia computadorizada de cabeça em lesão cerebral traumática pediátrica

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Abstract

Introduction Over-investigation of head computed tomography (CT) has been observed in children with TBI. Long-term effects from a head CT brain scan have been addressed and those should be balanced. A nomogram is a simple prediction tool that has been reported for predicting intracranial injuries following a head CT of the brain in TBI children in literature. This study aims to validate the performance of the nomogram using unseen data. Additionally, the secondary objective aims to estimate the net benefit of the nomogram by decision curve analysis (DCA).

Methods We conducted a retrospective cohort study with 64 children who suffered from traumatic brain injury (TBI) and underwent a CT of the brain. Nomogram's scores were assigned according to various variables in each patient; therefore sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy and F1 score were estimated by the cross-tabulation of the actual results and the predicted results. Additionally, the benefits of a nomogram were compared with "None" and "All" protocols using DCA.

Results There were 64 children with TBI who underwent a head CT in the present study. From the cross-tabulation, the nomogram had a sensitivity of 0.60 (95%CI 0.29–0.90), specificity of 0.96 (0.91–1.0), PPV of 0.75 (0.44–1.0), NPV of 0.92 (0.86–0.99), accuracy of 0.90 (0.83–0.97), and an F1 score of 0.66 (0.59–0.73). Also, the area under the curve was 0.78 which was defined as acceptable performance. For the DCA at 0.1

Keywords
- External validation
- Nomogram
- intracranial hematoma
- pediatric traumatic brain injury
- head injury

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high-risk threshold, the net benefit of the nomogram was 0.75, whereas the "All" protocol had the net benefit of 0.40 which was obviously different.

Conclusion A nomogram is a suitable method as an alternative prediction tool in general practice that has advantages over other protocols.

Resumo

Introdução A investigação excessiva da tomografia computadorizada (TC) de crânio tem sido observada em crianças com TCE. Os efeitos a longo prazo de uma tomografia computadorizada de crânio foram abordados e devem ser equilibrados. Um nomograma é uma ferramenta de predição simples que foi relatada na literatura para prever lesões intracranianas após uma tomografia computadorizada de crânio em crianças com TCE. Este estudo tem como objetivo validar o desempenho do nomograma usando dados não vistos. Adicionalmente, o objetivo secundário visa estimar o benefício líquido do nomograma por meio da análise da curva de decisão (DCA).

Métodos Realizamos um estudo de coorte retrospectivo com 64 crianças que sofreram traumatismo cranioencefálico (TCE) e foram submetidas a tomografia computadorizada de crânio. As pontuações do Nomograma foram atribuídas de acordo com diversas variáveis em cada paciente; portanto, sensibilidade, especificidade, valor preditivo positivo (VPP), valor preditivo negativo (VPN), acurácia e escore F1 foram estimados pela tabulação cruzada dos resultados reais e dos resultados previstos. Além disso, os benefícios de um nomograma foram comparados com os protocolos "Nenhum" e "Todos" usando DCA.

Palavras-chave
- validação externa
- nomograma
- hematoma intracraniano
- lesão cerebral traumática pediátrica
- ferimento na cabeça

Resultados Houve 64 crianças com TCE que foram submetidas a tomografia computadorizada de crânio no presente estudo. A partir da tabulação cruzada, o nomograma apresentou sensibilidade de 0,60 (IC95% 0,29–0,90), especificidade de 0,96 (0,91–1,0), VPP de 0,75 (0,44–1,0), VPN de 0,92 (0,86–0,99), acurácia de 0,90 (0,83–0,97) e uma pontuação F1 de 0,66 (0,59–0,73). Além disso, a área sob a curva foi de 0,78, definida como desempenho aceitável. Para o DCA no limiar de alto risco de 0,1, o benefício líquido do nomograma foi de 0,75, enquanto o protocolo "Todos" teve o benefício líquido de 0,40, o que foi obviamente diferente.

Conclusão Um nomograma é um método adequado como ferramenta alternativa de predição na prática geral que apresenta vantagens sobre outros protocolos.

Introduction

Mortality and physical disabilities following traumatic brain injury (TBI) in children have been a concern of major public health problems.[1,2] Head computed tomography (CT) is the gold standard investigation of intracranial injuries. According to Larson et al, the rate of head CT in patients following TBI rose from 13.1% in 1996 to 40.7% in 2007.[3] However, the long-term side effects of CT have been mentioned. From prior studies, children who underwent CTs between 1985–2002, were significantly associated with leukaemia and brain tumors.[4,5] Therefore, the balancing of the unnecessary ionizing radiation exposure in children has been considered in over-investigations.

Investigation criteria has been performed and proposed from previous studies, for example, Children's Head Injury Algorithm for the Prediction of Important Clinical Events,[6] Canadian Assessment of Tomography for Childhood Head Injury,[7] and the Pediatric Emergency Care Applied Research Network[8] that are clinical prediction rules to identify children who need a head CT following mild TBI. Nomogram is one of the clinical prediction tools that has been used for predicting clinical outcomes and prognosis in various neurological conditions such as TBI, neuro-oncology and neurosurgical complications. According to Tunthanathip et al., a clinical nomogram was developed for the prediction of intracranial injuries following TBI from 900 TBI children in 2009–2018. The performance of the prediction tool was reported at an acceptable level as follows: accuracy (0.83), sensitivity (0.42), specificity (1.00), positive predictive value (1.00), and negative predictive value (0.81).[9] Also, this nomogram was further developed as a web-based application for user-friendly application in general practice.[9]

External validation is one of the processes to estimate the nomogram's performance using new and unseen data.[10] Therefore, this study aimed to validate the performance of the nomogram at predicting intracranial injuries following a head CT which was proposed from a prior study. Moreover, the secondary objective aimed to estimate the net benefit of the nomogram by decision curve analysis.

Methods

Study Designs and Study Population

A retrospective cohort study design was performed with patients suffering from TBI registered in the Trauma Registry of the trauma center of southern Thailand between January 2019 and December 2020. Patients were excluded for the following reasons: (1) patients died before arrival or at the emergency department; (2) patients who did not have a head CT. In detail, electronic medical records were reviewed to collect clinical characteristics, treatment, and functional outcomes. The findings from the head CT were evaluated by a neurosurgeon. Severities of TBI were defined according to the Glasgow Coma Scale (GCS) as follows: patients with a GCS score of 13–15 were defined as mild TBI, moderate TBI were patients with a GCS score of 9–12, and severe TBI were patients with a GCS score of 3–8 [4]. The hospital-discharge Glasgow Outcome Scale (GOS) was estimated in the present study. In detail, GOS was divided into 5 scores as follows: Death (1 score), vegetative state (2 scores), severe disability (3 scores), moderate disability (4 scores), good recovery (5 scores).[2,11] Moreover, the GOS was dichotomized into unfavorable outcome (GOS of 1–3) and favorable outcome (GOS of 4–5) for binary proposes.[11] The study was approved by the institutional research ethical committees.

Statistical Analysis

Descriptive statistics were performed for describing the baseline characteristics of the present cohort: mean with standard deviation (SD) or median with interquartile range (IQR) were used for describing continuous variables, while the categorical variables were described in percentages.

According to the primary objective, scoring for the present cohort was performed based on a clinical nomogram of Tunthanathip et al.[9] Nomogram scores were assigned according to various variables in each child; therefore, the cross-tabulation between the actual result and predicted result was done to estimate the nomogram's performance. In detail, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy and F1 score were estimated from the cross-tabulation. Additionally, the receiver operating characteristic (ROC) curve and area under the curve (AUC) were performed. An AUC of $\geq$ 0.7 was defined as acceptable performance, whereas an AUC of $\geq$0.8 and $\geq$0.9 was defined as good and excellent performance, respectively.[12,13]

For the secondary objective, a decision curve analysis (DCA) was conducted to evaluate the benefit of the nomogram compared with other protocols: "None" and "All" protocols. The cost-benefit ratio was used at a threshold of 0.1 according to prior studies.[14–16] The statistical analysis was done by the R version 3.6.2 software (R Foundation, Vienna, Austria).

Results

There were 204 children with TBI in the present study with 140 children being excluded because they did not undertake

Table 1 Demographic data of the present cohort ($N = 64$)

Factor	N (%)
Gender	
Male	39 (60.9)
Female	25 (39.1)
Age -month	
$<$ 60	5 (7.8)
$\geq$ 60	59 (92.2)
Mean of age- month (SD)	92.2 (7.6)
Injured mechanism	
Motorcycle crash	22 (34.4)
Fall at ground level	19 (29.7)
Object hit at the head	7 (10.9)
Pedestrians' injury	6 (9.4)
Bicycle accident	6 (9.4)
Vehicle crash	3 (4.7)
Fall from height	1 (1.6)
Road traffic injury	21 (48.4)
Sign and symptoms	
Scalp wound/hematoma	41 (64.1)
Loss of consciousness	21 (32.8)
Amnesia	19 (29.7)
Vomiting	7 (10.9)
Hypotension	4 (6.3)
Seizure before CT of the brain	2 (3.1)
Bleeding per nose/ear	2 (3.1)
Motor weakness	1 (1.6)
Initial Glasgow Coma Scale score	
13–15	57 (89.1)
9–12	1 (1.6)
3–8	6 (9.4)
Pupillary light reflex	
Normal reactivity both eyes	62 (96.9)
Fixed one eye	2 (3.1)
Fixed both eyes	–
Positive findings on CT of the brain	10 (15.6)
Calvarium skull fracture ($N = 3$)	3 (4.7)
Linear	2 (3.1)
Compound depressed	1 (1.6)
Basilar skull fracture	3 (4.7)
Epidural hematoma	3 (4.7)
Subdural hematoma	4 (6.3)
Contusion	1 (1.6)
Brainstem hemorrhage	1 (1.6)
Subarachnoid hemorrhage	5 (7.8)
Intraventricular hemorrhage	2 (3.1)

Table 2 Nomogram score of Tunthanathip et al.[9]

Variable	Score
Age group	
$<=$ 5 years	0
$>$ 5 years	14
Road traffic injury	
No	0
Yes	9
Loss of consciousness	
No	0
Yes	12
Motor weakness	
No	0
Yes	52
Scalp injury	
No	0
Yes	31
Bleeding per nose/ear	
No	0
Yes	100
Glasgow Coma Scale score	
13–15	0
9–12	37
3–8	72
Pupillary light reflex	
React both eyes	0
Fixed one eye	69
Fixed both eyes	35

*Prediction of positive intracranial injury used the cut off of >0.5 probability (total score more than 79)

a head CT. Hence, the present study enrolled 64 children whose baseline characteristics are presented in ►**Table 1**. The mean age was 92.2 months (SD 7.6), with a range of 4–168 months, whereas the median age was 384 (IQR 132). For the mechanism of injury, road traffic accidents were found in 48.4% of all cases. A motorcycle crash was the most common cause of injury, whereas a fall at ground level was found in 29.7%. More than two-thirds of children had a scalp injury and post-traumatic seizure was observed in 3.1% of them. According to the severity of TBI, major patients were mild TBI and 11% of the cohort were moderate-severe TBI. Therefore, intracranial injuries were found at 15.6%. Subdural hematoma and subarachnoid hemorrhage were common findings following a CT of the brain.

Therefore, children in the present cohort were individually allocated scores as shown in ►**Table 2**. The prediction of positive intracranial injury was assigned when the total score was more than 79 (probability of positive results more than 0.5). Cross-tabulation between actual results and predicted results are presented in ►**Table 3**. From the cross-tabulation, the nomogram's sensitivity, specificity, PPV, NPV, accuracy, and F1 score using the unseen data was 0.60 (95%CI 0.29–0.90), 0.96 (0.91–1.0), 0.75 (0.44–1.0), 0.92 (0.86–0.99), 0.90 (0.83–0.97), respectively. Additionally, the F1 score was 0.66 (0.59–0.73) and the AUC was 0.78, as shown in ►**Fig. 1**.

For the secondary objective, DCA was performed for evaluating the net benefit of the nomogram compared with other situations, as shown in ►**Fig. 2A**. In detail, the DCA comprises of three lines; None (black line), All (gray line), and Nomogram (red line). "None" means nobody received a head CT brain in the present study; therefore, no net benefit is observed in Y-axis. "All" means a head CT is performed on all children, while "Nomogram" means using the nomogram score in the present cohort for selecting head CT. Vicker et al. used the high-risk threshold of 0.1 (cost: benefit ratio or harm: benefit ratio)[14] That meant that 1 normal person was harmed from treatment/investigation (such as head CT with unnecessary radiation exposure) and 9 actual patients underwent necessary treatment/investigation from a total of 10 children. When we set the harm benefit ratio at 1:9, the net benefit of the nomogram is higher than the head CT all cases protocol (All), as shown in ►**Fig. 2B**.

Discussion

The overall performance of the nomogram was at an acceptable level for predicting intracranial injury in pediatric TBI when we performed temporal external validation. We observed the stability of nomogram's performance in variations of baseline risk (intercept) and covariate effects (regression coefficients) of the prediction model in different time periods.[17,18] The tool had a high specificity and PPV that may be useful for ruling in children who were at high risk of intracranial injury. According to Baeyens et al., SPIN is the acronym for 'Specific test when Positive rules IN the disease' and SPIN relates with the high specificity and high PPV.[19]

Moreover, the DCA was plotted in the present study, which is a novel framework for estimating prediction tools by Vicker et al in 2006.[14] In the field of oncology, Calster et al.

Table 3 Cross-tabulation between actual and predicted results

	Actual results of head CT	
Predicted results of head CT	**Positive finding**	**Negative finding**
Predicted positive finding	6	2
Predicted negative finding	4	52

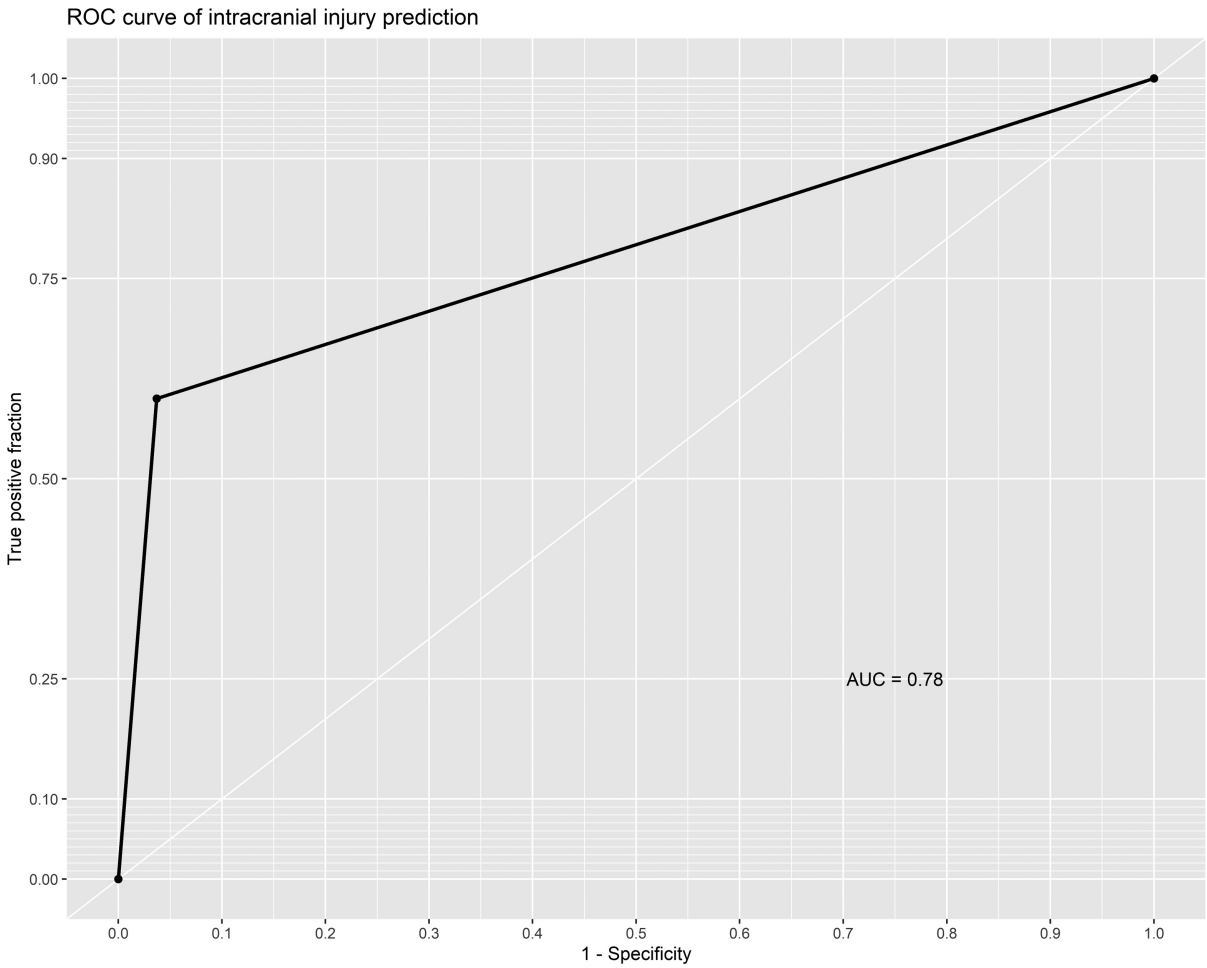

Fig. 1 Receiver operating characteristic curve with area under the curve.

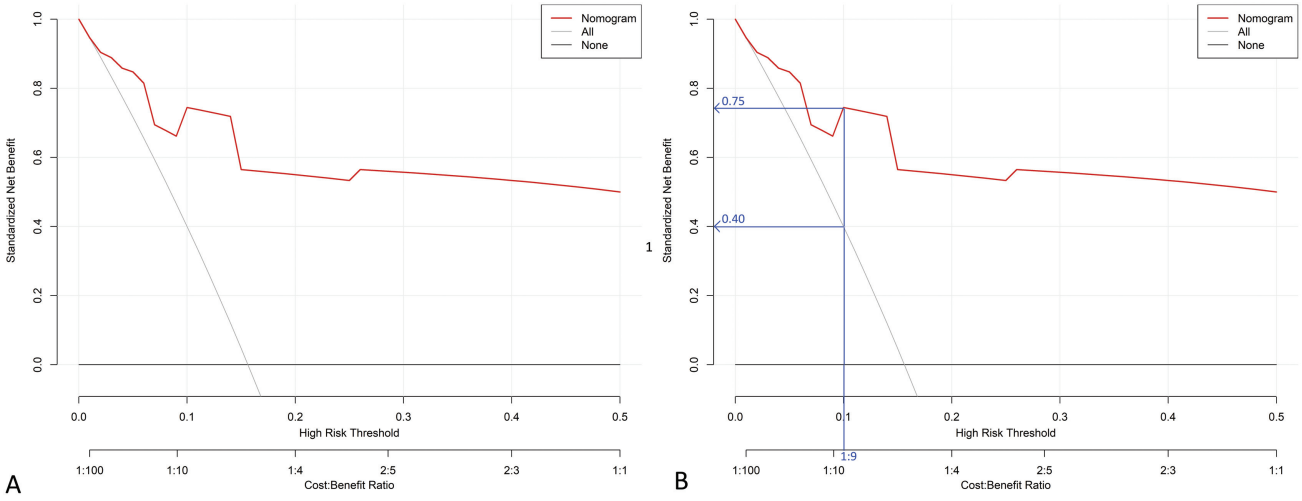

Fig. 2 (A) Decision curve analysis of nomogram. (B) Decision curve analysis with comparison between "All" protocol (gray line) and "Nomogram" protocol (red line). At cost: benefit ratio of 1:9, net benefit of "Nomogram" protocol is higher than "All" protocol (blue line).

used DCA for evaluating the net benefit of the prediction model for high-grade prostate cancer to select who should undertake a biopsy.[16] Therefore, DCA was concluded that it could help the clinicians to make better clinical decisions for treatment or investigation. As a result of the present study, the predictive model of the nomogram has estimated a benefit using DCA and found that it had potential value for implication in general practice.[10,20]

A nomogram is one of the clinical prediction tools that has been used for predicting various outcomes such as neuro-oncology,[10] trauma,[9,20] and various clinical outcomes.[21] Because the scoring system of the nomogram was quite difficult to remember, a web-based application of the nomogram has been developed in the literature review.[9] Moreover, machine learning algorithms have been proposed as alternative approaches for predicting clinical outcomes. Tunthanathip et al. used various algorithms of machine learning and found that the naive Bayes algorithm was highlighted for the prediction of infection following neurosurgical operations.[22] The comparison of predictive performances among various clinical prediction tools should be conducted in the future for selecting the best predictive performance. Hence, the tools will be deployed in general practice.

However, certain limitations should be recognized. First, although high accuracy was observed in the present study, the imbalance of negative and positive findings on head CT may be misleading.[23] Therefore, the F1 score has been suggested for estimating in this situation. The F1 score is calculated from the weighted average of PPV (precision) and sensitivity (recall). This tool may not be appropriate to use for a screening tool, because diminishing vales of recall and F1 score were observed. As mentioned above, the nomogram in the present study may be used for ruling in high-risk patients with an accepted F1 score.[24] Second, the sample size was limited in the present study; therefore, a multicenter study should be conducted in the future to increase the number of TBI children.

For future study, geographic external validation should be performed for estimating the generalizability from differences of both baseline risk and covariate effects of the nomogram's predictive model in different settings and time periods.[17,25] Also, an impact analysis should be conducted to evaluate the diminishing rate of head CT over-investigation in children.[26]

Conclusion

A nomogram is a suitable method for applying an alternative prediction tool in general practice that has advantages over other protocols.

Abbreviations Used in this Paper

AUC: Area under the curve, CT: computed tomography, DCA: decision curve analysis, GCS: Glasgow Coma Scale, GOS: Glasgow Outcome Scale, IQR: interquartile range, NPV: negative predictive value, PPV: positive predictive value, ROC: Receiver operating characteristic, SD: standard deviation, SPIN: Specific test when Positive rules IN the disease, TBI: traumatic brain injury

Declarations

All procedures performed in the study that involved studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee or both and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Author Contributions

AJ and TT conceived the study and designed the method. TT supervised the conduct of the data collection. AJ and TT managed the data, including quality control. AJ and TT provided statistical advice on the study design and analyzed the data and AJ drafted the manuscript, and TT contributed substantially to its revision. TT takes responsibility for the paper.

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Conflict of Interest

The authors declare to have no competing interests

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Nasal Cerebrospinal Leaks in the Milieu of COVID-19 Pandemic

Vazamentos nasais cerebroespinhais no meio da pandemia de COVID-19

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Abstract

Background The unintentional ingestion of oropharyngeal or gastric contents into the respiratory tract is known as aspiration. Rhinorrhea can cause aspiration pneumonia (cerebrospinal fluid leakage).

Objective There are only a few reports in the literature about pneumonia as a complication of rhinorrhea. There are no reports on how to handle such cases if they present to the clinic at the peak of COVID-19 disease and distinguish between these two conditions.

Methods We reviewed the literature and retrospectively analyzed the clinical information and treatment protocols used to treat the two clinical cases.

Results By screening the COVID-19 PCR and antibodies more than twice, surgery was postponed for 10–14 days in both cases to rule out COVID-19-induced pneumonia. Chest CT scans still revealed ground glass opacities. In both cases, the skull base defect was repaired. In both cases, radiological signs of rhinorrhea-induced pneumonia had completely resolved at the 24- and 30-day follow-ups.

Conclusion CSF aspiration causes radiological changes in the lungs in rhinnorhea. This is a short-term local decrease in lung tissue airness (partial filling of alveoli with fluids), which is visible radiographically (ground-glass opacities). To rule out COVID-19 infection, surgery should be postponed for 10–14 days, and PCR and antibodies (IgG, IgM) should be performed at least twice. If the COVID-19 screening test is negative, repair surgery can be scheduled.

Keywords
- CSF liquor rhea
- COVID-19
- aspiration
- pneumonia
- skull base repair surgery

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Resumo

Introdução A ingestão não intencional de conteúdo orofaríngeo ou gástrico no trato respiratório é conhecida como aspiração. A rinorréia pode causar pneumonia por aspiração (vazamento de líquido cefalorraquidiano).

Objetivo Existem poucos relatos na literatura sobre pneumonia como complicação da rinorréia. Não há relatos sobre como lidar com esses casos se eles se apresentarem à clínica no pico da doença COVID-19 e distinguirem entre essas duas condições.

Métodos Revisamos a literatura e analisamos retrospectivamente as informações clínicas e os protocolos de tratamento utilizados para tratar os dois casos clínicos.

Resultados Ao rastrear a PCR e os anticorpos da COVID-19 mais de duas vezes, a cirurgia foi adiada por 10 a 14 dias em ambos os casos para descartar pneumonia induzida pela COVID-19. A tomografia computadorizada de tórax ainda revelou opacidades em vidro fosco. Em ambos os casos, o defeito na base do crânio foi reparado. Em ambos os casos, os sinais radiológicos de pneumonia induzida por rinorréia foram completamente resolvidos nos acompanhamentos de 24 e 30 dias.

Conclusão A aspiração do LCR causa alterações radiológicas nos pulmões na rinorreia. Esta é uma diminuição local de curto prazo na leveza do tecido pulmonar (preenchimento parcial dos alvéolos com fluidos), que é visível radiograficamente (opacidades em vidro fosco). Para descartar infecção por COVID-19, a cirurgia deve ser adiada por 10 a 14 dias e a PCR e anticorpos (IgG, IgM) devem ser realizados pelo menos duas vezes. Se o teste de rastreio da COVID-19 for negativo, pode ser agendada uma cirurgia reparadora.

Palavras-chave

- Ema licorosa do LCR
- COVID 19
- aspiração
- pneumonia
- cirurgia de reparo da base do crânio

Introduction

Nasal liquorrhea is a leakage of cerebrospinal fluid from the cranial cavity into the nasal cavity or paranasal sinuses caused by a congenital or acquired defect in the bones and meninges of the skull base.[1]

Meningitis, meningoencephalitis, pneumocephalus, and brain abscess are all potentially fatal complications of rhinorrhea. Complications such as aspiration bronchopneumonia and gastritis are possible.[2,3] With pronounced outflow of cerebrospinal fluid in the supine (horizontal) position, cerebrospinal fluid can frequently enter the lower respiratory pathways from the nasal cavity/nasopharynx, resulting in aspiration bronchopneumonia and patients presenting clinically with complaints of cough that is most often reproduced in the supine position.[4] The epidemiology of pneumonia has been reported to be between 5 and 10 cases per 1000 inhabitants in Europe and North America.[5] According to one study, more than 1.5 million of the country's adult population suffers from pneumonia, and the death rate can reach thousands each year.[6] The statistics presented here emphasizes the importance of early diagnosis and treatment of the condition. Viral pneumonia is the most difficult to diagnose, and it has a seasonal nature, occurring primarily during the winter session. A new epidemic of coronavirus infection caused by SARS-CoV-2 occurred in December 2019.[7–11] The primary manifestation of the disease is pneumonia, but asymptomatic or mildly symptomatic involvement of the upper respiratory tracts may also occur, which resolves within a week of infection.[12,13] The detection of viral RNA with real-time reverse transcription test (PCR) is currently the gold standard for the diagnosis of COVID-19, and the combination of computed tomography data with PCR false-negative results in COVID-19 suspected patients is another important addition for the differential diagnosis.[14,15] We present the diagnosis and treatment modalities of our two cases with rhinorrhea and COVID-19 positivity, as well as a review of the relevant literature.

Case Presentation

Clinical Case-1

Sixty-seven-year-old patient complained of clear fluid discharge from the nose while tilting head down for six months, with a gradual increase later in the course. The patient was initially diagnosed and treated for allergic rhinitis, but no improvement was observed. Three months after the onset of symptoms, the patient developed a high-grade fever (100,4°-102,2°F) and a headache. In this case, suspected meningitis was ruled out, and an MRI revealed a pituitary adenoma with no neurological deficits at the time [►**Fig. 1**]. IgM and IgG antibodies for the (SARS-CoV-2) virus was found to be negative in an RNA PCR test. Chest CT revealed hyper dense opacities in the "ground glass" pattern in the bilateral lower lobes of the lungs and the 3, 4, and 5 segments of the right lung. There was no dilation in the roots of the lungs, and no fluid was found in the pleural cavity. There were no simultaneous diaphragm changes, and the mediastinum was not displaced [►**Fig. 2**]. The patient has no prior knowledge of the Covid-19 case. Leukocytes were 4.351009/l in laboratory tests, neutrophils were 72.4 percent, granulocytes were 1.1 percent, and lymphocytes

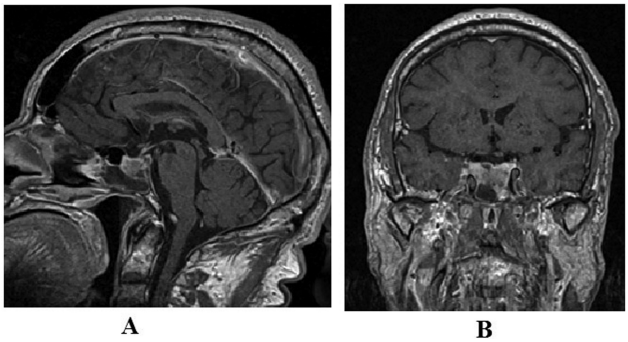

Fig. 1 Endo-infra-sellar lesion of hypophyseal gland. MRI with contrast enhancement in sagital view (A) and coronal view (B).

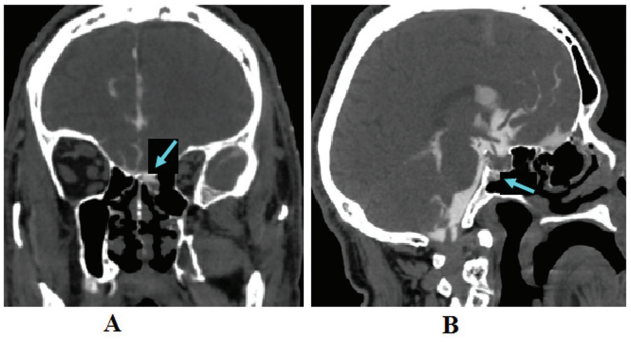

Fig. 3 CT cisternography. Show two defects at different sites of skull base; one at the bottom of Turkish saddle (B), Posterior ethmoid bone cells from the rightside (A). Defects are shown by arrows.

were 0.85109/l. SARS-CoV-2 induced pneumonia was suspected based on the pandemic spread of COVID-19 infection, decreased lymphocytic count, and ground glass opacities in chest CT. In contrast, given the chronic nature of the nasal discharge and chest, CT changes could have resulted from CSF aspiration into the lungs.

As per the protocol in a pandemic, we in our hospital do not hospitalize patients with active or suspected coronavirus infection. The patient's scheduled surgery was postponed for 10–14 days so that dynamic changes in the new chest CT could be evaluated, new swabs from the nose and throat could be administered, blood re-screened for IgG and IgM antibodies could be administered, and a decision about hospitalization and surgical treatment could be made based on the results. However, no COVID-19 RNA was detected by PCR, no IgM and IgG antibodies (ELISA) were found, and a repeat Chest CT done after 16 days revealed multiple focal infiltrative changes in the lungs but no significant dynamic shift in comparison to the previous one. According to a negative PCR for COVID-19 and negative (IgM, IgG) antibodies, chest CT changes were interpreted as a result of CSF aspiration and the resulting CSF induced aspiration Pneumonia, and the patient was admitted to the hospital for surgical repair of the defect.

A CT cisternography was also performed prior to surgery, which revealed defects at two different sites at the skull base, one in the sella floor and the second in the posterior ethmoid bone cells from the right side (►**Fig. 3**). Endoscopic transnasaltranssphenoidal adenoma resection was combined with plasty of the two CSF fistulas, one at the base of sella turcica and the other at the level of posterior ethmoid cells from the right side, using allograft and autograft materials. Pituitary adenoma resection was performed first, followed by soft tissue (fat and fascia) removal from the superolateral aspect of the thigh. The sellar cavity was filled with fat, and a piece of fascia lata was used to close the gap at the level of the posterior ethmoid cells. A free flap of mucosal pedicle with maintained circulation was used to cover and reinforce the defect, which was then fixed in place with fibrin-thrombin glue.

The postoperative period was uneventful. There were no somatic or neurological deficits revealed. There were no signs of nasal liquor rhea after the surgery, and the patient was discharged from the hospital on the ninth day. The histopathological examination confirmed the adenoma diagnosis. The inflammatory changes in the lungs were significantly improved on a repeat chest CT performed 24 days after surgery.

Clinical Case-2

A forty-year-old man presented with complaints of clear nasal discharge for the previous year. The defect was discovered during imaging at the base of the skull, near the sphenoid bone. Plasty of the skull base defect was performed

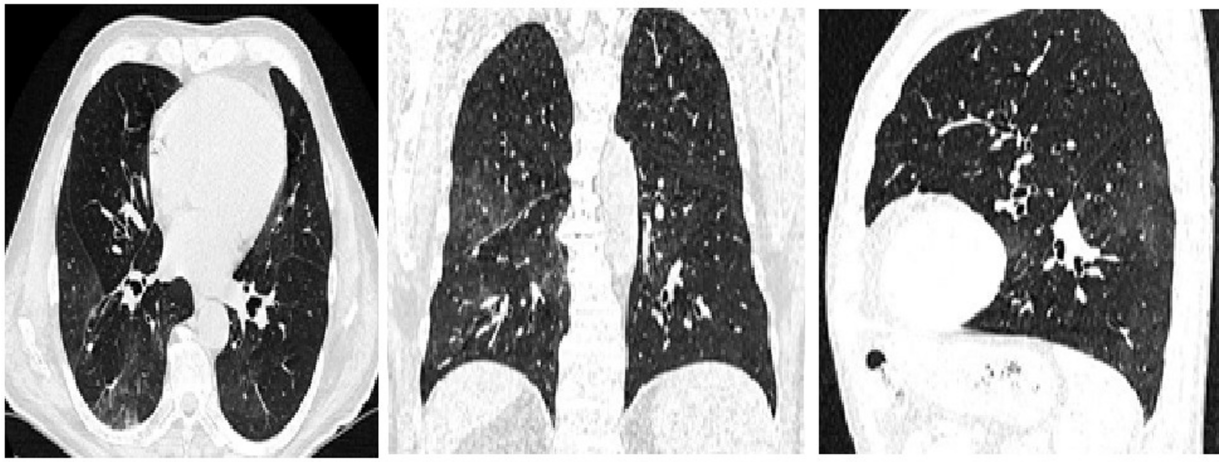

Fig. 2 CT chest prior to surgery.

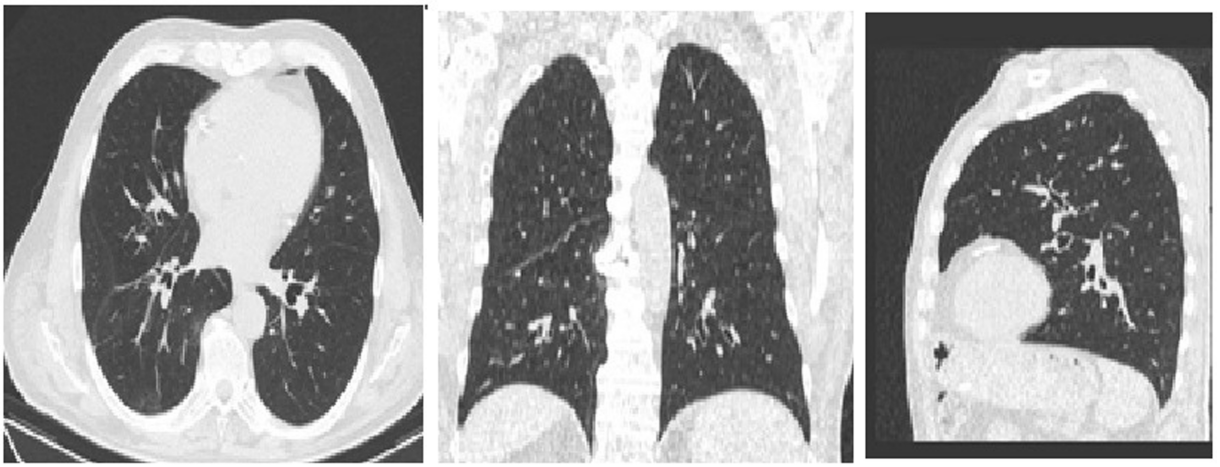

Fig. 4 CT of lungs after plasty of the skull base defects causing liquorrhea (regression of inflammatory changes).

using a transsphenoidal approach, and the patient was discharged with no postoperative leakage complaints. Nonetheless, three months later, the patient complained of nasal liquorrhea, a cough during the night, and headaches. A second defect was discovered in the sphenoid sinus's lateral pocket from the right side during a repeat examination, in addition to the meningoencephalocele (►**Fig. 5**).

In a ground-glass pattern, inflammatory changes were seen bilaterally on chest CT (►**Fig. 6**). A PCR test for SARS-CoV-2 was performed twice, and no coronavirus RNA was detected, as well as no IgM or IgG antibodies to the coronavirus. Clinical and biochemical blood tests were also normal, and there were no signs of intoxication. There was no positive history of contact with the COVID-19 patient, and no family members were also infected with SARS-CoV-2. This patient was also kept under dynamic observation for 14 days, and a repeat SARS-CoV-2 (PCR) analysis was performed, which came back negative, with no IgM/IgG antibodies detected. After a repeat chest CT revealed no dynamic changes, the patient was admitted to the hospital for a second surgical repair of the defect. The defect was plastyed using an endoscopic transnasal approach; the defect was approached via the pterygoid approach, and the meningoencephalocele was removed. The defect was filled with fat, and a large piece of fascia lata was removed from the leg; all layers of plasty were reinforced and fixed with fibrin-thrombin glue. The recovery period was uneventful. There was no nasal liquorrhea in the early postoperative period. Five days after surgery, the patient was discharged with instructions to remain under observation at the regional hospital. The radiological signs of pneumonia on a new chest CT regressed completely in the late postoperative period (one month after surgery), and no antibodies to SARS-CoV-2 were detected.

Discussion

Aspiration refers to the unintentional ingestion of oropharyngeal or gastric contents, liquids, or other hard materials into the lower respiratory tracts. The nature of the aspirated materials, microbiocenosis of the respiratory mucosa, and colonisation by pathogenic microflora all influence clinical response to aspiration.[16,17] Aspiration of CSF into the lungs is possible with severe nasal leaks, which can cause respiratory tract inflammation. Patients suffering from liquor rhea typically complain of coughing while lying in a supine position. There are only a few reports in the literature about

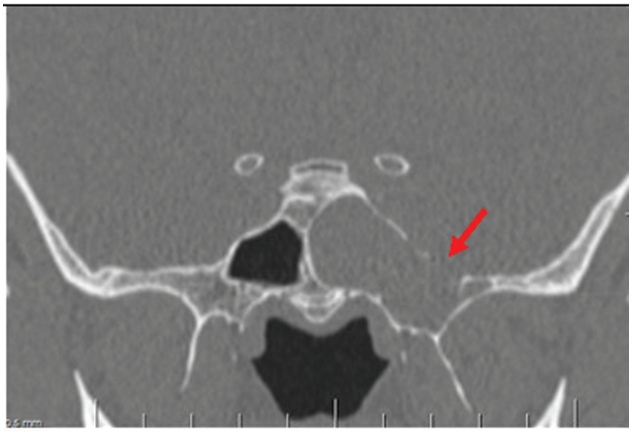

Fig. 5 Defect at the lateral pocket of sphenoid sinus in the right side (red arrow).

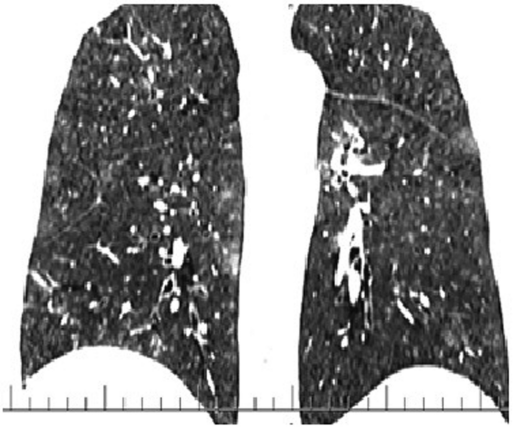

Fig. 6 CT chest of patient with nasal liquor rhea. (Ground glass appearances are present).

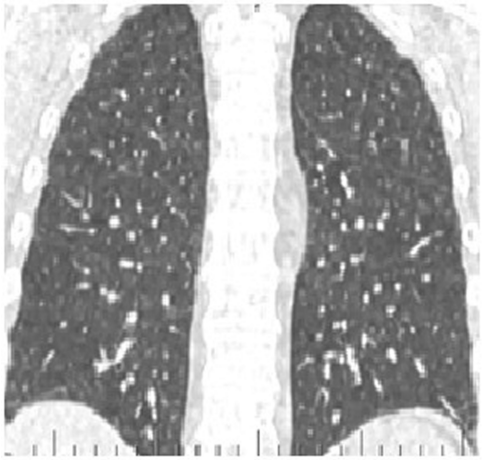

Fig. 7 CT of lungs after plasty of the skull base defect. (regression of inflammatory changes).

pneumonia as a complication of nasal liquor rhea.[18] Until Justin Seltzer et al[19] published their first article on this issue in 2016, reports on this complication were only given in series dedicated to the treatment of nasal liquor rhea. There were no reports on the clinical/diagnostic signs or treatment methods for aspiration pneumonia. It was most likely due to the fact that this complication was not considered important in clinical practice but gained significant importance during the SARS-CoV-2 pandemics.[11,20–26]

From 2016 to 2020, four articles related to aspiration pneumonia were reported in the PubMed search engine, which included nine patients with nasal liquor rhea. ►**Table 1** summarizes the findings of these patients. In the given articles, the average age of the patients was 51 years (33–76 years). Many patients (8,88.9%) were females. 7 (77.8 percent) were overweight, and 5 (55.6 percent) were obese. At the time of presentation, the most common complaints were nasal discharge, cough, and shortness of breath. In 2 (22.2 percent) of the cases, elevated body temperature and classic signs of intoxication were observed. In most cases, radiological studies of the lungs revealed ground glass opacities 7 (77.8 percent). There was no correlation found between the side of the defect and the involvement of the right or left sided lung; in many cases, involvement was bilateral (88.9 percent).

Table 1 Summeries of aspiration pneumonia cases associated with nasal liquor rhea

Authors	Gender	Age	Etiology of leakage	ИМТ	Complaints	Radiography/ CT chest	Localization of defect
[Justin Seltzer][19]	F	44	Spontaneous	36,5	Discharge from the right nostril, cough, dyspnea during physical stress, snoring	Deranged respiratory exchange in bilateral lower lobes of lungs	Roof of ethmoid sinus from the right side
[Maya Or][27]	F	76	Spontaneous	37	Discharge per right nostril, dyspnea, cough	Peri-bronchial ground glass opacities in all lobes	Roof of ethmoid sinus from the right side
[Maya Or][27]	F	51	Spontaneous	36	Discharge from right nostril, periodic cough, meningitis	Bilateral ground glass opacities, thickening of bronchial walls	Sphenoid sinus from the right
[Maya Or][27]	F	44	Spontaneous	37	Periodical discharge from right nostril, dyspnea during physical stress, snoring.	Bilateral disturbance of respiratory gas exchange in lungs (left > right)	Lamina cribrosa from the right side
[Maya Or][27]	F	54	Spontaneous	41	Discharge from left nostril, headache	Ground glass opacities in right side.	Roof of ethmoid sinus from the left side
6[Maya Or][27]	F	36	Spontaneous	31	Discharge from left nostril, cough, dyspnea, snoring	Ground glass opacities in bilateral in both upper lobes + left lowere lobe.	Roof of ethmoid sinus from the left side
[Maya Or][27]	M	64	Spontaneous	21	discharge from left nostril	ground glass appearance bilaterally, thickening of the bronchial wall, bronchiectasis	Pyramids of Temporal bone
[Mark G Jones][28]	F	33	Spontaneous	no given	Nasal discharge, cough, chest discomfort and pain in chest, raised temperature	Ground glass opacities in both lungs	Lamina Cribrosa
[Wasgewatta][29]	F	53	Spontaneous	35	Nasal discharge, cough, raised temprature.	Bilateral Ground glass opacities in lower lobes.	Lamina cribrosa from the right side

Justin Seltzer et al.[19] and Mark G Jones et al.[19] report that they were unable to exclude nasal liquorrhea as the causative agent of pneumonia at the outset. In both cases (patients 1 and 8), they receive several courses of antibiotic therapy as well as other symptomatic treatment; however, the symptoms of pneumonia recur and worsen after the antibiotics are discontinued. Following that, a lung biopsy was performed in both cases, which revealed no evidence of chronic pneumonitis or bronchiolitis. Following a joint discussion, the hypothesis of aspiration induced pneumonia was advanced, and endoscopic endonasalplasty of the skull base defect was performed in both cases after the diagnosis of nasal liquor rhea. According to the authors, after performing a control chest CT in both cases, complete resolution of pneumonia was observed in the postoperative period.

Maya O.R et al.[27] reported on six cases of pneumonia caused by nasal liquorrhea. According to the authors, they performed plasty of the skull base defect without treating pneumonia in the pre and postoperative periods. In all the cases presented, the signs of pneumonia regressed in the postoperative period following treatment of the defect closure. Sanjiwika Lalanjani Wasgewatta et al[16] described a case of spontaneous nasal liquorrhea and pneumonia during CPAP therapy for obstructive sleep apnea syndrome. Following CPAP treatment, the patient developed a cough, headache, nasal discharge, and fever. Following that, the patient underwent endoscopic endonasalplasty of the skull base defect as well as ventriculoperitoneal shunting. A week after the operation, a repeat CT of the chest was performed, and the signs of lung tissue involvement vanished. In our cases, the patients' pneumonia completely resolved after the CSF fistula was closed. During the rapid spread of COVID-19 infection, the neurosurgery center continued to provide patients with cutting-edge medical care. An algorithm was developed to reduce and prevent the nosocomial spread of infection among patients, considering epidemiological data (history of contact with patients infected with COVID-19), laboratory data (detection of SARS-CoV-2 virus RNA by PCR), and data from chest CT before hospitalization.

COVID-19 lung changes are quite variable; however, most authors agree that the most common and distinctive findings are parenchymal thickening in the form of ground glass opacities (single or multiple) or a combination of these changes with consolidation and/or reticular changes (cobblestone changes).[30] The appearance of bilateral changes in the lungs, predominantly in sub-pleural localization and in the absence of pleural effusion, is one of the most common chest CT manifestations of covid-19 pneumonia. However, the dorsal allocation of CT changes with involvement of multiple lobes of the lungs, particularly the lower ones. In our case, the patient's chest CT revealed ground glass opacities. This sign, however, is not pathognomonic; rather, it is an indicator of lung tissue thickening and an indication of interstitial type of infiltration. Certain areas of the lungs with "ground glass" opacities have a moderately reduced airiness index. The occurrence of this phenomenon is caused by thickening of the inter-alveolar septa as well as partial filling of the alveoli with inflammatory contents.[31,32] In the context of the COVID-19 pandemic, it is now necessary to perform a chest CT on all patients to look for the disease's characteristic "ground glass" opacities. Patients with profuse nasal liquor rhea pose a serious problem in terms of differential diagnosis in this scenario, as they have similar chest CT findings, which is dangerous during hospitalization of these patients in hospitals where patients with corona virus are also treated. In our opinion, dynamic observation of chest CT findings, repeated tests for IgG and IgM antibodies, and PCR for COVID-19 RNA allow us to exclude or confirm the diagnosis of COVID-19 and determine a further plan of care for such cases. In cases of nasal liquor, detection of CSF-induced aspiration pneumonia is possible by performing a chest CT scan; however, due to the current COVID-19 pandemic, PCR for coronavirus RNA is recommended in such cases, along with IgM and IgG antibodies for at least two times. If the results of both tests are negative and there are no clinical signs/symptoms of COVID-19, there are no contraindications to general anesthesia and surgery, and the patient can be hospitalized in a separate ward and plastic surgery of the skull base defect can be performed.

Conclusion

Aspiration of cerebrospinal fluid causes radiological changes in the lungs in patients with nasal liquorrhea. In such cases, radiological changes may manifest as a short-term local decrease in the airiness of lung tissue ("ground glass" opacities), representing the partial filling of the alveoli with fluids but with no clinical manifestations. In such cases, patients should have a PCR diagnostic test for SARS-CoV-2 virus RNA and antibodies (IgM, IgG) performed at least twice, as well as a CT of the chest. If there are signs of ground-glass opacity, it is recommended that the operation be postponed for 10–14 days to reassess chest CT changes and repeat the coronavirus detection test to rule out the viral nature of the lung tissue involvement.

Consent for Publication

Proper informed and written consent in local understandable language was taken from the patient regarding the publication of the same cases.

Ethics Approval

There is no ethics issue in this paper.

Data Availability Statement

The data will be available from address of correspondence on reasonable request.

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Conflicts of Interest

There are no conflicts of interest.

Acknowledgment
Nothing to Declare.

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Modified 30-Degree Head-Up Tilt Park Bench Position in Semielective Posterior Fossa Surgery in a Patient with Pheochromocytoma

Posição de banco de apoio de inclinação de cabeça para cima de 30 graus modificada em cirurgia de fossa posterior semieletiva em paciente com feocromocitoma

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Abstract

Von Hippel–Lindau (VHL) disease is a rare genetic disorder associated with the central nervous system and visceral organs. Pheochromocytomas occur in 10% of VHL patients, while cerebellar tumors are common tumors in VHL syndrome, with an incidence of 60%. The most common position for posterior fossa operations is the park bench or lateral decubitus position. These positions have primarily replaced the sitting position. However, the advantages of the supine position cannot be overlooked. The coexistence of pheochromocytoma and the cerebellar tumor may require modification in surgical position and anesthesia management in line with possible pathophysiological changes. We present the anesthesia management in posterior fossa surgery in patients with postponed pheochromocytoma surgery. The present case highlights the importance of a multidisciplinary team approach and anesthetic management.

Keywords
- von hippel–lindau
- park bench position
- pheochromocytoma
- general anesthesia

Resumo

A doença de Von Hippel-Lindau (VHL) é uma doença genética rara associada ao sistema nervoso central e órgãos viscerais. Feocromocitomas ocorrem em 10% dos pacientes com VHL, enquanto os tumores cerebelares são tumores comuns na síndrome de VHL, com incidência de 60%. A posição mais comum para operações da fossa posterior é o banco do parque ou posição de decúbito lateral. Essas posições substituíram principalmente a posição sentada. No entanto, as vantagens da posição supina não podem ser negligenciadas. A coexistência de feocromocitoma e tumor cerebelar pode exigir modificação da posição cirúrgica e manejo da anestesia de acordo com possíveis alterações fisiopatológicas. Apresentamos o manejo da anestesia na cirurgia da fossa posterior em pacientes com cirurgia de feocromocitoma adiada. O presente caso destaca a importância de uma abordagem de equipe multidisciplinar e do manejo anestésico.

Palavras-chave
- von hippel - lindau
- posição de banco de parque
- feocromocitoma
- anestesia geral

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Introduction

The park bench position is widely used in posterior fossa operations. It has replaced the sitting position for most neurosurgery procedures. However, this position has been modified since the advantages of the sitting position cannot be achieved. The modified 30-degree head-up tilt park bench position can provide the same advantages as the sitting position, and it also reduces the risk of venous air embolism and hypotension.[1–4] Von Hippel–Lindau (VHL) disease is a rare genetic disorder associated with cerebellar tumor and pheochromocytoma. Catecholamine discharges in the pheochromocytoma can lead to dangerous cardiovascular consequences and produce raised intracranial pressure (ICP).[1,5] We present the anesthesia management in a woman with pheochromocytoma for the excision of a cerebellar hemangioblastoma due to neurological symptoms.

Case

A 57-year-old female was admitted with complaints of hypertensive attack and vomiting. She was diagnosed with VHL disease. Neurological worsening and disorientation developed. A right cerebellar hypermetabolic mass measuring 19×21 mm was seen on positron emission tomography (PET) (►**Fig. 1**). Single-photon emission computed tomography (SPECT) images revealed an adrenal nodule consistent with pheochromocytoma. Adrenalectomy was postponed, and it was decided to perform posterior fossa surgery first. The patient had hypertension for 10 years. She had undergone Coronary artery bypass graft surgery 6 years before. Esmolol, phentolamine, doxazosin and methyldopa were started for blood pressure control. Written informed consent was obtained from the patient for the present study. The patient was monitored with electrocardiograms (leads II, V1), peripheral SpO_2, cutaneous temperature, Patient State Index (PSI), invasive blood pressure (BP) assessments (right radial artery), and central venous pressure (right subclavian catheter) in the operating room. Her heart rate (HR) was 100 beats/minute, her BP was 70/98 mmHg, and her body temperature was 36.6° C. Anesthesia was induced with fentanyl 1 µg/kg, propofol 2.5 mg/kg, and rocuronium 0.6 mg/kg, and the patient was intubated. Maintenance of anaesthesia was achieved with sevoflurane/oxygen/air, combined with a remifentanil 0.25–0.5 mcg/kg/minute infusion. The PSI value remained between 25 and 50. After the intubation in the supine position, the patient was turned into the park bench position. Description of the modified park bench position: The head of the operating table and the thorax were elevated $\sim$ 30 ° to be higher than the feet. The head was fixed with a three-pin head holder. During this time, the head was kept coaxial with the thorax without any lateral flexion, but the lateral side of the craniotomy was rotated and slightly bent forward as in the semisitting position (►**Fig. 2**).[2] No hemodynamic problems occurred during the positioning. The BP of the patient shot up to 185/105 mmHg. Esmolol infusion was used for BP control. Hemodynamics were stable during surgery, with a maximum drop in BP to 100/70 mmHg. After surgery, the patient was sent to the intensive care unit (ICU), where she was extubated within 4 hours. Neurological impairment was not observed. One day later, the patient was sent to the neurosurgery clinic with an excellent general condition.

Discussion

Pheochromocytoma is observed in between 10 and 20% of cases of VHL disease, but the incidence of cerebellar tumor is of 60%. The association of a pheochromocytoma with

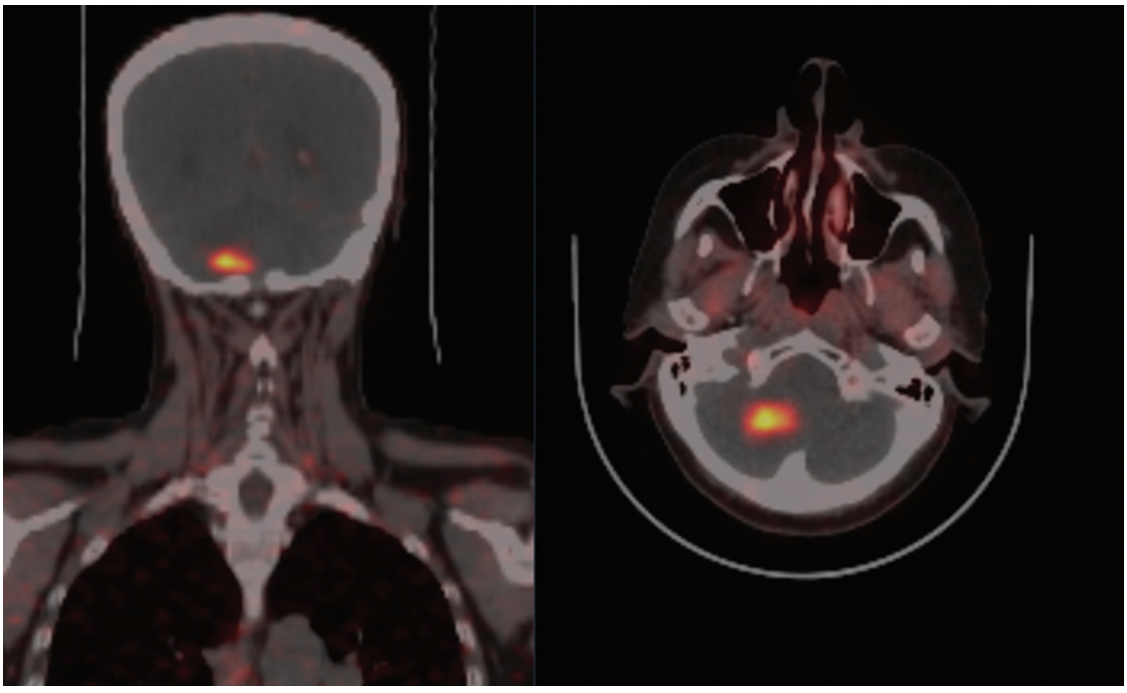

Fig. 1 A right cerebellar hypermetabolic mass measuring 19×21 mm on PET/CT.

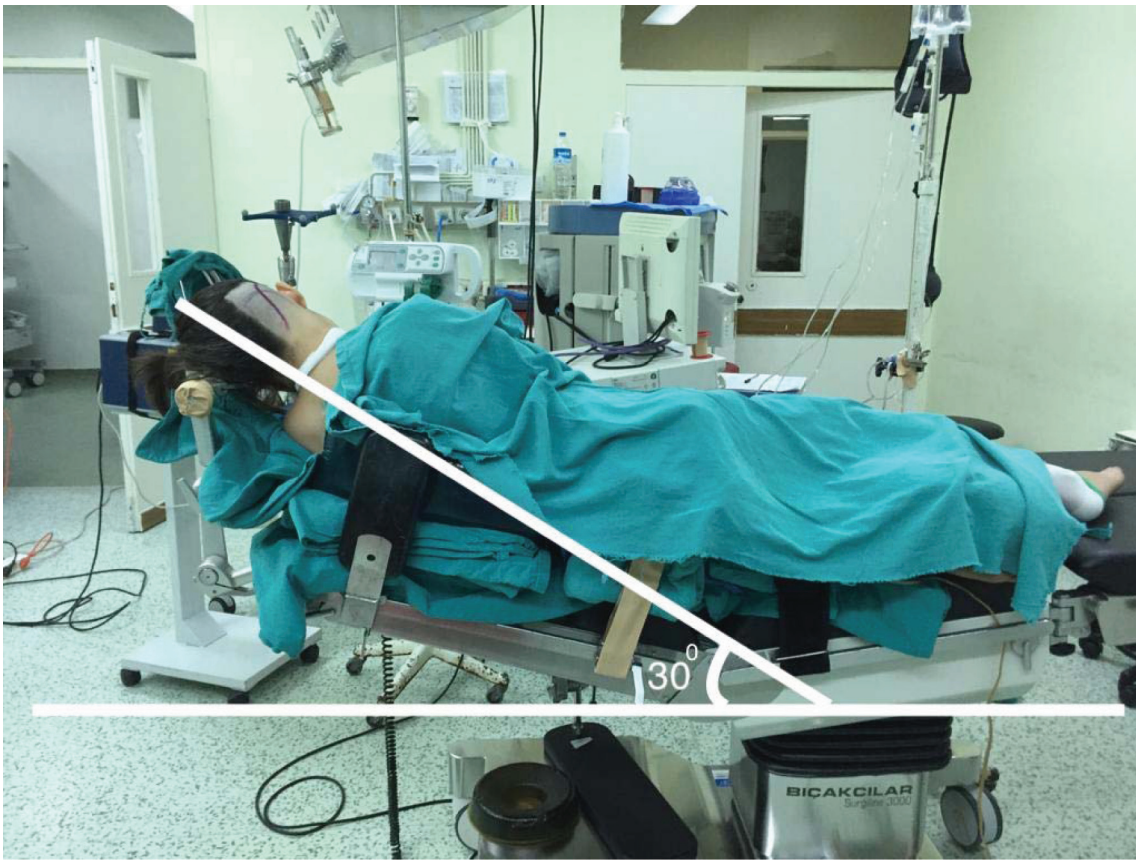

Fig. 2 Modified 30-degree head-up tilt park bench position.

cerebellar mass further increases the complications rate. The release of excessive amounts of catecholamines, especially during anesthesia induction or during surgery, can cause life-threatening cardiovascular complications and cause raised ICP.[1,5,6]

Anesthesia management is challenging in patients with pheochromocytoma. The catecholamine storm can raise ICP and result in lethal complications. In the perioperative period, cardiac complications such as severe hypertensive attacks and arrhythmias may occur. Thiopental can cause histamine release, which needs to be avoided in pheochromocytoma. Propofol is preferred because it causes vasodilation and reduces the hypertensive response to laryngoscopy and intubation. Sevoflurane can be used as an inhalation agent as it provides cardiac stability. Vecuronium, rocuronium, and cisatracurium can be used as muscle relaxant agents since they do not release histamine.[7,8] In our case, providing anesthesia depth with brain function monitoring facilitated hemodynamic stabilization.

Besides the anesthetic agents, the position of the patient used in the operation can help preventing complications and serious adverse events. Although each position applied in posterior fossa operations has its advantages and disadvantages, the surgeon should choose the most suitable for the patient and the pathology. The sitting position for posterior fossa surgery modified to the semisitting or "beach chair" position keeps most of its advantages and allows a rapid trendelenburg in the case of air embolism.[3] The classical sitting position causes postural hypotension in $\sim$ ⅓ of the patients, and severe hypotension occurs in between 2 and 5% of the patients.[3,4] The hypotension effect of the sitting position may be an advantage for high BP in pheochromocytoma. Excellent surgical exposure, drier area, less blood loss, and reduced facial swelling are the advantages of the sitting position. However, we cannot ignore venous air embolism and the increased risk of pneumocephalus.[3] In addition, the prone and sitting positions can increase abdominal compression, causing catecholamine surge. Mugawar et al.[9] preferred the prone position in a cerebellar mass excision in a patient who had bilateral pheochromocytoma and detected VHL because the hemodynamic reactions caused by the sitting position during surgery might not be tolerated by the patient. They were careful to avoid any excessive pressure over the abdomen, as there might be excessive endocrine discharges from the adrenal glands due to abdominal compression in the prone position. Another case performed in a similar position is that described by Tempelhoff et al.[10] They reported anesthetic management of a patient with multiple posterior fossa tumors and pheochromocytoma. After the induction of anesthesia, the patient had a cardiac arrest after an attempt at pulmonary artery catheterization. After successful cardiopulmonary resuscitation, surgery was performed on the following day in the prone position. When the advantages and disadvantages were evaluated, the modified park bench position was considered suitable for our patient. This position allows a neural and vascular

manipulation and control of the cerebellopontine angle. In addition, it may result in a decrease in the posterior fossa pressure.[2] Wajekar et al.[1] reported that they had performed posterior fossa surgery in the sitting position in a patient with pheochromocytoma. Hemodynamic stabilization in the sitting position was achieved by central venous pressure (CVP) monitoring. We preferred a modified park bench position in our patient due to cardiac instability.

Conclusion

The management of anesthesia in the modified park bench position can be safer than other positions, especially in posterior fossa surgery in patients with postponed adrenalectomy and cardiac instability. Careful monitoring and titration of anesthesia are essential in providing a successful outcome at such high-risk patients.

Main Points

- The coexistence of pheochromocytoma and a cerebellar tumor may require a modification in the surgical position in line with possible pathophysiological changes.
- The modified 30-degree head-up tilt park bench position can provide the same advantages as the sitting position, and it also reduces the risk of venous air embolism and of hypotension
- The modified park bench position may be safe in posterior fossa surgery in patients with postponed adrenalectomy and cardiac instability.

Informed Consent

Written informed consent was obtained from the patient who participated in the present study.

Financial Disclosure

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Conflict of Interests

The authors have no conflict of interests to declare.

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Rare Presentation of *Morganella morganii* Microorganism as Epidural and Subdural Empyema

Apresentação rara de Morganella morganii Microrganismo como Empiema Epidural e Subdural

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Abstract

Background *Morganella morganii* is a gram-negative bacterium that rarely infects the central nervous system (CNS). Few reports described such an infection in the CNS. We present a case of extremely invasive *M. morganii* infection in the CNS. In addition, we performed a literature review of *M. morganii* infection in the CNS.

Case report A 53-year-old male was admitted to the hospital due to fever, general weakness, and left-sided facial muscle twitching. He had a history of diabetes mellitus, hypertension, brain tumor, and epilepsy. Multiple left frontal scalp ulcers were revealed. In addition, a computed tomography (CT) scan and magnetic resonance imaging (MRI) revealed a left side epidural abscess and subdural empyema. Moreover, the patient had left frontal bone osteomyelitis. The next day, the patient underwent craniectomy, was transferred to the intensive care unit and started an empirical antibiotic course. *Morganella morganii* was identified from the infected scalp ulcers. On the 13th day, the patient passed away due to uncontrolled status epilepticus.

Conclusion *M. morganii* can cause isolated or multiple types of CNS infections, including brain abscess, meningitis, and subdural empyema. The mortality rate may differ according to age and to the use of surgical evacuation.

Keywords
- subdural empyema
- morganella morganii
- brain infection
- scalp ulcer

Resumo

Introdução Morganella morganii é uma bactéria gram-negativa que raramente infecta o sistema nervoso central (SNC). Poucos relatos descreveram tal infecção no SNC. Apresentamos um caso de infecção extremamente invasiva por M. morganii no SNC. Além disso, realizamos uma revisão da literatura sobre a infecção por M. morganii no SNC.

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Relato de caso Um homem de 53 anos foi admitido no hospital devido a febre, fraqueza geral e espasmos da musculatura facial do lado esquerdo. Ele tinha história de diabetes mellitus, hipertensão, tumor cerebral e epilepsia. Múltiplas úlceras no couro cabeludo frontal esquerdo foram reveladas. Além disso, uma tomografia computadorizada (TC) e uma ressonância magnética (RM) revelaram um abscesso epidural do lado esquerdo e empiema subdural. Além disso, o paciente apresentava osteomielite do osso frontal esquerdo. No dia seguinte, o paciente foi submetido à craniectomia, foi transferido para a unidade de terapia intensiva e iniciou curso empírico de antibiótico. Morganella morganii foi identificada a partir das úlceras do couro cabeludo infectadas. No 13° dia, o paciente faleceu devido a estado de mal epiléptico não controlado.

Conclusão M. morganii pode causar tipos isolados ou múltiplos de infecções do SNC, incluindo abscesso cerebral, meningite e empiema subdural. A taxa de mortalidade pode diferir de acordo com a idade e com o uso da evacuação cirúrgica.

Palavras-chave
- Empiema Subdural
- Morganella morganii
- Infecção cerebral
- Úlcera do couro cabeludo

Introduction

Morganella morganii is a gram-negative aerobic bacilli that belongs to the Enterobacteriaceae family and is part of the normal gut microbiota.[1–3] *Morganella morganii* infection can cause urinary tract infection, blood sepsis, soft tissue, wound, and hepatobiliary tract infection.[1,2] Central nervous system (CNS) infection with *M. morganii* is rarely encountered and reported in the literature, including brain abscess, meningitis, and subdural empyema.[3] In the present case report, we present a case of aggressive *M. morganii* CNS infection using case report (CARE) guidelines.[4] Moreover, we performed a literature review by searching for articles related to CNS infection by *M. morganii* in the PubMed and Scopus databases.

Case Presentation

A 53-year-old male patient with multiple comorbidities, including diabetes mellitus and hypertension, was admitted to our hospital as an emergency case of a 1-week history of intermittent fever, general weakness, and left-sided facial muscle twitching. He had a history of left side temporoparietal brain tumor excision (astrocytoma) 20 years ago. He was found to be neglected by the family as all his relatives live far away from him. Besides, he had been diagnosed with right side acute subdural hematoma (SDH) and was treated surgically 8 months before, and he had been diagnosed with epilepsy 8 years before, which was managed with phenytoin as a single antiepileptic medication. Physical examination revealed high-grade fever (38.3 C°) and other vital signs were within normal ranges. Multiple left frontal scalp ulcers and necrosis were detected (►**Figure 1**). The patient's Glasgow coma scale was 11 as he could open his eyes spontaneously (4), as well as producing sounds when in pain (2) and flexion to pain (5). Pupils were normal sized and reactive to light. Power examinations showed right-side weakness. Blood laboratory exams showed elevation in white blood cell (WBC) count (13.4 $^{*} \times 10^{9}$/L), mainly neutrophils (81%), C-reactive protein (140 mg/L), erythrocyte sedimentation rate (ESR) (62 mm/hr). Other lab results were within normal ranges. Both CT scan and MRI images revealed left side epidural abscess, subdural empyema, cerebral atrophy, and cerebritis in the frontal area (►**Figure 2**). The patient was prepared for surgery and, on the next day, he underwent left decompressive craniectomy surgery and evacuation of the epidural abscess, the subdural empyema, and the infected part of the skull. The artificial dura of the previous tumor excision was also removed. Pus biopsy was taken and sent to the microbiology lab.

MacConkey agar or blood agar were used for bacteria while sabouraud dextrose agar was used to detect any fungal growth. Although no growth was detected from the pus culture, the scalp ulcer culture was positive for *M. morganii*. The antibiotic susceptibility test showed resistance against fluoroquinolones, cefixime, and ampicillin with sulbactam. On the other hand, it was sensitive to aminoglycosides and other cephalosporins. The patient was kept on phenytoin for seizure control and treated with vancomycin, ceftriaxone, and metronidazole at the initial period, then the antibiotics regimen changed to gentamicin and ceftriaxone IV according to the susceptibility to antibiotics.

The patient was observed in the intensive care unit for 13 days, then he passed away due to uncontrolled status epilepticus.

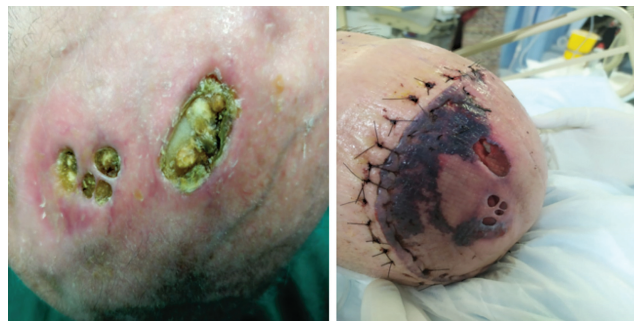

Fig. 1 Patient scalp before surgery (left) and after surgery (right). We see evidence of multiple necrotic infected areas on the scalp with redness around them, which indicated signs of active infection.

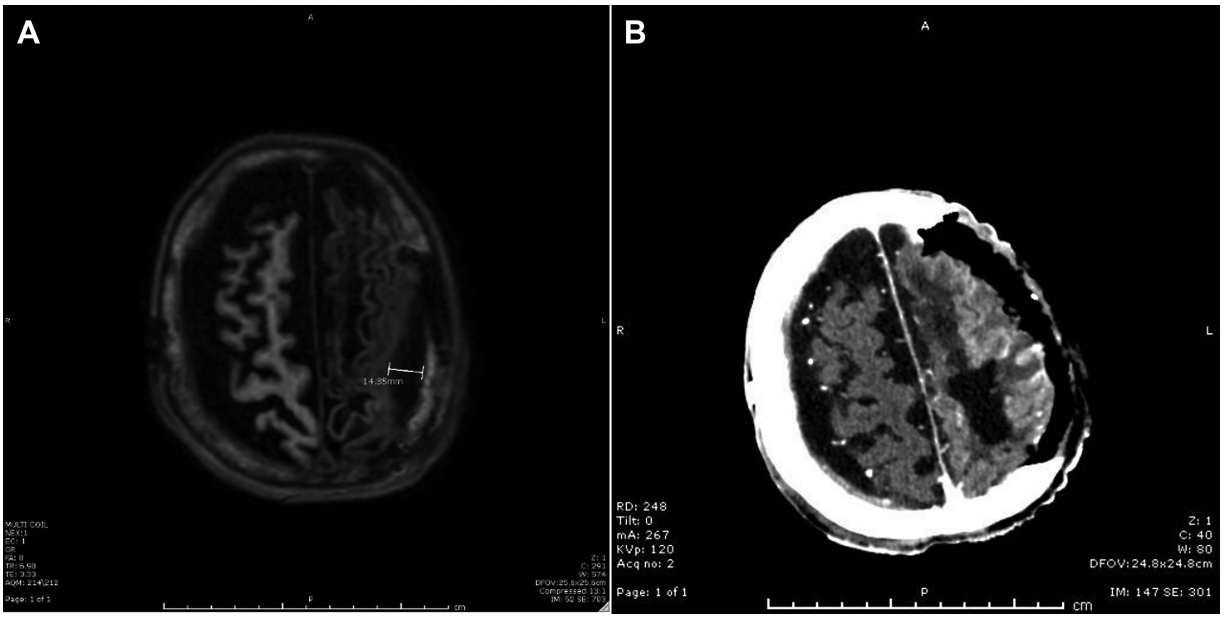

Fig. 2A Brain axial view T1 magnetic resonance imaging with IV contrast showing left frontal epidural and subdural empyema measuring about 1.4 cm in it maximum thickness, associated with a hypodense area involving the underlying left frontal lobe suggesting for encephalitis, the left frontal lobe appears edematous with effacement of the sulci and leptomeningeal enhancement. **Fig. 2B** Brain computed tomography scan with IV contrast showing interval resolution of the previously noted left frontal convexity empyema with a large area of pneumocephalus at its site. The left frontal lobe appears edematous with effacement of the sulci and leptomeningeal enhancement, suggesting for encephalitis.

Discussion

Morganella morganii is a rare causative agent of intracranial infections. Previous studies have reported brain abscesses, meningitis, and subdural empyema with this infection.[5,6] In the present case report, we reported the first case of extremely invasive *M. morganii* CNS infection involving the scalp, the skull, and the epidural and subdural spaces.

Risk factors and the source of the infection in the brain are unclear due to the scarcity of cases reported in the literature. However, iatrogenic, otogenic, wound infections, and urinary tract infection (UTI) as possible sources of infection have been reported previously.[1,2,5] In our case, tumor excision surgery was performed on the same side of the infection but was performed 20 years ago which was an unusual risk factor.

In the previously reported studies, the age of the patients ranged from 1 day to 78 years old (►**Tables 1** and **2**). There were more male cases than female cases (nine male cases, seven female cases, and one unreported case). The mortality rate of the reported studies in the literature, including our case, was 27.8%. The most common presentation was meningitis, with 10 cases; 5 cases were isolated meningitis,[7–11] 2 were combined with brain abscesses,[3,12] 1 was combined with subdural empyema,[13] 1 was combined with encephalitis,[14] and 1 was combined with sepsis.[15] The second most common presentation was brain abscess, with seven cases; five cases were isolated brain abscesses,[5,16–18] two cases were combined with meningitis,[3,12] and one case was combined with subdural empyema.[19] Eight cases were < 2 years old (►**Table 1**). A total of 47% of the cases were infants with a history of trauma,[6,13] preterm infants,[15] born from mothers with chorioamnionitis,[11] and delivered by vacuum-assisted vaginal delivery.[20] No significant prior history or possible risk factors were identified in the remaining infant cases.[9,17,18] Surprisingly, none of the infants had died.

In the cohort of patients > 2 years old (►**Table 2**), the mortality rate was high, reaching 50%. Three patients had a history of chronic suppurative otitis media. Brain abscess and meningitis have been previously reported as possible intracranial complications of chronic suppurative otitis media.[21]

Only three cases described osteomyelitis caused by *M. morganii*.[20,22,23] Staudt et al. reported a case of skull osteomyelitis and infected cephalohematoma with *M. morganii* in a 1-day old infant.[20] Our case is the second case of skull osteomyelitis and the fourth case of osteomyelitis in general. Subdural empyema can be caused by a superimposed infection of a previous SDH.[6] The identification of *M. morganii* is based on culturing the biopsy on MacConkey agar or blood agar.[3] In our case, both were negative for the aspirated pus but positive for the superficial scalp lesions. The rate of negative pus culture from subdural empyema is reported to range from 7 to 53%.[24] In our case, possible sources of such a rare pathogen might be iatrogenic from the previous burr-hole drainage to clear the SDH, but the infection was in the contralateral side from the intracranial potential space created from his previous tumor excision,[25] which was performed 20 years before.

Morganella morganii also contains an inducible ampC β -lactamase gene, making it resistant to penicillin and to first- and second-generation cephalosporins.[26] In addition, overproduction of ampC β -lactamase by the loss of *ampD* gene expression can cause treatment failure with third-

Table 1 Reported cases of patients younger than 2 years old

Name	Age (gender)	Description of the infection	Treatment	Outcome	Notes
Bond et al., 2020[6]	13 months old (female)	Subdural empyema	Meropenem and surgical evacuation	Recovery	First case of sterile empyema
Milligan et al., 2013[9]	3 weeks old (female)	Meningitis	Cefotaxime and gentamicin	Recovery	
Park et al., 2004[13]	7 months old (male)	Meningitis and subdural empyema	Ceftriaxone, metronidazole and surgical evacuation	Recovery	History of meningitis
Paul et al., 2020[15]	32 + 5 gestational weeks (male)	Meningitis and sepsis	Meropenem and gentamicin	Recovery	Preterm infant due to fetal distress
Sinha et al., 2006[11]	6 days old (female)	Meningitis	Cefotaxime, gentamicin, and meropenem	Recovery	Mother had chorioamnionitis before the delivery
Staudt et al., 2016[20]	1 day old (male)	Cephalohematoma and osteomyelitis	Vancomycin, meropenem and surgical evacuation	Recovery	Delivered via vacuum extraction
Thomas et al., 2007[17]	2 months old (male)	Brain abscess	Unspecified antibiotics and surgical evacuation	Discharged	Patient discharged on oral chloramphenicol with no follow-up
Verboon-Maciolek et al., 1995[18]	8 days old (male)	Brain abscess	Cefotaxime, gentamicin, and surgical evacuation	Recovery	Cultures of pus aspirated from the abscess were sterile

Table 2 Reported cases of patients older than 2 years old

Name	Age (gender)	Description of the infection	Treatment	Outcome	Notes
Abdalla et al., 2006[5]	38 years old (female)	Brain abscess	Cefepime and surgical evacuation	Death	History of craniotomy due to a motor vehicle accident
Águeda et al., 2013[19]	9 years old (male)	Brain abscess and subdural empyema	Ceftriaxone, vancomycin, ceftriaxone, and surgical evacuation	Recovery	History of chronic suppurative otitis media
Isaacs et al., 1987[7]	78 years old (female)	Meningitis	Pefloxacin mesylate	Death	The reason of death was coronary heart disease
Lu et al.,1999[12]	55 years old (female)	Brain abscess and meningitis	Imipenem/ cilastatin and surgical evacuation	Recovery	The patient underwent caniotomy, then developed the infection
Mastroianni et al., 1994[8]	45 years old (male)	Meningitis	Netilmicin and ceftriaxone	Death	History of AIDS
Ndiaye et al., 2010[14]	12 years old (male)	Meningoencephalitis	Cefotaxime and gentamicin	Recovery	History of chronic otitis media
Patil et al., 2010[3]	12 years old (male)	Brain abscess and meningitis	Amikacin, ceftriaxone, and metronidazole	Recovery	History of chronic suppurative otitis media
Rau et al., 2002[16]	Not reported (not reported)	Brain abscess	Third-generation cephalosporins and surgical evacuation	Recovery	
Samonis et al., 2001[10]	25 years old (female)	Meningitis	Cefotaxime and amikacin	Death	
Present study	53 Years old (male)	Skin, skull, encephalitis, epidural abscess, and subdural empyema	Gentamicin, ceftriaxone, and surgical evacuation	Death	History of hypertension, diabetes, epilepsy, and brain tumor treated with craniotomy

generation cephalosporins.[26] In our case, the antibiotic susceptibility test showed resistance to cefixime, a third-generation cephalosporin. This was also noted by Sinha et al., who described a case of cefotaxime-resistant *M. morganii* during treatment due to overexpression of ampC β -lactamase.[11] Thus, the use of third-generation cephalosporins should be monitored continuously even if the bacterium showed an initial susceptibility and response. Third-generation cephalosporins, meropenem, and gentamicin were the most used antibiotics in the literature (►**Tables 1** and **2**). In most cases, surgical evacuation by burr-hole drainage or craniotomy was performed. In our case, the patient underwent craniectomy due to the presence of osteomyelitis. The mortality rate when the surgical evacuation was performed was 20%, compared with 37.5% when the surgical evacuation was not performed. Therefore, surgical management with the administration of the appropriate antibiotics is needed to increase the chances of survival.

Conclusion

In the present case report, we reported a very rare case of *M. morganii* infection in an adult patient that involved the scalp, the skull, and the epidural and subdural spaces with unusual presentation and unknown risk factors. Clinical presentation and mortality rate may differ according to age. The use of surgical evacuation resulted in a decreased mortality rate.

Ethics Approval and Consent to Participate

Written informed consent was obtained from the patient for publication of the case report and any related images.

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Conflict of Interests

The authors have no conflict of interests to declare.

Contribution of the Authors

Daoud S. S.: Supervision and critical review of the manuscript.

Jarrar S.: Supervision and literature review.

Ababneh O. E.: Writing of the manuscript, data collection, and review.

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Is There a Genetic Relationship between Acute Lymphoblastic Leukemia and Meningioma? A Case Report of the Analyses of Three Genes

Há alguma relação genética entre leucemia linfoblástica aguda e meningioma? Relato de caso das análises de três genes

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Abstract

Meningiomas are the most common tumors of the central nervous system, and they are generally slow growing and benign. Acute lymphoblastic leukemia (ALL) is a life-threatening ltype of cancer that involves the accumulation of peripheral blood vessels and immature cells in the bone marrow. Genetic mutations play an important role in the etiology of both diseases. Therefore, in the case herein presented, we investigated the *meningioma 1* (*MN1*), *nucleophosmin 1* (*NPM1*), and *Wilms tumor 1* (*WT1*) genes for possible genetic mutations. A 27-year-old female with a chief complaint of headache and history of lllALL presented with a mass in the left frontal lobe. The pathological analysis revealed a fibroblastic meningioma. However, the three genes were found to be normal in the analysis. In light of these findings, we did not encounter any evidence of a genetic relationship between meningioma and ALL in the present study.

Keywords
- acute lymphoblastic leukemia
- meningioma
- MN1
- NPM1
- WT1

Resumo

Os meningiomas são os tumores mais comuns do sistema nervoso central e geralmente apresentam crescimento lento e são benignos. A leucemia linfoblástica aguda (LLA) é um tipo de câncer com risco de vida que envolve o acúmulo de vasos sanguíneos periféricos e células imaturas na medula óssea. As mutações genéticas desempenham um papel importante na etiologia de ambas as doenças. Portanto, no caso aqui apresentado, investigamos os genes do meningioma 1 (MN1), nucleofosmina 1 (NPM1) e tumor de Wilms 1 (WT1) para possíveis mutações genéticas. Uma mulher de 27 anos com queixa principal de cefaleia e história de LLL apresentou uma massa no lobo frontal esquerdo. A análise anatomopatológica revelou um meningioma fibroblástico. No entanto, os três genes foram considerados normais na análise. À luz desses achados, não encontramos nenhuma evidência de relação genética entre meningioma e LLA no presente estudo.

Palavras-chave
- linfoblástico agudo leucemia
- MN1
- NPM1
- WT1

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Introduction

Meningiomas are widespread primary central nervous system tumors originating from the arachnoid cap cells. The growth rate of meningiomas is usually considered slow that associated with low mortality and high morbidity. Genetic mutations have been reported to play a role in the development of meningiomas.[1]

Acute lymphoblastic leukemia (ALL) is a life-threatening malignant tumor involving the accumulation of lymphoblast cells in hematopoietic tissues such as the bone marrow, the spleen, the peripheral blood, and the lymph nodes.[2] LLIt is the most common type of acute leukemia in pediatric patients, accounting for $\sim$ 25% of childhood malignancies. In addition, ALL is responsible for 20% of adult acute leukemia.[2] LLThe etiology of ALL probably environmental, socioeconomic, infectious, and genetic factors are currently under investigation.

The *meningioma 1* (*MN1*) gene is a transcriptional coactivator encoding a 136 kDa protein located in the 22q12 chromosome.[3] The *MN1* gene was first identified as part of a translocation in meningiomas.[4] Overexpression of this gene is related to poor prognosis, poor treatment response, and short survival. Further, it has been reported that *MN1* overexpression plays an important role in acute myeloblastic leukemia (AML), and is associated with poor clinical outcomes in normal-karyotype AML.[5]

The *Wilms tumor 1* (*WT1*) gene encodes a C2H2-type zinc finger transcription factor located in the 11p13 chromosome, and is known to present distinct isoforms in mammals.[6] Further, it is involved in processes such as transcriptional regulation, RNA metabolism, and participation in protein–protein interactions.[6] The *WT1* gene was first described in AML overexpression, a childhood malignancy.[3] Although *WT1* is not associated with a specific leukemic disease, many studies have reported that this gene may be a sensitive parameter in the onset or reappearance of the disease.[7] In adults, *WT1* overexpression leads to lung, brain and breast cancers.[7]

The *nucleophosmin 1* (*NPM1*) gene is located in chromosome 5q35. It is composed of 12 exons and a histone chaperone that can bind to broad H3–H4 tetramers and can constitute nucleosomes in chromatins.[8] The associated proteins bind to histones and transfer them to the naked DNA.[8] Overexpression of the *NPM1* gene results in high mitotic index and proliferation. This can lead to solid organ tumors like oral, prostate, ovary, colon, and bladder cancers.

Several studies have reported on the *MN1*, *NPM1*, and *WT1* genes. Associations between *MN1* gene mutations and AML have been frequently investigated, and there are studies that report poor prognosis.[9] The relationship of the *MN1* gene with meningiomas has also been reported.[4] However, in the literature, we could not find any studies reporting a relationship between the *MN1*, *NPM1*, and *WT1* genes and ALL; no association between meningiomas and ALL has been identified.

We examined a young female with a history of ALL who underwent surgery for a convexity meningioma at our clinic. We investigated the possible gene mutations, such as those in the *MN1*, *WT1*, and *NPM1* genes, to determine whether there is an association between ALL and meningiomas.

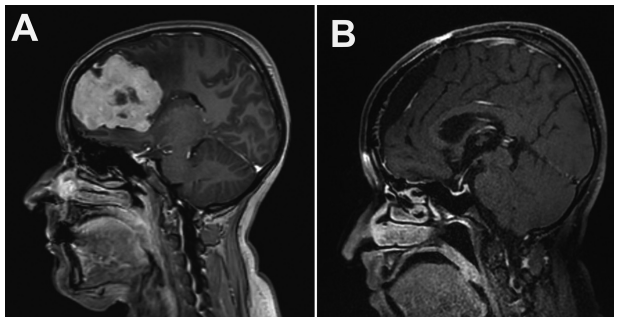

Fig. 1 Contrast-enhanced cranial magnetic resonance imaging identified a 66cm2 calcified mass in the left frontal lobe (**A**). When the patient's history was examined, it was found that B-cell common ALL (CALLAB) had been diagnosed and treated 10 years prior to presentation. The intraoperative mass was totally resected, and there were no complications. Remarkably, the patient's headache and visual complaints improved, and no recurrence was observed during the follow-up visit 1 year postoperatively (**B**).

Case Report

A 27-year-old female presented to our clinic with headache and blurred vision. No motor and sensory deficits were detected on the physical examination. Further, the cranial nerves were intact. Contrast-enhanced cranial magnetic resonance imaging identified a $6 \times 6\,cm^2$ calcified mass in the left frontal lobe (►**Fig. 1 A**). When the patient's history was examined, it was found that B-cell common ALL (CALLA-B) had been diagnosed and treated 10 years prior to presentation. The intraoperative mass was totally resected, and there were no complications. Remarkably, the patient's headache and visual complaints improved, and no recurrence was observed during the follow-up visit 1 year postoperatively (►**Fig. 1 B**). The pathology report was interpreted as fibroblastic meningioma (Grade 1). The patient had not received radiotherapy before, and intrathecal medication was not administered.

An *MN1* gene mutation has been detected in meningioma and AML. However, there are insufficient articles in the literature about common gene mutations that coexist in meningiomas and ALL. A peripheral blood sample and paraffin block preparation were transferred to the gene analysis laboratory to investigate the *MN1*, *WT1*, and *NPM1* genes.

Analysis of the DNA Sequence l

Genomic DNA was isolated from the paraffin block with the use of the QIAamp DNA FFPE Tissue Kit (Qiagen inc., Hilden, Germany), and from the peripheral blood sample with the QIAamp DNA Blood Mini Kit (Qiagen, Inc.), according to the manufacturer's instructions. The DNA isolates are stored at −20°C until the polymerase chain reaction (PCR) step. The primers were designed for the coding and exon–intron junction regions of the three genes: *WT1* (NM_024426, ENST00000452863), *MN1* (NM_002430, ENST00000302326), and *NPM1* (NM_002520, ENST00000296930). In total, 10 pairs of PCR primers were designed to amplify 10 coding exons of the *WT1* gene, 3 pairs, to amplify 2 coding exons of the *MN1* gene, and 8 pairs, to amplify 11 coding exons of the *NPM1* gene. The PCRs were performed on isolated DNA samples using the

designed primers and the MyTaq Mix (lMeridian Biosciences, Cincinnati, OH, US) according to the manufacturer's instructions. The reactions were examined using 2% agarose gel electrophoresis. The PCR products from the same sample were combined to obtain PCR pools, and they were purified with the NucleoFast 96 PCR kit, (Macherey-Nagel GmbH & Co., Dueren, Germany). The purified PCR pools were quantified with the ND1000 microvolume spectrophotometer (Thermo Fisher Scientific, Inc., Waltham, MA, US), and standardized to 0.2 ng/ul, which was needed for sample preparation. The samples were prepared for next-generation sequencing with the NexteraXT l(illumina, Inc., San Diego, CA, US) sample preparation kit, and they were subsequently sequenced with the Miseq system (illumina, Inc.). The data were visualized and analyzed with the IGV 2.3 software (Broad institute, Cambridge, MA, US), to search for possible pathogenic mutations.

As a result of these DNA analyses, no clinically important mutations of the *MN1*, *WT1* and *NPM1* genes were detected.

Discussion

Meningiomas are the most common benign intracranial lesion. Although the etiology of meningiomas remains unclear, various proto-oncogenes and tumor-suppressor genes have been reported to play a role.[1]

The subtypes of ALL may differ in terms of biological, cellular, and molecular characteristics, treatment response, and risk of relapse, and they usually present different outcomes.[10] B-cell precursor ALL (BCP-ALL) is a disease characterized by the proliferation of the blast forms of immature B cells in the bone marrow and/or peripheral bone, which can be caused by some known molecular changes.[11] Reportedly, the Epstein–Barr virus and human immunodeficiency virus (HIV) type 1 are closely related to the underlying infectious agents in the etiology of BCP-ALL.[12] Our patient, who was diagnosed with BCP-ALL, had no history of infection.

Although the mechanism of action of the *MN1* gene and its contribution to leukemogenesis are not completely known, its overexpression has been reported to cause myeloid malignancies.[5] The *MN1* gene mutation has also been reported in meningiomas.

It is unclear how the *WT1* gene contributes to malignant transformation in adults.[6] However, it is known that the gene plays a role in processes such as apoptosis, proliferation, differentiation, and mRNA processing in the genitourinary system, sensory system, and heart cells in the wide embryological process.

The *NPM1* gene plays an important role in RNA transport, ribosome biogenesis, regulation of apoptosis, and genomic hemostasis in large cells.[13] Its mutation or fusion is predominantly observed in acute myeloid leukemia, and it is present in $\sim$ 30% of the patients. Overexpression of the *NPM1* gene is associated with poor prognosis and malignancies such as glioblastoma multiforme, oral squamous cell carcinoma, colon cancer, non-small cell lung cancer, hepatocellular carcinoma, ovarian cancer, and endometrial carcinoma, in addition to leukemia.[13]

Carturan et al.[9] studied the *MN1*, *WT1*, and *NPM1* genes in 136 patients with AML and 50 healthy volunteers, and, according to their study, overexpression of these genes is indicative of poor prognosis in patients with AML.

Is there a relationship between meningiomas and ALL, or is it a random association? We examined a possible molecular genetic mutation in this patient who presented with leukemia and meningiomas. A genetic analysis of the tumor tissue and blood sample identified CALLA-B and fibroblastic meningioma. The *MN1*, *WT1*, and *NPM1* genes were analyzed and found to be normal.

Although we cannot have a definitive understanding about the relationship between these two diseases based on a single case, our case can trigger future studies. Since the number of cases has been increasing, the relationship between these two diseases is expected to become clearer. Therefore, large-scale clinical trials are needed.

Conflict of Interests

The authors have no conflict of interests to declare.

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Surgical Management of the Armored Brain: Case Report of the Treatment of a Chronic Calcified Subdural Hematoma*

Manejo cirúrgico do cérebro blindado: Relato de caso do tratamento de hematoma subdural crônico calcificado

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Abstract

Calcified chronic subdural hematomas (CCSDHs) are rare entities, whose yearly incidence ranges from 1.72 to 20.6 per every 100 thousand persons. Several different approaches to their management are reported in the literature, ranging from conservative treatment to craniotomy with full removal of the neomembranes. Currently, there are no guidelines or consensus that establish the best technique. We herein report a case of symptomatic CCSDH initially drained through a burr-hole craniotomy, with no resolution of the symptoms. Later, our patient underwent a craniotomy and partial membranectomy, which resulted in full symptomatic recovery.

Keywords
- neurosurgery
- chronic subdural hematoma
- pathologic calcification

Resumo

Hematomas subdurais crônicos calcificados (HSDCCs) são entidades raras, cuja incidência anual varia de 1,72 a 20,6 casos a cada 100 mil pessoas. Várias abordagens diferentes para seu manejo são relatadas na literatura, desde o tratamento conservador até a craniotomia com remoção total das neomembranas. Atualmente não há diretrizes ou consensos que estabeleçam a melhor técnica. Nós relatamos um caso de HSDCC inicialmente drenado por meio de uma craniotomia por trepanação, sem resolução dos sintomas. Posteriormente, nosso paciente foi submetido a uma craniotomia e membranectomia parcial, que resultou em plena recuperação dos sintomas.

Palavras-chave
- neurocirurgia
- hematoma subdural crônico
- calcificação patológica

Introduction

Chronic subdural hematoma (CSDH) is an abnormal collection of blood in the subdural space that develops for three or more weeks.[1] Its overall yearly incidence ranges from 1.72 to

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20.6 per 100 thousand persons.[2] Between 0.5% and 2.0% of the cases of CSDH[3] undergo calcification, and they are known as calcified DSDHs (CCSDHs); their first known description was made by von Rokytansky in 1884.[4] Due to its similarity with an armor encapsulating the brain, this entity is sometimes referred to as *armored brain*.[5] In a review published in 2020, Turgut et al.[6] found only 114 reported cases of calcified or ossified CSDHs since 1930.

The purpose of the present report is to describe a case of a symptomatic CCSDH initially drained through a burr-hole craniotomy, with no resolution of the symptoms. Later, our patient was subjected to a craniotomy, which resulted in full symptomatic recovery.

Case Report

A 62-year-old male patient was brought to the emergency department (ED) by the emergency medical service. The accompanying family member reported that the patient felt dizzy after a meal and was unable to stand up. He also had nausea followed by vomiting with food content. His blood pressure was measured at 200/100 mmHg right after the symptoms. They denied any speech alteration or facial droop. Upon arrival at the ED, the patient had a Glasgow Coma Scale score of 14 due to confused verbal response, with an otherwise normal physical examination. His symptoms were gradually improving by the time he arrived at the ED. About five months before, the patient had a similar episode, which was treated as a hypertensive crisis with no organ damage. During the six months preceding the episode, the patient was suffering intermittent episodes of dysphasia and right hemiparesis, with spontaneous resolution. He also stated some episodes of syncope.

He was submitted to a brain magnetic resonance imaging (MRI) scan, which revealed a well-organized chronic subdural hematoma with focal compression of the underlying brain parenchyma (►**Figs. 1** and **2**).

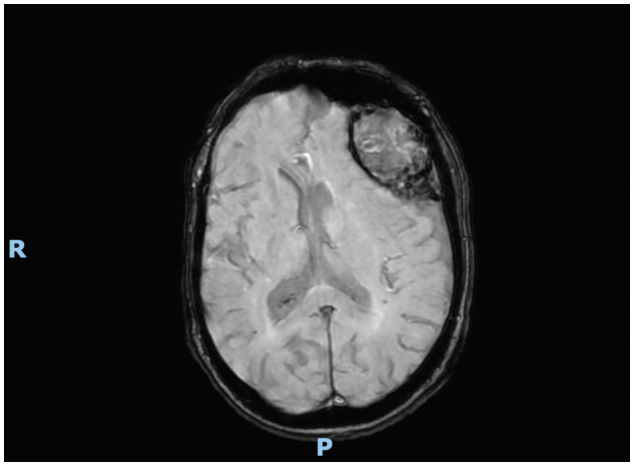

Fig. 1 T2 susceptibility-weighted angiography (SWAN) sequence showing a well-circumscribed subdural hemorrhagic collection which exerts a mass effect on the left frontal lobe, causing an 8-mm midline shift. Abbreviations: R, right; P, posterior.

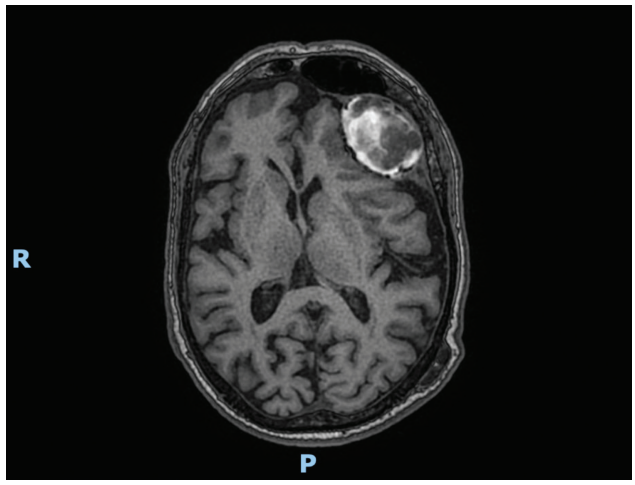

Fig. 2 T1-weighted non-contrast magnetic resonance imaging (MRI) scans of the brain in the axial plane, showing the same collection as ►**Fig. 1**. Abbreviations: R, right; P, posterior.

The patient was also subjected to a computed tomography (CT) scan of the brain, which showed calcifications around the hematoma.

We opted for the surgical management of the subdural hematoma through a burr hole right under the coronal suture on the left side. During the procedure, a minimum volume of hematic fluid was drained, and a suction drain was left in the subgaleal space. A postoperative contrast-enhanced MRI showed that the volume of the hematoma had not changed. This finding led us to conclude it was a CCSDH, and we indicated a reintervention.

The patient was then subjected to a left frontal craniotomy, through which the hematoma was drained, and its cavity was opened to communicate with the subdural space, without complete removal of the calcified membrane. A CT scan performed after this second operation showed that the volume of the hematoma had decreased and that the calcified cavity was communicating with the subdural space beneath (►**Fig. 3**).

The patient had no surgical complications or neurological deficits and his symptoms improved. He was discharged after 48 hours and remained neurologically intact at the 6-month follow-up visit.

Discussion

It is known that the pathological finding that distinguishes chronic from acute subdural hematomas is the development of neomembranes that encapsulate the bleeding in a cavity between the dura and the arachnoid.[7] With time, these neomembranes may evolve into firm collagen tissue that forms a fibrotic layer around a hygroma or liquefied hematoma.[8] It is not known why the fibrotic capsule of some of these CSDHs undergoes a process of calcification, creating a CCSDH.[9]

Although sometimes used interchangeably,[10,11] the term *ossification* is best used when referring to CCSDHs that show

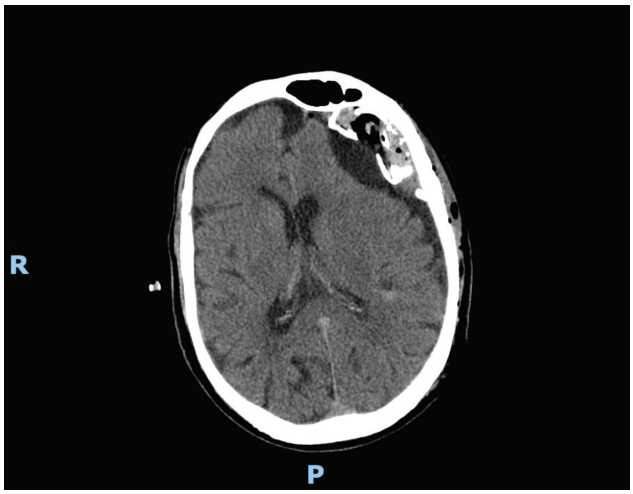

Fig. 3 Computed tomography scan performed after the second surgical procedure showing a decreased hematoma volume, as well as the communication of the calcified capsule with the subdural space. Abbreviations: R, right; P, posterior.

microscopic evidence of bone formation, which may be considered a terminal phase of organization.[12]

The etiologic factor for CCSDH most commonly identified is repeated brain injuries,[6] although some cases may be related to shunt overdrainage[13] or meningitis.[14]

There are no guidelines regarding the ideal management of CCSDHs. Several authors[15–18] have reported that craniotomy has no effect on long-standing symptoms, and thus recommend surgery only when acute or progressive neurological deficits are present. When indicated, the procedure of choice is a matter of controversy. Some authors advocate a craniotomy with full membranectomy,[10,19–21] but there are also reports of satisfactory results with burr hole craniotomy.[22] When a hematoma reaccumulates after an initially satisfactory burr-hole drainage, a craniotomy may be necessary.[5] The same may be the case for infection of the subdural space after burr-hole drainage.[23] A rare but reported complication of a not sufficiently large membranectomy is the herniation of the brain into the subdural space.[24] Our patient was managed with a craniotomy and partial membranectomy, which were enough for the resolution of the symptoms.

Conclusion

Calcified chronic subdural hematoma is a rare entity whose management lacks guidelines or expert consensus. The case herein reported shows that drainage through a craniotomy and communication of the capsule with the subdural space through partial removal of the calcified membrane may be a feasible and effective option when surgical treatment is warranted.

Conflict of Interests

The authors have no conflict of interests to declare.

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Spinal Cord Paracoccidioidomycosis: Case Report

Paracoccidioidomicose na medula espinhal: Relato de caso

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Abstract

Paracoccidioidomycosis (PCM) is a systemic mycosis caused by fungi *Paracoccidioides brasiliensis* and *Paracoccidiodes Lutzii*. Its distribution is limited to subtropical regions of Central and South America, where it is endemic, and Brazil accounts for ∼ 80% of the reported cases. Even in endemic zones, its incidence is low, ranging from 3 to 4 new cases per million to 1 to 3 new cases per 100 thousand inhabitants per year. Granulomas in the spinal cord are rare, and they account for 0,6% of all cases of systemic PCM. The authors report a case of a woman with crural paraparesis caused by dorsal spinal cord PCM granulomasin T7-T8 and T8-T9, with no evidence of systemic disease. The patient was submitted to microsurgery, with total excision of the lesions, and is experiencing positive neurological recovery. Though rare, PCM intramedullary granulomas must be considered in differential diagnosis of the tumoral expansive process of the spinal cord, especially in patients coming from endemic rural zones.

Keywords
- paracoccidioidomycosis
- spinal cord
- granuloma

Resumo

A paracoccidioidomicose (PCM) é uma micose sistêmica causada pelos fungos *Paracoccidioides brasiliensis* e *Paracoccidioides Lutzii*. A doença é endêmica nas regiões subtropicais das Américas do Sul e Central, sendo o Brasil responsável por aproximadamente 80% dos casos relatados. A sua incidência, até mesmo em zonas endêmicas, é baixa, e varia de 3 a 4 casos novos por milhão até 1 a 3 casos novos por 100 mil habitantes ao ano. Os granulomas intramedulares são raros, e acometem 0,6% dos indivíduos com PCM. Os autores relatam o caso de uma paciente de 81 anos com paraparesia crural devido a granulomas intramedulares de PCM em T7-T8 e T8-T9, sem evidências de doença sistêmica. A paciente foi submetida a microcirurgia, com boa evolução pós-operatória. Embora raros, os granulomas intramedulares de PCM devem ser considerados no diagnóstico diferencial das lesões da medula espinhal, especialmente naqueles pacientes provenientes de zonas rurais endêmicas.

Palavras-chave
- paracoccidioidomicose
- medula espinhal
- granuloma

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Introduction

Paracoccidioidomycosis (PCM) is a systemic granulomatous chronic mycosis caused by fungi *Paracoccidioides brasiliensis* and *Paracoccidioides Lutzii*.[1–3] It is endemic in the subtropical areas of South and Central America,[1,4,5] and Brazil accounts for ~ 80% of the reported cases, followed by Colombia, Venezuela, Argentina, and Peru.[2,3,5,6]It occurs more often in rural areas of the Brazilian south, southeast and midwest, especially in the states of São Paulo and Minas Gerais.[1,2,7,8]

After being inhaled, the *Paracoccidioides* fungi cause pulmonary infection that is often subclinical in immunocompetent individuals. And, should the occasion arise, such fungi might spread to other organs, either through hematological or lymphatic routes, in special to the oropharynx, the mucocutaneous tissue, the lymph nodes, the adrenal glands, the liver, as well as to the central nervous system (CNS).[1–3,9]

Involvement of the CNS is rather variable, occurring in 0% to 27% of the series of patients with PCM.[1–3,6] The granulomatous form predominates in 96% of the cases, occurring especially in cerebral hemispheres.[1,10,11] Intramedullary granulomas are rare, affecting 0,6% of PCM cases and 4% of cases of neuroparacoccidioidomicosys.[1,9] Reviewing the Medline and LILACS databases, we identified 19 reports of patients with intramedullary granulomas.[6,7,9,12–23] Due to their rarity, we herein report the case of a patient with two dorsal intramedullary lesions which were approached surgically.

Case Report

An 81-year-old woman presented with a history of progressive weakening of muscular strength on the lower limbs which had started one month before the consultation. Four months before, she had presented herpes zoster on the dorsal region of the skin at the level of the roots of T4 and T5 to the right. There was no other neurologic symptomatology. The patient had been a smoker since she was an adolescent, and had systemic arterial hypertension. She had lived and worked in a rural area of the state of Rio Grande do Sul, Brazil. Upon neurological examination, the patient presented crural paraparesis with grade force II, bilateral Babinsky, and sensorial level in T9. She was investigated with magnetic resonance imaging (MRI), and two intramedullary spinal cord images were suggested granuloma or metastasis in T7-T8 and T8-T9 (►**Fig. 1**). Due an increase in the weakening of muscular strength on the lower limbs, the patient was submitted to laminectomy from T6 to T9, as well as to a total microsurgical excision of the lesions (►**Fig. 2**). Intraoperative ultrasonography was performed to locate the intramedullary granulomas (►**Fig. 3**). The histopathological examination was compatible with PCM (►**Fig. 4**). We used dexamethasone 16 mg/day preoperatively and postoperatively.

The patient was referred to an infectious disease specialist, performing a chest computed tomography, which revealed a lump in the posterior segment of the right upper lobe, and another one in the left upper basal segment. Furthermore, small calcified granulomas were observed, spread bilaterally in the lung parenchyma. There were no signs suggestive of either skin or oral lesions, and no involvement of other organs and systems. The patient was treated with sulfamethoxazole and trimethoprim.

A year after the surgical treatment, the patient presented a positive evolution, and was capable of ambulation with the aid of metal bars.

Fig. 1 Magnetic resonance imaging (MrI) scan of the sagittal spinal cord showing two nodular lesions compatible with granulomas or metastasis.

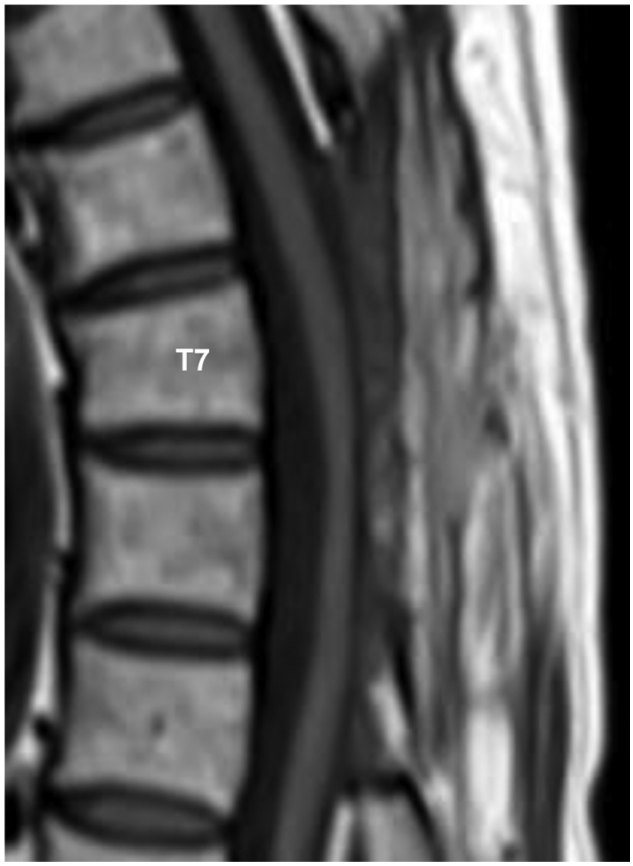

Fig. 2 Postoperative sagittal MRI scan shows total resection of the lesions.

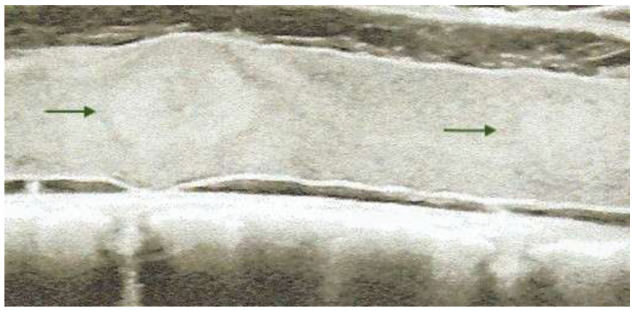

Fig. 3 Intraoperative ultrasonography with identification of intramedullary spinal cord granulomas.

Discussion

Paracoccidioidomycosis is not a disease of compulsory notification; therefore, there is no precise data about its incidence and prevalence in Brazil. It is believed that its incidence in endemic areas may vary from 3 to 4 new cases per million to 1 to 3 new cases per 100 thousand inhabitants per year.[1–3,9] However, recent records of incidence in the state of Rondônia, Brazil, report 9,4 cases per 100 thousand inhabitants.[10] Clinical findings generally occur between the ages of 30 to 50 years, old and male patients are more affected in the proportion of 10 to 15 for 1 female.[1–3,9]

Once inhaled, the fungus may be either destroyed in the lung parenchyma by phagocytic cells or multiply and produce an infection source, forming a primary complex. Such lesions may either recede in immunocompetent individuals or the fungi contained in these complexes may spread to other organs, causing the acute form of the disease. Many individuals remain with the primary scarring complex containing viable fungi, called quiescent lesions, which may be reactivated and evolve to chronic PCM many years after the initial infection. In the tissues, reactivity of the host induces an inflammatory response and the formation of granulomas. In this respect, granuloma represents an immune response triggered by the host to the wall components released by the offending agent.[1–3,6,9] Involvement of the CNS is always secondary to the primary focus, and there is usually a widespread illness affecting multiple organs. However, simultaneous involvement of other organs or systems may not occur.[1,6,9,15] Smoking and alcoholism are often associated.[2]

One of the reasons for the difficulty in establishing a diagnosis in patients without systemic disease is that the neuroradiological characteristics of the lesions are not specific, being impossible to differentiate them from granulomas caused by tuberculosis, toxoplasmosis, cysticercosis, cryptococcosis or even glial and metastatic neoplasia.[1,11–14,16,19,22,23] The hypothesis of granuloma must be considered when multiple lesions are observed.[13,23] Besides intramedullary spinal cord involvement, intradural extramedullary granulomas may occur, as well as epidural bone lesions involving the spinous process, the lamina and the vertebral bodies, causing osteomyelitis and spondylodiscitis.[24–28]

There is evidence that the concomitant use of corticosteroids with antifungal therapy can reduce the inflammatory process in patients with PCM.[2] The drugs most used in the antifungal treatment are itraconazole, sulfamethoxazole/trimethoprim, and amphotericin B.[2] Microsurgical treatment is recommended in those patients who present neurological signs of spinal cord lesions.[1,2,6,9] In the case herein reported, intraoperative ultrasonography facilitated the identification of the lesions and the surgical approach.

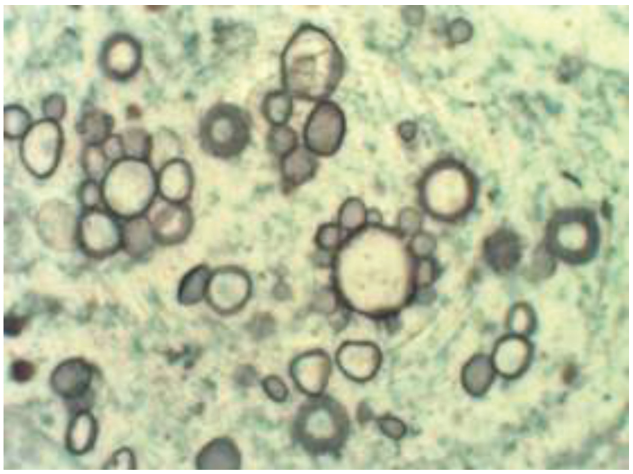

Fig. 4 Histopathology showing helm-shaped yeasts compatible with paracoccidioidomycosis (prata metenamina de Gomori [Gromori methenamine silver, GMS], 400x).

Although there was an assumption of granuloma, the PCM diagnosis came to us as a surprise. Even though PCM is a rare disease, it must be considered in the differential diagnosis of intramedullary and intracranial expanding processes, especially in those patients coming from endemic rural areas and, furthermore, awareness of this disease must be raised, to make the diagnosis easier and enable physicians to provide early treatment.

Conflict of Interests

The authors have no conflict of interests to declare.

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Correspondence to "Intracranial Pressure Monitoring and Unfavorable Outcomes"

Correspondência a "Monitorização de pressão intracraniana e resultados desfavoráveis"

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We would like to express our surprise after reading the reply to Dr. Chiara Robba's *Intracranial pressure monitoring and unfavorable outcomes* correspondence, written by Brazilian physicians Welling et al., in which the possibilities and tools available for intracranial pressure monitoring in both national and international scenarios are described, stating that "*intracranial pressure monitoring is not included in the management strategy for neurocritical patients*", using BEST TRIP[1] as such reference. Our astonishment lies in the fact that we, authors of this letter, use intracranial pressure (ICP) monitoring as a daily practice in our neurocritical care unit. As representatives of The Neurocritical Care Committee of the Brazilian Association of Intensive Care Medicine (AMIB, in the Portuguese acronym), we recommend monitoring intracranial pressure in neurocritical patients, since monitoring-guided treatment of intracranial hypertension is associated with a potential improvement in treatment outcomes.

It is important to highlight that Brazil is an enormous country, as big as the European continent itself, and to generalize a medical conduct in a country this big, with different social and geographical realities, is at the very least inconsequential. Intracranial pressure monitoring has been performed in Brazil since 1990,[2] and current protocols are based on guidelines or consensus statements published in the medical literature. It is undeniable that neurointensivism knowledge is applied in clinical practice according to a structured and properly trained medical team, as well as to the availability of resources and technologies, both in developed and developing countries. Thus, ICP monitoring is administered differently both in different centers in the same country and in different countries, for reasons related to the local reality and infrastructure.[1,3]

We believe that it is important not to undervalue BEST TRIP just as much as overestimate SYNAPSE-ICU,[3] but it is necessary to understand the limitations of BEST TRIP[1], since in modern medicine and intensive care unit patient care, other methods need to be included and personalized. A sole ICP value and strategy is not suitable for every single individual, especially when considering our critical care patients with highly compromised cerebral autoregulation.[4,5]

The magical number that defines high ICP has greatly digressed in medical literature. The current 22 mmHg has previously varied between 15 and 25 mmHg, leading to the questions: does one size fit all? Are all hypertensions equal?

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Should oligemia and hyperemia receive the same treatment? We can conclude with three key elements: point of care, multimodality monitoring, and nongeneralization.

Conflict of Interests

The authors have no conflict of interests to declare.

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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.

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