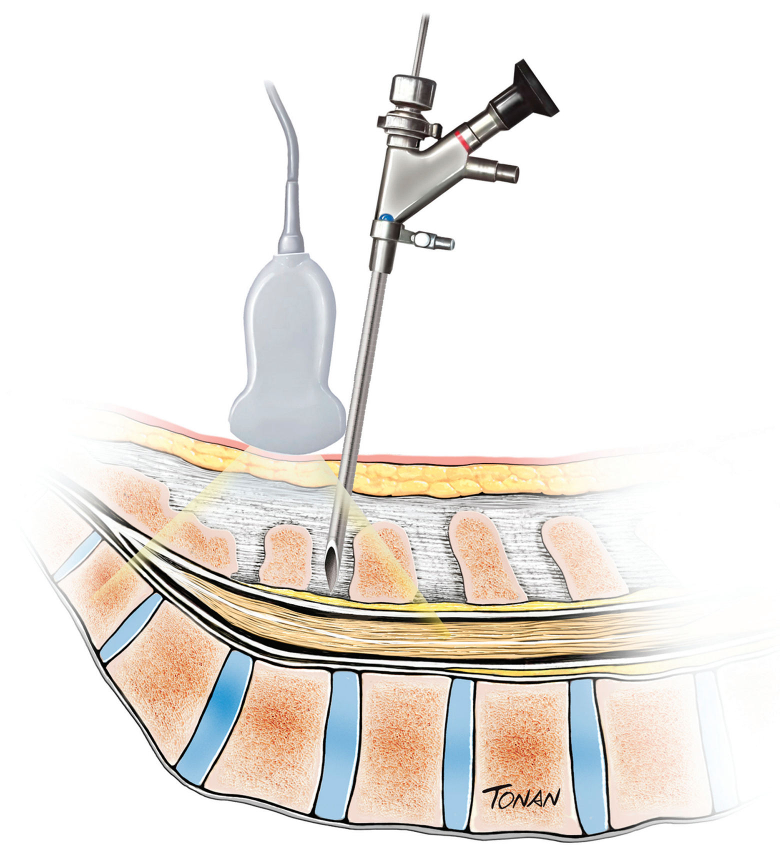
ISSN 0103-5355

Brazilian Neurosurgery

Arquivos Brasileiros de Neurocirurgia

Number 4 • Volume 41 • Pages 311–396 • December 2022



SBN
Sociedade Brasileira de Neurocirurgia

OPEN ACCESS

Thieme

ISSN 0103-5355

Brazilian Neurosurgery
Arquivos Brasileiros de Neurocirurgia

ISSN 0103-5355

Brazilian Neurosurgery
Arquivos Brasileiros de Neurocirurgia

Volume 41, Number 4/2022

Brazilian Neurosurgery
Arquivos Brasileiros de Neurocirurgia

Thieme Revinter Publicações Ltda

online www.thieme-connect.com/products

Case Reports

Technical Note

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

Cover design: © Thieme
Cover image source: © Sociedade Brasileira de Neurocirurgia
(Castro JPS, Brock RS, Teixeira MJ, Figueiredo EG. Ultrasound-Guided In-Plane Interlaminar Lumbar Endoscopic Approach with Smartphone and Portable Light Source: Description of a New Surgical Technique. Arq Bras Neurocir 2022;41(4): 391–396)

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

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

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

ISSN 0103-5355

Multi-Level Cervical Disc Degeneration and Vertigo

Degeneração do disco cervical em múltiplos níveis e vertigem

Serdar Ercan[1] Murat Baloglu[2]

[1] Department of Neurosurgery, School of Medicine, Atilim University, Ankara, Turkey
[2] Department of Neurosurgery, Eskisehir City Hospital, Eskisehir, Turkey

Address for correspondence Serdar Ercan, associate professor, Department of Neurosurgery, School of Medicine, Atilim University, Ankara, Turkey, Kizilcasar Mah, 1184. Cad, No:13, Incek, Golbasi, Ankara, Turkey (e-mail: srdrercn@gmail.com).

Arq Bras Neurocir 2022;41(4):e311–e315.

Abstract

Objective While complaints of pain, loss of strength, and numbness radiating to the neck and arm are common in patients due to cervical disc degeneration, vertigo is a rare symptom. The articles previously published on the subject focus on single-level disk degeneration and its correlation with vertigo. However, in the case of multilevel cervical discopathy, its effect on the severity of vertigo and its response to surgical treatment has not been clarified. Therefore, the objective of the present study is to shed light on the topic.

Methods Patients with vertigo complaints in whom all known etiological causes of vertigo had been excluded, but with cervical disc degeneration, were included in the study. The scores on the Visual Analog Scale (VAS) and Cervical Vertigo Evaluation Scale (CVES) were analyzed in terms of numbers of discopathy, spine levels, and differences regarding the preoperative and postoperative status.

Results A total of 24 patients (14 with single-level and 10 with multi-level disc degeneration) underwent anterior cervical discectomy. The preoperative CVES score was significantly decreased after surgery. Multi-level disc degeneration causes fewer vertigo symptoms than the single-level kind. No significant correlation between the severity of pain and vertigo was observed.

Conclusion Multi-level disc degeneration causes fewer vertigo symptoms. These symptoms decreased after anterior cervical discectomy in cases of single-level disk herniation at upper segments. The surgical intervention could be a favorable choice of treatment. However, the mechanism and treatment approach to cervical vertigo is still a controversial issue.

Keywords
- vertigo
- dizziness
- cervical
- disc degeneration

received
March 21, 2022
accepted
April 25, 2022

DOI https://doi.org/10.1055/s-0042-1749369.
ISSN 0103-5355.

Resumo

Objetivo Embora as queixas de dor, perda de força e dormência com irradiação para o pescoço e braço sejam comuns em pacientes devido à degeneração do disco cervical, a vertigem é um sintoma raro. Os artigos publicados anteriormente se concentram na degeneração do disco de nível único e na sua correlação com a vertigem. No entanto, no caso da discopatia cervical em múltiplos níveis, seu efeito sobre a gravidade da vertigem e sua resposta ao tratamento cirúrgico não foi esclarecido. Portanto, o objetivo do presente estudo foi lançar luz sobre essa questão.

Métodos Foram incluídos no estudo pacientes com queixa de vertigem nos quais foram excluídas todas as causas etiológicas conhecidas de vertigem, mas que apresentavam degeneração discal cervical. As pontuações na Escala Visual Analógica (EVA) e na Escala de Avaliação da Vertigem Cervical (Cervical Vertigo Evaluation Scale, CVES, em inglês) foram analisadas em termos dos números de discopatia, dos níveis da coluna, e das diferenças entre o estado pré e pós-operatório.

Resultados A todo, 24 pacientes (14 com degeneração discal de nível único e 10 com degeneração em múltiplos níveis) foram submetidos a discectomia cervical anterior. A pontuação pré-operatória no CVES sofreu redução significativa após a cirurgia. A degeneração do disco em múltiplos níveis provoca menos sintomas de vertigem do que a de nível único. Não se observou correlação significativa entre a gravidade da dor e a vertigem.

Conclusão A degeneração discal em múltiplos níveis provoca menos sintomas de vertigem. Os sintomas de vertigem diminuíram após a de discectomia cervical anterior em hérnia de disco de nível único nos segmentos superiores. A intervenção cirúrgica pode ser uma escolha favorável no tratamento. No entanto, o mecanismo e a abordagem do tratamento da vertigem cervical ainda é uma questão controversa.

Palavras-chave
- vertigem
- tontura
- cervical
- degeneração discal

Introduction

Dizziness is the illusion of spinning, with the sensation of rotational movement of the surrounding objects. It is among the most common complaints in medicine, and it affects approximately 20% to 30% of the general population.[1–3] The etiology of vertigo varies; insufficient activity of the semicircular canals of the ear, unequal neural activity of left and right vestibular nuclei at the central nervous system, and blood pressure irregularity due to cardiac disorders are the most common factors that cause dizziness and vertigo. Many treatment protocols have been developed considering the etiology, and the patients are treated by specialist physicians. However, there are reports of[1,3,4] a group of patients who were have cervical disc degeneration with complaints of dizziness despite the absence of the aforementioned vertigo etiologies. With this new finding, the highly-controversial concept of cervicogenic vertigo was introduced in the literature.

In a study by Colledge et al.[4] on the causes of vertigo in the elderly, the authors attributed vertigo to cervical spondylosis in 65% of the cases. While complaints of pain, loss of strength, and numbness radiating to the neck and arm are common in patients due to cervical disc degeneration, vertigo is a rare symptom.[2,5,6]

There are authors[4] who oppose as well as supporters of cervical vertigo. The lack of an established diagnostic test for the syndrome is the most important cause of controversy. In studies[7–10] on this subject, single-level disc pathologies and treatment methods are generally discussed; however, the severity of vertigo in patients with multi-level disc degeneration and the treatment protocols to be applied in these cases are not mentioned. In the present study, we aimed to investigate how it will affect vertigo both between cervical spine levels and in the presence of additional adjacent disc degeneration. In addition, among the treatment options, the effect of the surgical treatment on vertigo was investigated.

Materials and Methods

All patients underwent vestibular and hearing tests. Then, regular consultations were held to exclude any ear, neurologic and cardiologic disorders. Cervical magnetic resonance imaging (MRI) scans, radiographs, and computed tomography (CT) scans were assessed. Patients who have vertigo but no etiological disorders except cervical spondylosis were included. The vertigo symptoms were evaluated based on the Cervical Vertigo Evaluation Scale (CVES), which was first described by Wang and Zhou in 1998.[7] The duration of the cervical disc degeneration was examined retrospectively from the hospital archive. The data obtained were used to understand whether there is a link between the severity of

Table 1 Demographics of patients with cervical disk degeneration and vertigo

Mean age (years)		62 ± 4
Number of patients	Male	10
	Female	14
		2
Duration of disk degeneration (years)	< 1	7
	1-5	9
	> 5	8
Average score on the Visual Analog Scale	Preoperative	7
	Postoperative	3
Mean score on the Cervical Vertigo Evaluation Scale	Preoperative	11 ± 2
	Postoperative	24 ± 2
Cases of single-level disc degeneration		14
Cases of multi-level disc degeneration		10
Cases of degeneration in the upper cervical segments		11
Cases of degeneration in the lower cervical segments		13

vertigo and the duration of the degeneration. Preoperative and postoperative changes in CVES and Visual Analog Scale (VAS) scores were examined to assess whether there was a difference between vertebral segments.

Operative procedure: anterior cervical discectomy (ACD) was performed using the standard approach.[8] Under general anesthesia, the disc was completely removed, and the cervical cage was inserted.

Postoperative management: non-steroidal anti-inflammatory drugs (NSAIDs) were used for the next five days.

Follow up: the preoperative and postoperative CVES scores were used to evaluate the clinical outcomes.[9] Preoperativ spine level in which disc degeneration occured, and number of spine level and surgery performed for the disc degeneration were recorded.

Statistical analysis: for the statistical analysis, we used the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, IBM Corp., Armonk, New York, US) software, version 22.0. We compared significant preoperative and postoperative CVES values through the Mann-Whitney U test.

Results

A total of 24 patients (14 female and 10 male subjects) were included. All patients had neck and arm pain along with vertigo. The ages of the patients were between 56 and 72 (mean: 62 ± 4) years. The mean duration of the symptoms was 2 years; 15 patients had symptoms for less than 1 year, and the others, for about 3 years (►**Table 1**).

All patients underwent ACD, and a polyetheretherketone (PEEK) cage was installed at the level of deformity. In total, 14 patients had single-level disk degeneration (3 on C3-C4, 4 on C4-C5, 3 on C5-C6, and 4 on C6-C7), and 10 patients had multi-level disk degeneration (5 on C4-C5-C6 and 5 on C5-C6-C7).

The preoperative VAS scores were evaluated, and no significant differences between the patients with single- and multi-level disk degeneration were observed. However, the results regarding the CVES scores were different: the patients with multi-level disk degeneration had significantly fewer vertigo symptoms ($p = 0.03$). The upper cervical levels (C3-C4-C5) cause greater vertigo symptoms than the lower levels (C5-C6-C7), regardless of the number of degenerated discs (►**Figure 1**).

The preoperative and postoperative VAS scores were compared; the postoperative score was significantly lower than the preoperative scores both in cases of upper and lower cervical disc degeneration ($p = 0.01$ and 0.02 respectively) (►**Figure 1**). Moreover, significant recovery from pain was achieved in cases of single and multi-level disc degeneration ($p = 0.03$ and 0.01 respectively). Similar results were observed regarding the CVES scores ($p = 0.02$). No correlation was observed between the decline ratio of the VAS and CVES scores ($p = 0.1$). However, the efficacy of the surgical treatment for upper cervical levels

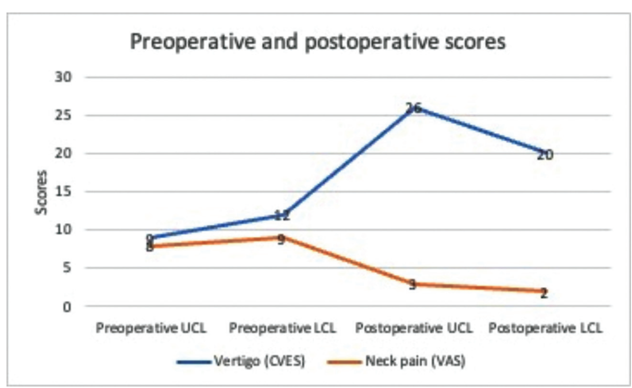


Fig. 1 Preoperative and postoperative CVES and VAS scores for the upper and lower cervical levels. Abbreviations: UCL, upper cervical level; LCL, lower cervical level.

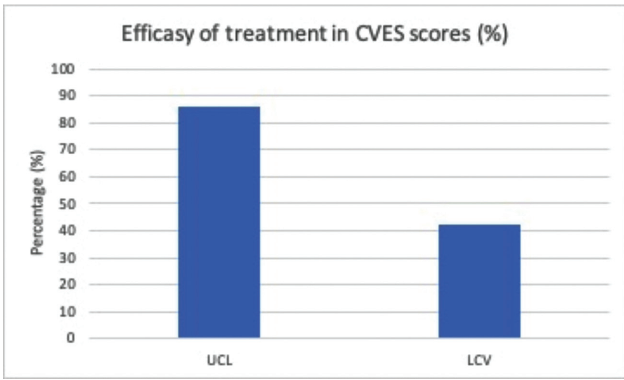


Fig. 2 After the surgical treatment, the improvement in the vertigo symptoms of patients with upper cervical level disc degeneration was significantly greater than that of those with lower cervical disc degeneration. Abbrevations: UCL, upper cervical level; LCL, lower cervical level.

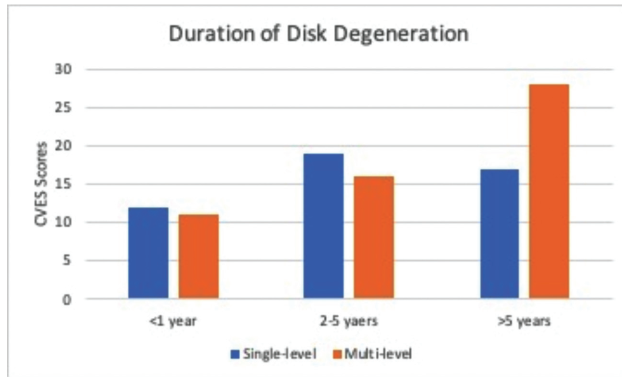


Fig. 3 In the multi-level disc degeneration group, patients with disc degeneration with a duration longer than 5 years had fewer vertigo symptoms. However, there was no significant difference in the single-level group regarding the duration of disc degeneration.

was significantly greater than the efficacy for lower cervical levels ($p = 0.03$) (►**Figure 2**).

In the multi-level disc degeneration group, patients with degeneration longer than five years had fewer vertigo symptoms. However, no significant differences were observed in the single-level group regarding the duration of the disc degeneration (►**Figure 3**).

Discussion

The exact cause of vertigo in cervical disc disorders is a controversial issue, and its mechanism has not yet been elucidated. Among the hypotheses is rotational malposition of the vertebral artery. Cervical balance changes due to cervical degenerative disc disorder, subsequent stenosis, or osteophytes may result in a decrease in the velocity of the flow of the vertebral artery. The resulting vertigo can be explained by the decrease in blood flow. However, Yin et al.[10] stated that changes in the diameter of the vertebral artery were not related to vertigo. They[10] claimed that there was no change in the vertebral artery after the treatment by percutaneous nucleoplasty (PCN), but vertigo decreased with the treatment.

Another hypothesis for the causes of cervicogenic vertigo is proprioceptive sensory dysfunction. The effect of Ruffini bodies in the etiology of cervicogenic vertigo was revealed for the first time, as studies[8,11] have found that patients with cervicogenic vertigo have more Ruffini bodies at degenerated levels than at healthy levels.[8] Zheng et al.[12] claimed that asymmetrical protrusion in cervical disc hernias causes asymmetric sensory input, which in turn causes cervical vertigo. But their study[12] only involved patients with single-level disc herniation. In the present study, we evaluated patients with single and multi-level disc herniation, and we observed that vertigo was severe especially in single-level discopathy, which occurred at the C3-4 and C5-6 levels ($p < 0.002$). However, we also observed that the vertigo in patients with multi-level cervical discopathy was less severe than in those with pathologies in two consecutive vertebral segments and those with healthy disc levels in between. Considering the duration of the degeneration in patients with two or more consecutive disc herniations, those with chronic degeneration (lasting longer than 5 years) had the least severe cases of vertigo, which was significant.

No significant correlation was found between the severity of pain and the severity of vertigo ($p = 0.2$). This inconsistency between pain and vertigo has been the most important claim by researchers who reject the diagnosis of cervical vertigo.[5,13]

Percutaneous nucleoplasty has been attempted primarily as a treatment option.[2] Hahn et al.[14] declare that short or medium term effectiveness of PCN is greater than long-term. In contrast, Li et al.[8] mention that long term effectiveness is better than short or medium term. Yin et al.[10] demonstrated that although there was no significant change in the diameter of the vertebral artery, the severity of the vertigo decreased in patients who underwent PCN. We observed that the severity of the vertigo decreased significantly in our patients who underwent discectomy ($p < 0.03$). However, in the comparison regarding the vertebral levels, we observed a significantly greater decrease in the severity of the vertigo in patients submitted to surgical intervention on the upper cervical vertebra than in the lower vertebral segments. With surgical discectomy, the disc protrusion that compresses the spinal cord is removed. This may explain the "asymmetric sensory input" hypothesis put forward earlier. In addition, complete disc removal means the disappearance of Ruffini bodies, which explains another vertigo hypothesis. However, the fact that the vertigo is less severe in multi-level disc hernia compared to single-level hernia and that it responds less to treatment, shows that all hypotheses should still be viewed with suspicion.

In the literature, there are very few studies approaching the degenerative disc with surgical intervention for the treatment of cervical vertigo, except for percutaneous procedures. Li et al.[15] submitted their patients diagnosed with cervical spondylosis to anterior fusion, and reported that nearly 80% of the vertigo symptoms improved. In similar study, Hong and Kawaguchi[16] obtained results close to those found by Li et al.[15] However, both studies only involved cases of single-level disc degeneration or spondylosis. In the study, we evaluated vertigo in cases of single- and multi-level disc degeneration.

Conclusion

Cervicogenic vertigo should be considered in patients who do not have any vertigo etiology other than cervical disc degeneration. We observed that vertigo symptoms decreased after ACD, especially in single-level upper segments. However, the mechanism and treatment approach to cervical vertigo is still a controversial issue. The fact that the physiopathology revealed in single-level discopathy is not compatible with that of multi-level discopathy increases the discussion.

Limitations of the Study

Since the tests used for vertigo in general are mostly subjective, it is very difficult to diagnose cervicogenic vertigo. There is no definitive diagnostic method that we can use for this syndrome. The diagnosis can only be established after all causes of vertigo have been ruled out by investigating other etiologies. However, an incorrectly-evaluated cause may lead to misdiagnosis.

Ethical Publication Statement
We confirm that we have read the Journal's position on issues involving ethical publication, and declare that the present report is consistent with those guidelines.

Authors' Contributions
Serdar Ercan and Murat Baloglu: collection and analysis of data, and writing if the manuscript.

Funding Statement
The authors declare that they have received no funding regarding the performance of the present research.

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

References

1 Hannaford PC, Simpson JA, Bisset AF, Davis A, McKerrow W, Mills R. The prevalence of ear, nose and throat problems in the community: results from a national cross-sectional postal survey in Scotland. Fam Pract 2005;22(03):227–233
2 Li Y, Peng B. Pathogenesis, Diagnosis, and Treatment of Cervical Vertigo. Pain Physician 2015;18(04):E583–E595
3 Yardley L, Owen N, Nazareth I, Luxon L. Prevalence and presentation of dizziness in a general practice community sample of working age people. Br J Gen Pract 1998;48(429):1131–1135
4 Colledge NR, Barr-Hamilton RM, Lewis SJ, Sellar RJ, Wilson JA. Evaluation of investigations to diagnose the cause of dizziness in elderly people: a community based controlled study. BMJ 1996; 313(7060):788–792
5 Brandt T. Cervical vertigo–reality or fiction? Audiol Neurotol 1996;1(04):187–196
6 Yacovino D. Cervical vertigo: myths, facts, and scientific evidence. Neurologia (Barcelona, Spain) 2012
7 Wang C, Zhuo D. A preliminary evaluation of symptoms and functions of patients with cervical vertigo. Chin J Rehabil Med 1998;13:245–247
8 Li C, Qi Y, Liu G, et al. Long-Term Clinical Outcomes of Percutaneous Cervical Nucleoplasty for Cervical Degenerative Diseases with Neck Pain and Cervical Vertigo. World Neurosurg 2020;133: e205–e210
9 Clements DH, O'Leary PF. Anterior cervical discectomy and fusion. Spine 1990;15(10):1023–1025
10 Yin HD, Zhang XM, Huang MG, et al. Curative effect and mechanism of radiofrequency ablation nucleoplasty in the treatment of cervical vertigo. Br J Radiol 2017;90(1072):20150772
11 Li Y, Peng B. Pathogenesis, Diagnosis, and Treatment of Cervical Vertigo. Pain Physician 2015;18(04):E583–E595
12 Zheng S, Muheremu A, Sun Y, Tian W, Wu CA. Preoperative imaging differences of patients with cervical spondylosis with cervical vertigo indicate the prognosis after cervical total disc replacement. J Int Med Res 2020;48(02):300060519877033
13 Brandt T, Bronstein AM. Cervical vertigo. J Neurol Neurosurg Psychiatry 2001;71(01):8–12
14 Hahn T, Halatsch ME, Wirtz C, Klessinger S. Response to cervical medial branch blocks in patients with cervicogenic vertigo. Pain Physician 2018;21(03):285–294
15 Li J, Jiang DJ, Wang XW, Yuan W, Liang L, Wang ZC. Mid-term outcomes of anterior cervical fusion for cervical spondylosis with sympathetic symptoms. Clin Spine Surg 2016;29(06):255–260
16 Hong L, Kawaguchi Y. Anterior cervical discectomy and fusion to treat cervical spondylosis with sympathetic symptoms. J Spinal Disord Tech 2011;24(01):11–14

The Effect of Ascorbic Acid Supplementation on the Time of Healing of Rats Submitted to Neurosurgical Procedures

Efeito da suplementação de ácido ascórbico no tempo de cicatrização de ratos submetidos a procedimentos neurocirúrgicos

Tiago Gonçalves Rosa[1]

[1] Hospital Universitário Evangélico Mackenzie, Curitiba, PR, Brazil

Arq Bras Neurocir 2022;41(4):e316–e323.

Address for correspondence Tiago Gonçalves Rosa, MD, Departmento de Neurocirurgia, Hospital Universitário Evangélico Mackenzie (HUEM), Faculdade Evangélica Mackenzie do Paraná (FEMPAR), Curitiba, PR, Brazil
(e-mail: neurocirurgia.irati@gmail.com).

Abstract

Introduction Vitamin C is an essential nutrient for both humans and rats and has been noted for its beneficial properties, among them, healing.

Objective To verify the effect of oral and subcutaneous vitamin C supplementation on the healing time of surgical wounds of rats skulls.

Statistical Methodology Thirty male Wistar rats were divided into 3 groups: 10 from the control group (GI), 10 from the group treated with oral vitamin C (GII), and 10 from the group treated with subcutaneous vitamin C (GIII). Vitamin C was administered to GI and GIII animals from the 3rd to the 7th postoperative day, totaling 10 days of administration at a dose of 100 mg/kg/day. On the 4th day of the study, the rats were submitted to a surgical procedure consisting of a 2-cm incision of the skin of the animals' heads and suturing with single stitches. After a determined period, the rats were killed and submitted to the collection of material for study by the picrosirius red technique for the evaluation of collagen types I and III, the degree of hematoxylin and eosin healing, and the rate of contraction of the wound on subsequent days. The results were described in averages, medians, minimum and maximum values, and standard deviations. For the comparison of the three groups, the analysis of variance with one factor (one-way ANOVA) or Kruskal-Wallis non-parametric test was used. The normality of the variables was evaluated by the Shapiro-Wilk test. Values of $p < 0.05$ indicated statistical significance. The data were analyzed using the IBM SPSS Statistics for Windows, v.20.0. software. (IBM Corp., Armonk, NY, USA).

Results The amount of collagen type III was higher in the groups that received vitamin C, however, without significant difference ($n = 0.292$). In relation to the rate of

Keywords
- scalp
- healing
- ascorbic acid
- Wistar rats

received
May 23, 2021
accepted
July 30, 2021

DOI https://doi.org/10.1055/s-0041-1740618.
ISSN 0103-5355.

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

contraction of the surgical wound, it was higher in the groups treated with vitamin C, with a significant difference between groups I and II ($p = 0.001$), and between groups I and III ($p < 0.001$). No significant difference was found between the groups that were treated with vitamin C ($p = 0.227$).
Conclusion Healing was more effective in the groups treated with vitamin C than in the group that did not receive vitamin supplementation. There was no significant difference in healing between the groups receiving oral or subcutaneous vitamin C.

Resumo

Introdução A vitamina C é um nutriente essencial tanto para humanos quanto para ratos e tem-se destacado por suas propriedades benéficas, entre elas, a cicatrização.
Objetivo Verificar o efeito da suplementação de vitamina C oral e subcutânea no tempo de cicatrização de feridas cirúrgicas do crânio de ratos.
Metodologia estatística: Foram utilizados 30 ratos *Wistar*, machos, divididos em 3 grupos, 10 do grupo controle (GI), 10 do grupo tratado com vitamina C oral (GII) e 10 do grupo tratado com vitamina C subcutânea (GIII). A vitamina C foi administrada aos animais de GII e GIII, do 3° dia ao 7° dia pós-operatório, totalizando 10 dias de sua administração, na dose de 100 mg/kg/dia. No 4° dia do estudo, os ratos foram submetidos ao procedimento cirúrgico, que consistiu na incisão de 2 cm da pele da cabeça dos animais e sutura com pontos simples. Após um período determinado, os ratos foram mortos e submetidos a coleta do material para estudo por meio da técnica de *picrosirius red* para avaliação do colágeno tipos I e III, o grau de cicatrização pela hematoxilina e eosina, e pela taxa de contração da ferida nos dias subsequentes. Os resultados foram descritos por médias, medianas, valores mínimos e máximos, e desvios padrões. Para a comparação dos três grupos, foi usado o modelo de análise da variância com um fator (ANOVA) ou o teste não-paramétrico de Kruskal-Wallis. A condição de normalidade das variáveis foi avaliada pelo teste de Shapiro-Wilk. Valores de $p < 0,05$ indicaram significância estatística. Os dados foram analisados com o programa computacional IBM SPSS Statistics for Windows, v.20.0. (IBM Corp., Armonk, NY, EUA).
Resultados: A quantidade de colágeno tipo III foi maior nos grupos que receberam vitamina C, porém, sem diferença significativa ($n = 0,292$). Em relação à taxa de contração da ferida operatória, ela foi maior nos grupos tratados com vitamina C, com diferença significativa entre os grupos I e II ($p = 0,001$), e entre os grupos I e III ($p < 0,001$), não sendo encontrada diferença significativa entre os grupos que foram tratados com vitamina C ($p = 0,227$).
Conclusão A cicatrização foi mais efetiva nos grupos tratados com vitamina C em relação ao grupo que não recebeu suplementação da vitamina. Não houve diferença significativa na cicatrização entre os grupos que receberam a vitamina C oral ou subcutânea.

Palavras-chave
- escalpe
- cicatrização
- ácido ascórbico
- ratos Wistar

Introduction

The healing process is common to all wounds, regardless of the agent that caused it, it is systemic and dynamic and is directly related to the general conditions of the organism. It consists of a perfect and coordinated cascade of cellular, molecular, and biochemical events that interact for tissue reconstitution to occur.

Tissue damage, the initial stimulus for the healing process, puts blood elements in contact with collagen, synthesized by fibroblasts, and other substances in the extracellular matrix, causing platelet degranulation and activation of the coagulation and complement cascades. With this, the release of several vasoactive and chemotactic mediators that guide the healing process by attracting inflammatory cells to the wound region occurs.

According to the literature, ascorbic acid acts as an electron donor for the proline hydroxylation process, during collagen synthesis, a fact that leads to suspicion of its increased demand in tissue repair processes.

Methodology

The present research was performed in the vivarium and in the laboratory of operative technique and experimental surgery at the institute of medical research (IPEM, in the Portuguese acronym) of Faculdade Evangélica Mackenzie do Paraná (FEMPAR). Thirty male Wistar rats were used, divided into 3 groups, 10 from the control group (GI), 10 from the group treated with oral vitamin C (GII), and 10 from the group treated with subcutaneous vitamin C (GIII).

Vitamin C was administered to animals from GII and GIII, from the 3rd to the 7th postoperative day, totaling 10 days of its administration, at a dose of 100 mg/kg/day. On the 4th day of the study, the rats were submitted to a surgical procedure that consisted of a 2-cm incision of the skin of the animals' heads and sutures with simple stitches. After a determined period, the rats were killed and subjected to the collection of material for study using the picrosirius red technique to assess collagen types I and III, the degree of healing by hematoxylin and eosin (HE), and the rate of wound contraction on subsequent days. The results were described by means, medians, minimum and maximum values, and standard deviations. For the comparison of the three groups, the one-way analysis of variance (one-way ANOVA) model or the Kruskal-Wallis non-parametric test was used. The condition of normality of the variables was assessed by the Shapiro-Wilk test. Values of $p < 0.05$ indicated statistical significance. The data were analyzed with the computer program IBM SPSS Statistics for Windows, v.20.0. (IBM Corp., Armonk, NY, USA).

All ethical parameters were respected, and this research was approved by the Ethics Committee on the Use of Animals of Faculdade Evangélica Mackenzie do Paraná (CEUAs / FEMPAR).

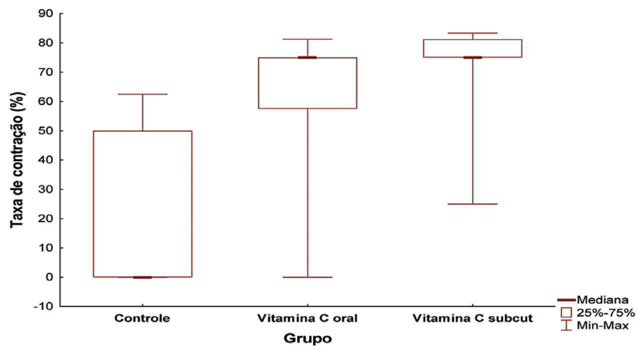
Results

A significant difference was found between the three groups in terms of the rate of contraction (►**Tables 1** and **2**). There was a significant difference between the control group and the groups treated with oral vitamin C ($p = 0.001$) and subcutaneous vitamin C ($p < 0.001$). No significant difference was found between the two groups treated with vitamin C ($p = 0.227$), the rates observed are shown in **Graph 1**.

►**Figs. 1**, **2**, and **3** demonstrate the evolution of the wound through the photos obtained on the 3rd, 5th, and 7th days of the study. It is possible to notice the reduction in the size of the wound and the gradual disappearance of the crust and granulation tissue.

Table 2 Comparison of the contraction rate in relation to each group

Compared groups	*p*-value*
Control versus oral vitamin C	**0.001**
Control versus subcutaneous vitamin C	< **0.001**
Oral vitamin C versus subcutaneous vitamin C	0.227



Graph 1 Contraction rate of the wound in percentage observed on day 7 of treatment.

Using the table adapted from the protocol created by Greenhalgh D. G. et al., the lesions were classified from 1 to 4, with 1 being the worst and 4 being the best degree of healing ►**Table 3**,**4**,**5**,**6**.

►**Figs. 4**, **5**, and **6** show the histological variation of the degree of healing in relation to each group.

The results indicate that there is no significant difference between the three groups in relation to the area of collagen I and the area of collagen III (**Graphic 2** and **Graphic 3**).

►**Fig. 7** shows the greater emphasis of type-I collagen fibers in relation to type-III collagen fibers in a control group rat. In the groups that received vitamin C, ►**Fig. 8** and **9**, especially in the group that received it subcutaneously, ►**Fig. 9**, the percentage of type-III collagen stands out in relation to type-I collagen.

Discussion

In our study, the highest amount of type-III collagen was identified in the groups that received vitamin C, however, with no significant difference. The rate of contraction of the surgical wound was higher in the groups treated with vitamin C, with a significant difference between groups I and II

Table 1 Comparison of percentage values of operating wound contraction rate in each group and among all groups

Variable	Group	N	Average	Median	Minimum	Maximum	Standard deviation	*p**-value*
Contraction rate	Control	10	20.8	0.0	0.0	62.5	26.5	
(%)	Oral vitamin C	10	64.9	75.0	0.0	81.3	23.4	**0.001**
	Subcutaneous vitamin C	10	70.0	75.0	25.0	83.3	18.4	

* Kruskal-Wallis non-parametric test, $p < 0.05$.

Fig. 1 Aspect of group I rat wound contraction (Control).

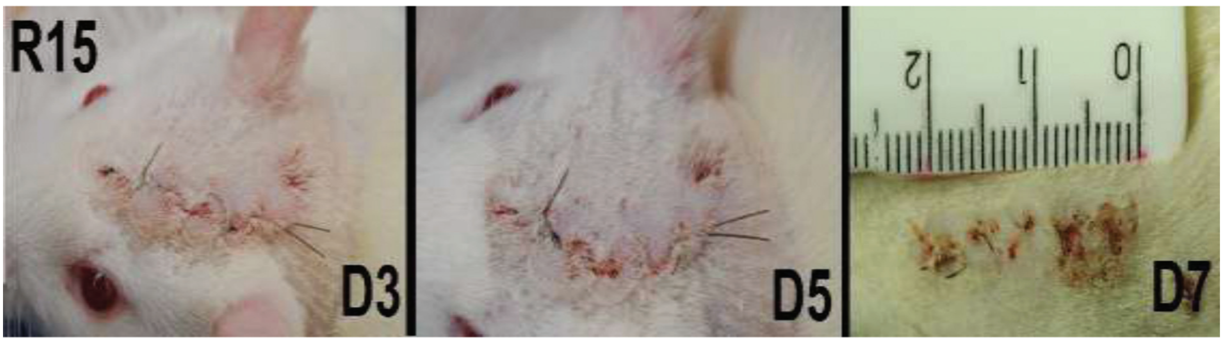


Fig. 2 Aspect of group II rat wound contraction (oral vitamin) for 7 days of observation.

Fig. 3 Aspect of Group III Rat Wound Contraction (Subcutaneous Vitamin C) DURING 7 DAYS OF OBSERVATION. NOTE: Animals in the control group on days 3, 5, and 7 of the study.

($p = 0.001$), and between groups I and III ($p < 0.001$). No significant difference was found between the groups that were treated with vitamin C ($p = 0.227$).

The dose of ascorbic acid was chosen based on previous studies, which verified that these are the minimum concentrations capable of affecting wound healing and that can be used in humans without leading to toxic and harmful effects when administered.

The surgical technique was chosen, as it is a technique that is easy to reproduce and standardize, based on previous works, which opted for the incision in the cranial region, of ~ 20 mm in length. The technique used to assess the intensity of the inflammatory process was HE, which is considered the main means of analysis when the objective of the study is the epithelial tissue.

Regarding the intensity of healing, the most advanced form was found in groups II and III in relation to the control group, that is, in the group that did not receive vitamin C supplementation, there was a greater degree of inflammation and a more pronounced granulation tissue.

The present study was based on previous works, cited in the bibliographic reference,[1–55] for the choice and organization of groups, surgical technique, dose of ascorbic acid, technique for evaluating the inflammatory process and intensity of healing, which observed a greater number and better arrangement of fibroblasts in animals in groups II and III when compared with the control group, since the use of ascorbic acid maintains an adequate concentration of the vitamin in the skin, which stimulates the proliferation of dermal fibroblasts.

Table 3 Comparison of percentage values according to hematoxylin and eosin groups and classifications

HE (degree)	Group (treatment)		
	Control	Oral	Subcutaneous
0	–	–	–
	–	–	–
1	–	–	–
	–	–	–
2	3	–	–
	30%	–	–
3	4	3	3
	40%	30%	30%
4	3	7	7
	30%	70%	70%
Total	10	10	10

Table 4 Comparison of the percentage values of healing assessed by hematoxylin and eosin

Hematoxylin and eosin (degree)	Group (treatment)		
	Control	Oral	Subcutaneous
0, 1, or 2	3	0	0
	30%	0%	0%
3 or 4	8	10	10
	80%	100%	100%
Total	10	10	10

The degree of scarring assessed by hematoxylin and eosin was higher in the groups that received vitamin C, however, with no significant difference between the groups.

The macroscopic evaluation was necessary since the wound contraction process is the fourth phase of the healing process and consists of the centripetal movement of the edges. The phase that precedes the contraction of the wound is that of proliferation, responsible for the closure of the lesion itself, and it is divided into three subphases, which are reepithelization, fibroplasia, and angiogenesis. Finally, the

Table 5 Comparison of the percentage values of the degree of healing in the groups assessing the statistical significance

Groups compared	*P*-value*
Control x oral	0.214
Control x subcutaneous	1
Oral x subcutaneous	0.472

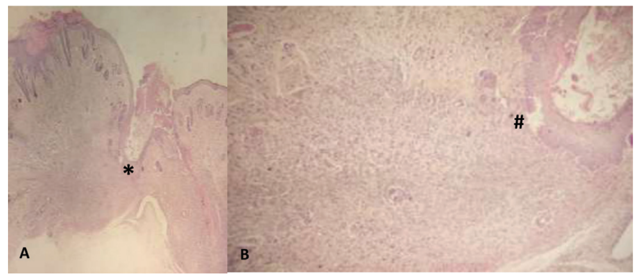


Fig. 4 Photomicrograph of the wound healing area in the Control group. LEGEND: (A) (HE 40x) - Granulation tissue of the epithelium (B) (HE200x). NOTE: (A) (*) Epithelium partially covering the surgical wound. (B) (#) Thin and immature granulation tissue, predominantly inflammatory cells, with few fibroblasts, capillaries, and collagen deposition.

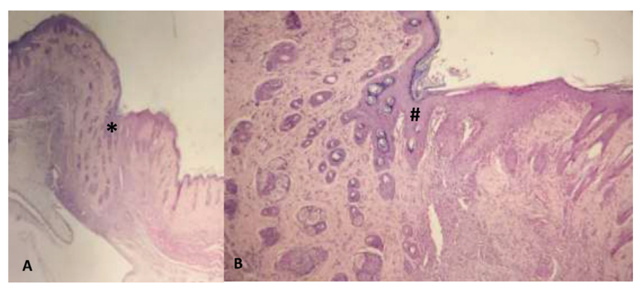


Fig. 5 Photomicrograph of the wound healing area of the subcutaneous vitamin C group. (A) (HE 40x) - Granulation tissue of the epithelium (B) (HE200x). NOTE: (A) (*) Epithelium fully covering the lesion. (B) (#) Medium-thickness granulation tissue, with few inflammatory cells with a predominance of fibroblasts with collagen deposition. Neovascularization present in good quantity.

Table 6 Comparison of the percentage values of the collagen I and Iii area in each group and among all groups

Variable	Group	N	Average	Median	Min	Max	Standard deviation	P-value*
Collagen I area	Control	10	50.7	50.0	12.3	84.0	23.7	
(%)	Oral vitamin C	10	48.5	45.3	31.7	82.0	15.0	0.292
	Subcutaneous vitamin C	10	37.5	39.0	1.7	64.8	20.1	
Collagen III area	Control	10	49.3	50.0	16.0	87.7	23.7	
(%)	Oral vitamin C	10	51.5	54.7	18.0	68.3	15.0	0.292
	Subcutaneous vitamin C	10	62.5	61.0	35.2	98.3	20.1	

*one-way ANOVA, $p < 0.05$.

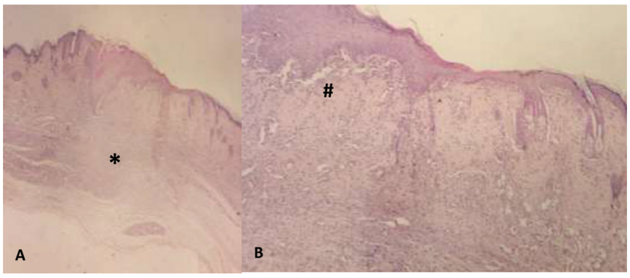
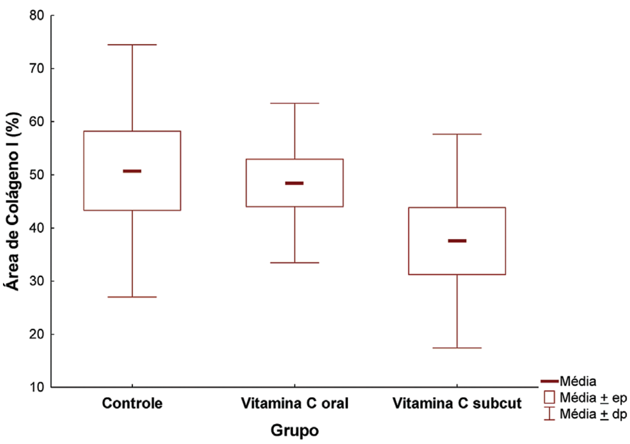
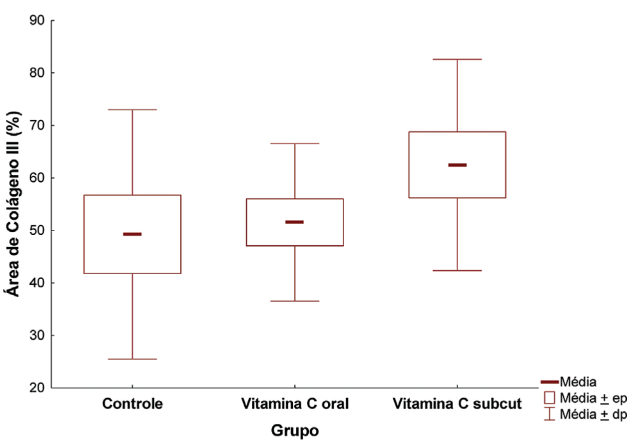


Fig. 6 Photomicrograph of the wound healing area of the oral vitamin C group. (A) (HE 40x) - Granulation tissue of the epithelium (B) (HE200x). NOTE: (A) (*) Epithelium fully covering the lesion with little crust formation. (B) (#) Thick and vascularized granulation tissue, predominance of fibroblasts and large collagen deposition.



Graph 2 Collagen I area (%) between the groups on the seventh day of treatment.



Graph 3 Collagen III area (%) between groups on the seventh day of treatment.

remodeling phase follows that of contraction of the wound and is the last stage of healing.

Conclusion

Ascorbic acid supplementation achieved more effective cranial healing compared with the group that did not receive

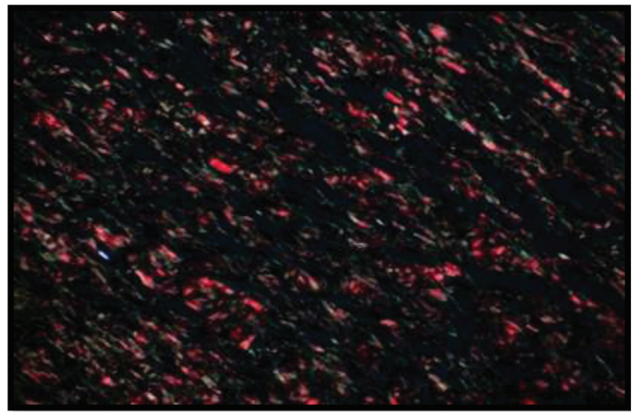


Fig. 7 Photomicrography of type-I and -III collagen fibers. 400x in histological staining with pricosirius red in an animal in the control group (GI) on the tenth day.

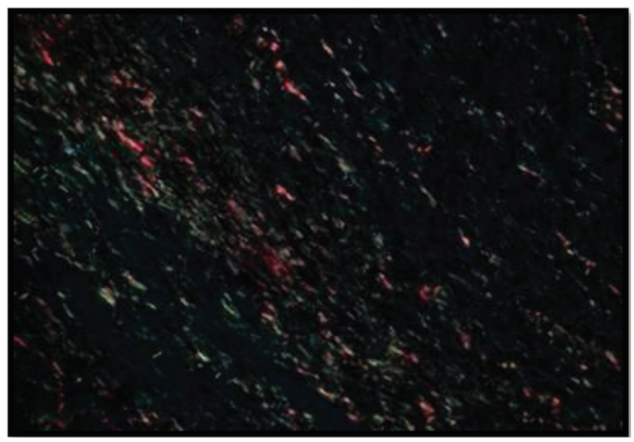


Fig. 8 Photomicrography of type I and III collagen fibers. 400x in histological staining with pricosirius red in an animal in the group treated with oral vitamin C (GII) on the tenth day.

Fig. 9 Photomicrography of type-I and -III collagen fibers. 400x in histological staining with picrosirius red in an animal in the group treated with subcutaneous vitamin C (GIII) on the tenth day. Type-I collagen represented by the symbol #. Type-III collagen represented by the symbol *

vitamin C supplementation. There was no significant difference in healing between the groups that received oral or subcutaneous vitamin C.

Regarding the rate of wound contraction, there was a significant difference between the control group and the groups treated with oral vitamin C ($p = 0.001$) and subcutaneous vitamin C ($p < 0.001$). No significant difference was found between the two groups treated with vitamin C ($p = 0.227$).

The degree of healing assessed by HE was higher in the groups treated with vitamin C, but without significant difference between oral and subcutaneous.

The amount of type-III collagen was higher in the groups that received vitamin C, with a significantly greater difference in the group that received it subcutaneously.

Funding
Coordination for the Improvement of Higher Education Personnel (CAPES).

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

References

1 Balbino CA, Pereira LM, Curi R. Mecanismos envolvidos na cicatrização: uma revisão. Ver Bras Cienc Farm 2005;41(01):27–51
2 Baptistella E, Malafaia O, Czeczko NG, et al. Comparative study in swines' vocal cords healing after excision of fragment with CO2 laser with mitomycin and 5-fluorouracil postoperative topical application. Acta Cir Bras 2009;24(01):13–18
3 Boyera N, Galey I, Bernard BA. Effect of vitamin C and its derivatives on collagen synthesis and cross-linking by normal human fibroblasts. Int J Cosmet Sci 1998;20(03):151–158
4 Camargo PAM, Campos ACL, Matias JEF, Rispoli DZ, Fonseca VR. Efeito da vitamina c tópica na cicatrização de prega vocal de suíno. Rev Bras Otorrinolaringol 2006;72:601–604
5 Carpenter KJ. The history of scurvy and vitamin C.. Cambridge University Press; 4231986
6 Carvalho MFP. Estudo histológico e imunohistoquímico comparativo da cicatrização de feridas em dorso de ratos tratados com mitomicina c ou proprionato de clobetasol. Tese (doutorado) São PauloFaculdade de Ciências médicas de São Paulo2012
7 Chan D, Lamande SR, Cole WG, Bateman JF. Regulation of procollagen synthesis and processing during ascorbate-induced extracellular matrix accumulation in vitro. Biochem J 1990;269(01):175–181
8 Chowcat NL, Savage FJ, Hembry RM, Boulos PB. Role of collagenase in colonic anastomoses: a reappraisal. Br J Surg 1988;75(04):330–334
9 Clark RA. The molecular and cellular biology wound repair. 2nd ed. New York: Plenum Press; 1996
10 Coltran R, et al. Inflamação aguda e crônica. In: Robbins. Patologia Estrutural e Funcional. 6.ed RJ Koogan, 2000:44–1000
11 Crandon JC, et al. Experimental human scurvy. N Engl J Med 1940;223:353–369
12 Talwar HS, Griffiths CE, Fisher GJ, Hamilton TA, Voorhees JJ. Reduced type I and type III procollagens in photodamaged adult human skin. J Invest Dermatol 1995;105(02):285–290
13 Dumas M, Chaudagne C, Bonté F, Meybeck A. Age-related response of human dermal fibroblasts to L-ascorbic acid: study of type I and III collagen synthesis. C R Acad Sci III 1996;319(12):1127–1132
14 Emanuel BS, Cannizzaro LA, Seyer JM, Myers JC. Human alpha 1 (III) and alpha 2(V) procollagen genes are located on the long arm of chromosome 2. Proc Natl Acad Sci U S A 1985;82(10):3385–3389
15 Englard S, Seifter S. The biochemical functions of ascorbic acid. Annu Rev Nutr 1986;6:365–406
16 Fenske NA, Lober CW. Structural and functional changes of normal aging skin. J Am Acad Dermatol 1986;15(4 Pt 1):571–585
17 Folkman J, Shing Y. Angiogenesis. J Biol Chem 1992;267(16):10931–10934
18 Hanson D, Langemo D, Thompson P, Anderson J, Hunter S. Understanding wound fluid and the phases of healing. Adv Skin Wound Care 2005;18(07):360–362
19 Hayashi T, Mizuno K. Collagen. Disponível em <. http://users.easystreet.com/kxm/eng/collagen.htm>/; acesso: 13/02/2018.
20 Hirshberg A, Lib M, Kozlovsky A, Kaplan I. The influence of inflammation on the polarization colors of collagen fibers in the wall of odontogenic keratocyst. Oral Oncol 2007;43(03):278–282
21 Hupp JR. Reparação de feridas. . In: PETTERSON, L. J. et al. Cirurgia oral e maxillofacial contemporânea. RJ: Guanabara Koogan; 2000:57–67
22 Junien C, Weil D, Myers JC, et al. Assignment of the human pro alpha 2(I) collagen structural gene (COLIA2) to chromosome 7 by molecular hybridization. Am J Hum Genet 1982;34(03):381–387
23 Junqueira LC, Bignolas G, Brentani RR. Picrosirius staining plus polarization microscopy, a specific method for collagen detection in tissue sections. Histochem J 1979;11(04):447–455
24 Kligman LH. Photoaging. Manifestations, prevention, and treatment. Clin Geriatr Med 1989;5(01):235–251
25 Kowalexski K, Yong S. Effect of hypothyroidism on bone and urinary hydroxyproline in rats with frature humerus. Indian J Orthop 1968;2(01):84–90
26 Lapière CM. The ageing dermis: the main cause for the appearance of 'old' skin. Br J Dermatol 1990;122(Suppl 35):5–11
27 Lind JA, et al. Treatise on the scurvy. Edinburgh University Press; 1953
28 Mandelbaum SH, Di Santis EP, Mandelbaum MHSA. Cicatrização: Conceitos atuais e recursos auxiliares – Parte I. Na Bras Dermatl 2003;788:393–410
29 Nagase H, Woessner JF Jr. Matrix metalloproteinases. J Biol Chem 1999;274(31):21491–21494
30 Nusgens BV, Humbert P, Rougier A, et al. Topically applied vitamin C enhances the mRNA level of collagens I and III, their processing enzymes and tissue inhibitor of matrix metalloproteinase 1 in the human dermis. J Invest Dermatol 2001;116(06):853–859
31 Oikarinen A, Kallioinen M. A biochemical and immunohistochemical study of collagen in sun-exposed and protected skin. Photodermatol 1989;6(01):24–31
32 Oikarinen A, Kallioinen M. A biochemical and immunohistochemical study of collagen in sun-exposed and protected skin. Photodermatol 1989;6(01):24–31
33 Pauling L. Evolution and the need for ascorbic acid. Proc Natl Acad Sci U S A 1970;67(04):1643–1648
34 Pereira MC, Repka CD, Camargo PA, Rispoli AC, Matias JE. Efeito da mitomicina –c tópica sobre os depósitos de colágeno na submucosa vocal de suínos. Ver Col Bras Cir. 2009;36:236–240
35 Piccinato CE, Netto JC, Cherri J. Cicatrizatização. In: CAMPOS, C. A. H de; COSTA, H. O. L. (ed). Tratado de otorrinolaringologia. São Paulo SP: Roca; 2003:189–200
36 Phillips CL, Combs SB, Pinnell SR. Effects of ascorbic acid on proliferation and collagen synthesis in relation to the donor age of human dermal fibroblasts. J Invest Dermatol 1994;103(02):228–232
37 Rabau MY, Dayan D. Polarization microscopy of picrosirius red stained sections: a useful method for qualitative evaluation of intestinal wall collagen. Histol Histopathol 1994;9(03):525–528
38 Reidling JC, Subramanian VS, Dahhan T, Sadat M, Said HM. Mechanisms and regulation of vitamin C uptake: studies of the

hSVCT systems in human liver epithelial cells. Am J Physiol Gastrointest Liver Physiol 2008;295(06):G1217–G1227
39 Rocha JCT. Terapia laser, cicatrização tecidual e angiogênese. RBPS 2004;17(01):44–48
40 Simões MJ, et al. Aspectos ultra-estruturais dos fibroblastos e dos macrófagos durante o processo de reparação da pele de ratos. Rev Paul Med 1986;104:132–135
41 Singer AJ, Clark RAF. Cutaneous wound healing. N Engl J Med 1999;341(10):738–746
42 Sharman IM, et al. Historical aspects in Vitamin C, Recent Aspects of its Physiological and Technological Importance. Halsted Press BookNew York 1974:1–15
43 Smith LT, Holbrook KA, Madri JA. Collagen types I, III, and V in human embryonic and fetal skin. Am J Anat 1986;175(04): 507–521
44 Sweat F, Puchtler H, Rosenthal SI. Sirius red F3BA as a stain for connective tissue. Arch Pathol 1964;78:69–72
45 Szendroi M, Meimon G, Bakala H, et al. On the presence of a metalloprotease in human skin fibroblasts that degrades the human skin elastic fiber system. J Invest Dermatol 1984;83(03): 224–229
46 Szent-Gyorgy A. Vitamin C. J Biol Chem 1928;22:1887–1409
47 Tajima S, Pinnell SR. Ascorbic acid preferentially enhances type I and III collagen gene transcription in human skin fibroblasts. J Dermatol Sci 1996;11(03):250–253
48 Trubian PS. Influência do octreotide na cicatrização de sutura gástrica em ratos: estudo tensiométrico e da morfometria do colágeno. Curitiba. 79f. [Dissertação]. Departamento de Cirurgia da Universidade Federal do Paraná. 2004
49 UNIVERSIDADE FEDERAL DO PARANÁ (UFPR) Normas para apresentação de documentos científicos 2° edição. Editora UFPR. 2007
50 Vaxman F, Olender S, Lambert A, Nisand G, Grenier JF. Can the wound healing process be improved by vitamin supplementation? Experimental study on humans. Eur Surg Res 1996;28(04): 306–314
51 Vaxman F, Olender S, Lambert A, et al. Effect of pantothenic acid and ascorbic acid supplementation on human skin wound healing process. A double-blind, prospective and randomized trial. Eur Surg Res 1995;27(03):158–166
52 Waugh WA, et al. Isolation and identification of vitamin C. J Biochem 1932;97:325–331
53 Welch RW, Bergsten P, Butler JD, Levine M. Ascorbic acid accumulation and transport in human fibroblasts. Biochem J 1993;294 (Pt 2):505–510
54 Witte MB, Barbul A. General principles of wound healing. Surg Clin North Am 1997;77(03):509–528
55 Yaar M, Gilchrest BA. Cellular and molecular mechanisms of cutaneous aging. J Dermatol Surg Oncol 1990;16(10): 915–922

Correlation between the Optic Nerve Sheath Diameter Measurement and Intracranial Hypertension Tomographic Findings from a Colombian Hospital

Correlação entre a medição do diâmetro da bainha do nervo óptico e os achados tomográficos da hipertensão intracraniana em um hospital colombiano

Andrés Fabricio Caballero-Lozada[1,2,3,4] Jorge Fernando Miño-Bernal[2]
Rene Alberto Espinosa-Marsiglia[1,2] Valentina Rojas-Rincón[4]

[1] Department of Anesthesiology and Resuscitation, Universidad del Valle, Cali, Colombia
[2] Department of Anesthesiology, Hospital Universitario del Valle, Cali, Colombia
[3] Fundación Hospital San José de Buga, Buga, Colombia
[4] Department of Anesthesiology, Unidad Central del Valle del Cauca, Tuluá, Colombia

Address for correspondence Andrés Fabricio Caballero-Lozada, MD, Department of Anesthesiology and resuscitation. Universidad del Valle, Street 4B # 36-00, Cali, Colombia (e-mail: andres.caballero@correounivalle.edu.co).

Arq Bras Neurocir 2022;41(4):e324–e330.

Abstract

Objective In the present study, we aimed at determining the correlation between tomographic findings of intracranial hypertension and ultrasound measurement of the optic nerve sheath diameter (ONSD).

Methods Observational, descriptive, prospective, cross-sectional pilot study. The present research was performed in a tertiary hospital in Cali, Colombia, from March 2019 to October 2019. Twenty-five patients constituted the intracranial hypertension group, and 25 patients without intracranial hypertension constituted the control group. Ultrasound measurements of the ONSD were assessed using a Sonosite Turbo (SonoSite Inc., Bothell, WA, USA) ultrasound. The computed tomography (CT) images obtained from each patient diagnosed with intracranial hypertension were available in the software of the hospital. The primary outcome was the ultrasound measurement of the ONSD.

Results The ONSD values of the right eye of the intracranial hypertension group ranged from 5.2 to 7.6 mm, and the ONSD of the left eye ranged from 5.3 to 7.3 mm. The global ONSD values, obtained from the average between the right and left eye, were recorded between 5.25 and 7.45 mm. Overall, our study indicated that ultrasound measurements of the ONSD were effective in differentiating a group with intracranial hypertension, previously diagnosed by CT scan images, from patients

Keywords
- Optic nerve
- Intracranial hypertension
- Ultrasonography
- Tomography, X-Ray Computed

received April 23, 2021
accepted July 30, 2021

DOI https://doi.org/10.1055/s-0041-1740174.
ISSN 0103-5355.

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

without this condition. According to the ROC curve, the optimal cutoff point for detecting intracranial hypertension was 5.2 mm.

Conclusions Ultrasound measurements of the ONSD correlated with the measurements obtained from CT scan images, suggesting that the ultrasound technique can be efficient in identifying patients with intracranial hypertension and valuable in cases when CT scan images are not an available option.

Resumo

Objetivo No presente estudo, pretendemos determinar a correlação entre os achados tomográficos da hipertensão intracraniana e a medida ultrassonográfica do diâmetro da bainha do nervo óptico (DBNO).

Métodos Estudo piloto, observacional, descritivo, prospectivo e transversal. A presente pesquisa foi realizada em um hospital terciário de Cali, na Colômbia, de março de 2019 a outubro de 2019. Vinte e cinco pacientes fizeram parte do grupo de hipertensão intracraniana e 25 pacientes sem hipertensão intracraniana fizeram parte do grupo controle. O ultrassom Sonosite Turbo (SonoSite Inc., Bothell, WA, EUA) foi utilizado para a medição ultrassonográfica do DBNO. As imagens tomográficas computadorizadas obtidas de cada paciente com diagnóstico de hipertensão intracraniana estavam disponíveis no software do Hospital. O resultado primário foi a medida ultrassonográfica do DBNO.

Resultados Os valores de DBNO do olho direito do grupo de hipertensão intracraniana foram de 5,2 a 7,6 mm e o DBNO do olho esquerdo foi de 5,3 a 7,3 mm. No que se refere aos valores globais de DBNO obtidos a partir da média entre o olho direito e o olho esquerdo, registrou-se entre 5,25 e 7,45mm. No geral, o presente estudo indicou que as medições ultrassonográficas do DBNO foram eficazes na diferenciação de um grupo com hipertensão intracraniana, previamente diagnosticada por imagens de tomografia computadorizada (TC), de pacientes sem essa condição. De acordo com a curva ROC, o ponto de corte ideal para detectar hipertensão intracraniana foi de 5,2 mm.

Conclusões De acordo com nossos achados, as medidas ultrassonográficas do ONSD se correlacionaram com as medidas obtidas nas imagens de TC, sugerindo que a técnica ultrassonográfica pode ser eficiente para identificar pacientes com hipertensão intracraniana e útil nos casos em que as imagens tomográficas não são uma opção disponível.

Palavras-chave
- Nervo Óptico
- Hipertensão Intracraniana
- Ultrassonografia
- Tomografia Computadorizada por Raios X

Introduction

Patients with neurological conditions make up 15% of admissions to the intensive care unit (ICU), where the management of cerebral edema, intracranial hypertension, vasospasm, and epileptic status is frequent.[1] The definition of intracranial hypertension is an intracranial pressure (ICP) > 20 mm Hg for > 5 minutes. It is a catastrophic neurological event associated with a poor prognosis for the life and functionality of the patient regardless of its etiology.[2] According to the clinical practice guidelines, the management of this condition must be done early and aggressively. Increased ICP reduces cerebral perfusion pressure, exacerbating a secondary brain injury jointly with ischemia and a fatal clinical prognosis.[3]

Clinically, this pathology manifests nonspecifically, and the use of computed tomography (CT) of the skull is necessary to document the displacement of vascular and parenchymal structures. Unfortunately, the availability of a CT scanner in specific regions or at certain times of the day is limited. Additionally, there is also a delay in taking the CT, which influences the neurological prognosis under the premise that "time is brain." Thus, the question arises: Is there a fast, noninvasive, accessible, and bedside method that can guide a diagnosis of intracranial hypertension? The answer would be with the ultrasound (US). In this context, our purpose was to determine the correlation between tomographic findings of intracranial hypertension and US measurement of the optic nerve sheath diameter (ONSD).

Materials and Methods

Study Design

This was an observational, descriptive, prospective, cross-sectional pilot study.

Setting

The present study was conducted from March 11, 2019 to October 27, 2019 at the Hospital Universitario del Valle (Cali, Colombia). Confidentiality of patients and control individuals was guaranteed; a unique alphanumeric code identified each participant. All participants gave informed consent.

Participants

A convenience sample of 25 patients constituted the intracranial hypertension group, and 25 patients without intracranial hypertension constituted the control group. The inclusion criteria were patients with clinical and tomographic signs of intracranial hypertension, without previous neurological pathology, admitted to the Emergency Department and to the ICU of the Hospital Universitario del Valle (Cali, Colombia), and with recent tomography < 24 hours at the time of measurement. The exclusion criteria were patients <18 years old with chronic neurological deterioration, basic ophthalmological comorbidities, optic neuritis, and/or ocular trauma. Likewise, outpatients with arachnoid cyst, lesions that compromise the cavernous sinus without good pain management, and operating difficulties in performing the procedure were excluded. Patients who withdrew after signing the informed consent or reported pain when performing the procedure were removed from the study.

Variables

The variables evaluated included US measurement of the global ONSD and the ONSD for the right and left eye, gender, age, pupil reactivity, intracranial hypertension condition, surgical management, tomographic findings, and successful intracranial hypertension diagnosis with US measurement of the ONSD.

Data Sources/Measurement

For data collection, a tabulated data collection format was designed in IBM SPSS Statistics for Windows, version 25 (IBM Corp., Armonk, NY, USA). The format included the variables to be evaluated. The ONSD was measured with the Sonosite Turbo ultrasound scanner (SonoSite Inc., Bothell, WA, USA), using a 13 to 6 MHz linear transducer (►**Fig. 1**). During the procedure, the participants were in a relaxed supine position. The procedure was based on the proposals made by Ohle et al.[4] and by Moretti et al.[5] The US equipment was placed in front of the operator, and the US gel was applied on the upper eyelid, obtaining an image of the optic nerve in the

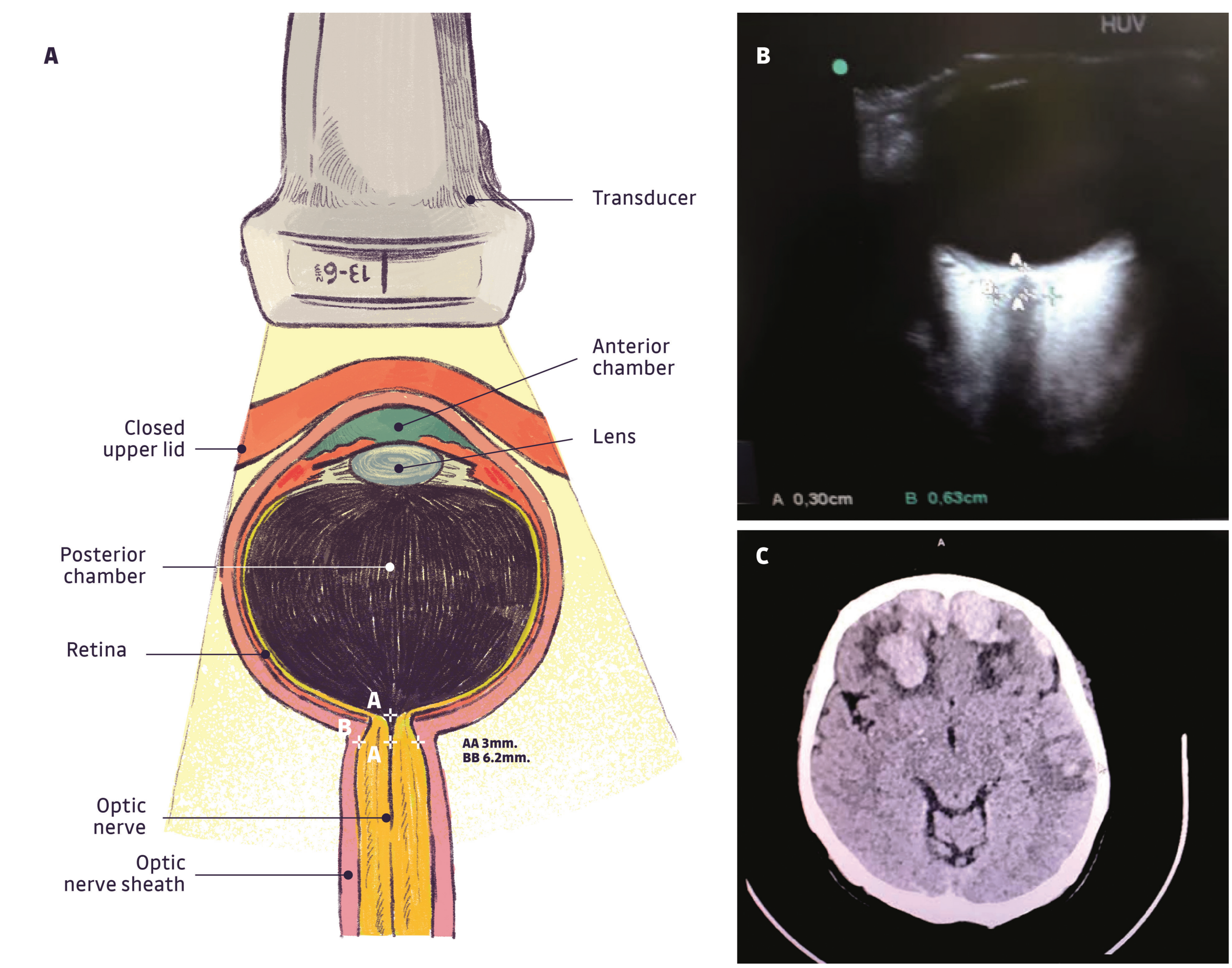


Fig. 1 (A) Illustration of ONSD measurement using the SONOSITE TURBO ultrasound scanner. (B) Ultrasonographic image of the optic nerve. (C) Tomographic image of the optic nerve.

axial plane. The ONSD measurements were performed at a depth of three behind the orbit, and three measurements were performed for each eye. The duration of the procedure was 5 minutes.

To compare the previous measurement with the tomographic images obtained from each patient, the information available in the "Integra" system was obtained. This information was part of the Hospital Universitario del Valle software for patients with symptoms of intracranial hypertension corroborated by previously mentioned tomographic findings.

Statistical Methods

A paired *t*-test was performed for independent samples (95% confidence intervals [CIs]), evaluating the distribution of the ONSD value in patients with intracranial hypertension versus the distribution of the ONSD value in the control population. In addition, a Pearson R correlation was performed between left and right ONSDs, looking to see if it is affected by the presence of anisocoria or by the spatial location of the lesion. The ONSD and age and ONSD and gender correlations were performed to assess whether the ONSD varies between the different age groups or if there are significant differences between genders. Also, it was studied if there are differences in the ONSD measurement between patients with intracranial hypertension undergoing surgical or conservative management.

The tomographic findings were used to identify signs of intracranial hypertension and were classified according to deviation from the midline, absence of cortical-subcortical differentiation, effacement of grooves, and ventricular megaly. Each of these variables was assigned a score of 1, and its sum was correlated with the ONSD value.

Several authors establish different cutoff points for the ONSD from 4.85 mm to 6.3 mm,[6,7] so it was defined by consensus a cutoff point of 5.5 mm.[8] This value was used to detect intracranial hypertension and represented a change in the CT images. This cutoff point defines the presence or absence of intracranial hypertension; a 2×2 test was performed among the population of cases and controls, looking for the sensitivity and specificity of this value in the study population. In this way, the likelihood ratio was defined, the probability of diagnosing intracranial hypertension using the ONSD measurement. Later, these data were unified in a ROC curve as a global and independent measure of the cutoff point.

Results

The data collection was performed between March 11 and October 27, 2019, at the Hospital Universitario del Valle. We recruited 50 individuals, of which 25 were patients with intracranial hypertension, and 25 individuals with no clinical history of intracranial hypertension were used as a control population. Of the intracranial hypertension group, 19 were men (76%), and the age varied between 19 and 82 years old. However, the most common age range was from 55 to 64 years old (28%). Of the control group, 16 subjects were men (64%), and the age varied between 18 and 72 years old; however, the most common age range was from 18 to 27 years old (40%).

Regarding surgical management, 18 (72%) patients with intracranial hypertension required decompressive neurosurgical management. The tomographic finding that suggested intracranial hypertension was the midline deviation, ventricular dilation compatible with hydrocephalus, effacement of the corticosubcortical relationship, and effacement of the grooves. A total of 2 tomographic findings were found in 12 (48%) patients, 1 finding in 6 (24%) patients, 3 findings in 5 (20%) patients, and 4 findings in 2 (8%) patients. A total of 22 (88%) patients presented reactive pupils. In the control group, the pupils of the 25 control individuals were reactive.

In the mean difference test of the ONSD values of the patients with hypertension, there were no significant differences between the measurements of both eyes ($p = 0.43$; 95% CI: - 0.16–0.36). Likewise, in the test for the mean difference of the ONSD values of the control individuals, there were no significant differences between the measurements of both eyes ($p = 0.89$; 95%CI: - 0.26–0.23). To compare the ONSD values of both groups, a paired *t*-test for independent samples was performed. Normality was first tested with the Shapiro-Wilk test, and homogeneity of variance with the Levene test for both groups. The paired test showed that there were significant differences between the means ($p < 0.05$; 95%CI: 1.31469–1.77331) (**►Table 1**).

In the Pearson correlation analysis between the ONSD of the right eye and the ONSD of the left eye of patients with intracranial hypertension, a coefficient of 0.68 was found, indicating a positive correlation (95%CI: 0.3816268–0.8447966). As for the control individuals, the average values of the right ONSD and the left ONSD correlated 0.58 (95%CI: 0.2333799–0.7907734). The correlation between the global ONSD values of patients with intracranial hypertension with age was - 0.20, indicating that the variables are inversely related (95%CI: - 0.5522713–0.2108760). For control individuals, a positive correlation of 0.29 between global ONSD values and age was found. Also, the correlation coefficient between the global ONSD values in patients with intracranial hypertension and the number of findings was 0.68 (95%CI: 0.3928022–0.8485192), indicating a positive correlation.

According to the results, of the 25 patients with intracranial hypertension diagnosed with CT, 24 were successfully

Table 1 Optic nerve sheath diameter values for the right and left eyes of the intracranial hypertension group and the control group

	ONSD (mm)			*p-value*
	Right eye	Left eye	Global	
Intracranial hypertension group	5.2–7.6	5.3–7.3	5.25–7.45	< 0.05
Control group	3.3–5.5	3.2–5.4	3.25–5.15	

Abbreviation: ONSD, optic nerve sheath diameter.

Table 2 Case-control study

Intracranial hypertension		Group		Total
		Cases	Controls	
	Present	24	0	24
	Absent	1	25	26
	Total	25	25	50

diagnosed with US (►**Table 2**). In addition, it was found that the specificity was high (100%), indicating that the disease will be ruled out when the result of the patient is negative. Likewise, the sensitivity was high (96%), indicating that the presence of the disease will be confirmed when a patient has a positive test result (►**Table 3**). In this case, the positive likelihood ratio, being infinite, is a measure of great magnitude since it allows us to confidently confirm the presence of intracranial hypertension when performing the measurement of ONSD by US. On the other hand, regarding the negative likelihood ratio, the lower it is, the better the study, since it rules out the disease; in this case, its value was 0.04 (►**Table 3**).

Subsequently, the patient data was unified to construct a ROC curve, finding an optimal cutoff point of 5.2 mm (►**Fig. 2**). Since the area under the curve (AUC) was 1, it can be inferred that the US ONSD measurement, used as a diagnostic test to classify patients with cranial hypertension and control patients, is ideal.

Discussion

Overall, the study indicated that US measurements of the ONSD were effective in differentiating a group with intracranial hypertension, previously diagnosed by CT scan images, from patients without this condition. However, as the study is limited by sample size, more studies should be made with a more significant sample to further validate the results. Nevertheless, the results are consistent with the findings of other studies. For instance, Blaivas et al.[9] sought to determine whether optic nerve sheath dilation, as detected

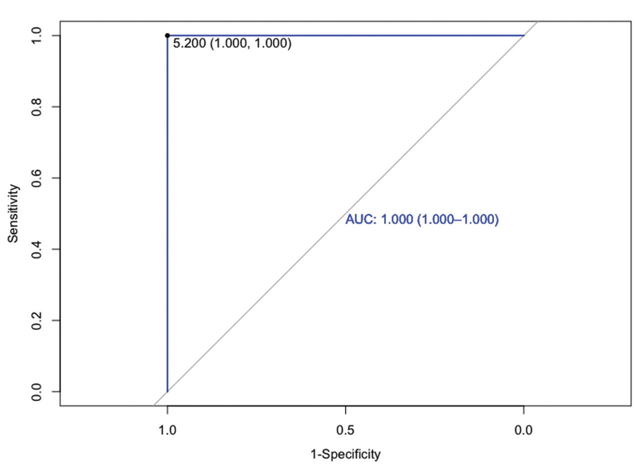


Fig. 2 ROC curve analysis.

Table 3 Characteristics of the case-control study

Characteristic	Value
Cutoff point	5.5mm
Sensitivity	96%
Specificity	100%
Positive likelihood ratio test	Infinite
Negative Likelihood ratio test	0.04
Positive predictive value	96%
Negative predictive value	100%
Area under the curve	Not built

in emergencies by the US with the Agilent Image Point Hx (Phillips, Andover, MA, USA) machine, could be reliably correlated with head CT findings suggesting elevated ICP in acute head injury patients. The authors found that all cases of CT-determined elevated ICP were correctly predicted by ONSD > 5 mm measured with US. The authors found for ONSD a sensitivity of 100% and a specificity of 95% in the measurement with US compared with CT. Likewise, Girisgin et al.[10] performed the ONSD measurement using a 7.5 MHz transducer in 28 patients with intracranial hypertension determined by CT, defined as effacement of the sulci, transfalcin herniation, and changes in the ratio of gray matter and white matter, and a control group of 26 patients without the illness. The average value of the ONSD in patients with intracranial hypertension was 6.4 mm, and 4.6 mm in control patients, finding a statistically significant difference between both groups ($p = 0.001$). The authors concluded that US use in the measurement of ONSD is helpful in the early and rapid detection of intracranial hypertension.

Moreover, Lee et al.[11] performed a multicenter study in which they identified 3 groups of patients, 1 with intracranial hypertension ($n = 81$), another with patients without intracranial hypertension ($n = 27$), and a control group ($n = 26$). The identification of intracranial hypertension, measured with a ProSound Alpha 6 13-MHz US probe (Hitachi Medical Corp., Tokyo, Japan), was extrapolated according to tomographic findings given by diffusion of cerebral sulci, significant cerebral edema, compression of cisterns, displacement of the midline, and absence in the differentiation of gray and white matter. The ONSD was significantly higher in patients with intracranial hypertension (5.9mm [5.8– 6.2]) than in those in the group without intracranial hypertension (5.2mm [4.8–5.4]) and in the control group (4.9mm [4.6–5.2]) ($p < 0.01$). There were no significant differences between patients without intracranial hypertension and the control population ($p = 0.31$). According to their results, the authors contemplated a cutoff point for ONSD of 5.5mm with a sensitivity of 99% (95%CI: 0.93–1.00) and a specificity of 85% (95%CI: 0.66–0.96%).

Ultrasound-guided ONSD measurement and ICP measurement have also been previously studied.[12–14] Cammarata et al.[15] studied 11 patients with severe head trauma admitted to an ICU with a Glasgow coma scale score < 8 points that required management with ICP monitoring. The authors measured ONSD by US with the Model Vivid Expert (General Electric Medical System, Milwaukee, WI) and found that the ONSD values among patients with ICP < 20 mmHg were similar to the values of patients without intracranial pathology. Also, the authors found a significant positive correlation between ONSD and ICP ($r = 0.74$; $p = 0.001$), concluding that ocular US may be considered as a good alternative for a rapid indirect evaluation of ICP in patients with head trauma. Similarly, Frumin et al.[16] evaluated 27 patients in a neurosurgical unit, of which 22% had an ICP > 20 mm Hg. According to the Spearman method, the authors reported a positive correlation between the ONSD measured by US with a SONOSITE M-TURBO (SonoSite Inc., Bothell, WA, USA) and intracranial hypertension AUC of 0.871 (95%CI: 0.67–0.96). Also, the authors recorded that an ONSD > 5.2 mm was a strong predictor of intracranial hypertension with a sensitivity of 83% (95%CI: 0.35–0.99) and a specificity of 100% (95%CI: 0.84–1.00).

Dubourg et al.[17] evaluated 6 studies that included 231 patients characterized by being homogeneous among themselves to compare ICP values with the measurement of the ONSD. The authors found a sensitivity of 90% (95%CI: 0.80–0.95), a specificity of 85% (95%CI: 0.73–0.93), with an AUC of 0.94% (95%CI: 0.91–0.96). With these results, they concluded that there was a correlation between the two variables and suggested using this proper US method in clinical decision-making.

Limitations

The present study has some limitations. First, given the nature of the study design used and the limited sample size, the results require further validation.

Conclusions

According to findings in the multimodal clinical context of the neurocritical patient, US would be a quick and noninvasive tool at the bedside of the patient. Therefore, it is suggested implementing US measurements to improve survival and neurological prognosis, detecting an elevated ICP in cases when CT scan images are not an available option. In addition, US measurements would allow the detection of increasing ICP before deciding an invasive neurosurgical monitoring. According to the ROC curve, the optimal cutoff point for detecting intracranial hypertension was 5.2 mm. Moreover, comparing the study that was made with others, in terms of the US machine used to measure the ONSD, it is likely that the equipment does not influence the effective results found here. Nevertheless, more studies should be made with a more significant sample to further validate the results.

Informed Consent and Patient Details

The authors declare that the present report does not contain any personal information that could identify the patient(s) or volunteers.

Presentation

Preliminary data for the present study were presented as an abstract European Anaesthesiology Congress 2020. European Journal of Anaesthesiology. 2020;37(e-Supplement 58):191

Ethics

The Institutional Committee for the Review of Human Ethics of the Universidad del Valle (Cali, Colombia) on February 28, 2019, gave the ethical approval for the present study (Ethical Committee N° 221–018).

Author Contributions

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

Funding Sources

The present research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interests

The authors have no conflict of interests to declare.

References

1 Kramer AH, Zygun DA. Neurocritical care: why does it make a difference? Curr Opin Crit Care 2014;20(02):174–181
2 Jordan CO, Aylward SC. Intracranial hypertension: a current review. Curr Opin Pediatr 2018;30(06):764–774
3 Smith M. Refractory Intracranial Hypertension: The Role of Decompressive Craniectomy. Anesth Analg 2017;125(06): 1999–2008
4 Ohle R, McIsaac SM, Woo MY, Perry JJ. Sonography of the Optic Nerve Sheath Diameter for Detection of Raised Intracranial Pressure Compared to Computed Tomography: A Systematic Review and Meta-analysis. J Ultrasound Med 2015;34(07): 1285–1294
5 Moretti R, Pizzi B. Ultrasonography of the optic nerve in neurocritically ill patients. Acta Anaesthesiol Scand 2011;55(06): 644–652
6 del Saz-Saucedo P, Redondo-González O, Mateu-Mateu Á, Huertas-Arroyo R, García-Ruiz R, Botia-Paniagua E. Sonographic assessment of the optic nerve sheath diameter in the diagnosis of idiopathic intracranial hypertension. J Neurol Sci 2016; 361:122–127
7 Amini A, Eghtesadi R, Feizi AM, et al. Sonographic Optic Nerve Sheath Diameter as a Screening Tool for Detection of Elevated Intracranial Pressure. Emergency (Tehran) 2013;1(01):15–19
8 Tayal VS, Neulander M, Norton HJ, Foster T, Saunders T, Blaivas M. Emergency department sonographic measurement of optic nerve sheath diameter to detect findings of increased intracranial pressure in adult head injury patients. Ann Emerg Med 2007; 49(04):508–514
9 Blaivas M, Theodoro D, Sierzenski PR. Elevated intracranial pressure detected by bedside emergency ultrasonography of the optic nerve sheath. Acad Emerg Med 2003;10(04):376–381
10 Girisgin AS, Kalkan E, Kocak S, Cander B, Gul M, Semiz M. The role of optic nerve ultrasonography in the diagnosis of elevated intracranial pressure. Emerg Med J 2007;24(04): 251–254
11 Lee SU, Jeon JP, Lee H, et al. Optic nerve sheath diameter threshold by ocular ultrasonography for detection of increased intracranial

pressure in Korean adult patients with brain lesions. Medicine (Baltimore) 2016;95(41):e5061

12 Sekhon MS, Griesdale DE, Robba C, et al. Optic nerve sheath diameter on computed tomography is correlated with simultaneously measured intracranial pressure in patients with severe traumatic brain injury. Intensive Care Med 2014;40(09):1267–1274

13 Raffiz M, Abdullah JM. Optic nerve sheath diameter measurement: a means of detecting raised ICP in adult traumatic and non-traumatic neurosurgical patients. Am J Emerg Med 2017;35(01):150–153

14 Jeon JP, Lee SU, Kim SE, et al. Correlation of optic nerve sheath diameter with directly measured intracranial pressure in Korean adults using bedside ultrasonography. PLoS One 2017;12(09):e0183170

15 Cammarata G, Ristagno G, Cammarata A, Mannanici G, Denaro C, Gullo A. Ocular ultrasound to detect intracranial hypertension in trauma patients. J Trauma 2011;71(03):779–781

16 Frumin E, Schlang J, Wiechmann W, et al. Prospective analysis of single operator sonographic optic nerve sheath diameter measurement for diagnosis of elevated intracranial pressure. West J Emerg Med 2014;15(02):217–220

17 Dubourg J, Javouhey E, Geeraerts T, Messerer M, Kassai B. Ultrasonography of optic nerve sheath diameter for detection of raised intracranial pressure: a systematic review and meta-analysis. Intensive Care Med 2011;37(07):1059–1068

Computed Tomography Predictors of Vascular Injury in Cranioencephalic Trauma Patients

Preditores tomográficos de lesão vascular em pacientes com traumatismo cranioencefálico

Miguel Velásquez-Vera[1,2] Juan David Rivera-García[1] Alejandro Gómez-Martínez[1] Juan Felipe Mier-García[1] Juan Camilo Salcedo-Moreno[1] Fernando Peralta-Pizza[1]

[1] Section of Neurosurgery, Universidad del Valle, Santiago de Cali, Colombia
[2] Section of Neurosurgery, Hospital Universitario del Valle, Santiago de Cali, Colombia

Address for correspondence Miguel Velásquez Vera, MD, Section of Neurosurgery, Universidad del Valle, Santiago de Cali, 760042, Colombia (e-mail: miguel.velasquez@correounivalle.edu.co).

Arq Bras Neurocir 2022;41(4):331–334.

Abstract

Objective A frequent challenge for the neurosurgeon when treating a patient with cranioencephalic trauma is to determine whether the patient has a vascular lesion, when to suspect it, and what studies to request. In this context, the objective of the present study was to identify the variables on cranial computed tomography (CT) scans that predict vascular injury in digital subtraction angiography in patients with cranioencephalic trauma.

Methods We conducted a cross-sectional study of patients with cranioencephalic trauma admitted to the Hospital Universitario del Valle between June 2016 and June 2019. Subjects with available simple CT images of the skull and digital subtraction angiography were included.

Results A total of 138 subjects who met the inclusion criteria were identified. The average age was 32 years, 82% were men, and the most frequent mechanism of injury was firearm wound (59%). The variables associated with vascular injury were fracture of the base of the temporal skull and sphenoid fracture.

Conclusion The presence of fractures of the base of the temporal skull and sphenoid fractures is associated with vascular injury in patients with cranioencephalic trauma.

Keywords

- traumatic brain injuries
- vascular system injuries
- X-ray computed tomography

Resumo

Objetivo Um desafio frequente para o neurocirurgião no cuidado de um paciente com traumatismo crânio-encefálico é determinar se o paciente tem lesão vascular, quando suspeitar que tem, e quais estudos pedir. Neste contexto, o objetivo deste estudo foi identificar as variáveis da tomografia computadorizada (TC) de crânio que predizem lesão vascular na angiografia por subtração digital em pacientes com traumatismo crânio-encefálico.

received
April 19, 2021
accepted
July 30, 2021

DOI https://doi.org/10.1055/s-0041-1739275.
ISSN 0103-5355.

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

Métodos Fez-se um estudo transversal de pacientes com traumatismo crânio-encefálico internados no hospital (cego) entre junho de 2016 e junho de 2019. Foram incluídos também pacientes com imagens de TC simples do crânio e angiografia de subtração digital disponíveis.

Resultados Foram identificados um total de 138 sujeitos que cumpriam os critérios de inclusão. A média de idade foi de 32 anos, 82% eram homens, e o mecanismo da lesão mais frequente foi o ferimento por arma de fogo (59%). As variáveis associadas à lesão vascular foram a fratura da base do crânio temporal e a fratura esfenoidal.

Conclusão A presença de fraturas da base do crânio temporal e fraturas do esfenoide está associada à lesão vascular em pacientes com traumatismo crânio-encefálico.

Palavras-chave
- lesões encefálicas traumáticas
- lesões do sistema vascular
- tomografia computadorizada por raios X

Introduction

Cerebrovascular injuries associated with cranioencephalic trauma can be classified according to their location, which can be extracranial or intracranial.[1] They are caused by external forces to the skull or neck and their contents,[2] compromising the microvasculature, the great vessels, or both.[3] The present study focuses on intracranial lesions, whose diagnosis is challenging. The most frequently occurring intracranial vascular lesions are pseudoaneurysms,[4,5] venous sinus thrombosis, arterial dissections, and arteriovenous fistulas, the most frequent of which is cavernous carotid fistula.

A frequent challenge for the neurosurgeon when treating a patient with cranioencephalic trauma is to determine whether the patient has a vascular lesion, when to suspect it, and what studies to request.[6] There are recommendations or criteria for screening in the literature, such as those of the Japanese guidelines for the management of cranioencephalic trauma.[2] According to some authors, the true positive rates of these screening methods are only between 31.3% and 42%.[2] Therefore, complementary clinical and radiological criteria should be established to more accurately determine who will benefit from additional studies or interventions to clarify the presence of a vascular lesion.[7] Such efforts are of utmost importance because, despite their low prevalence of approximately 1%, these pathologies are accompanied, in a large extent, by hemorrhagic and ischemic complications in up to 50% of the cases if the pathology involves the internal carotid artery, and in $\sim$ 25% of the cases if the vertebral arteries are involved.[8]

In this context, the present study aimed to characterize the radiological findings on simple computed tomography (CT) scans of the skull that are most frequently associated with intracranial vascular lesions in patients with cranioencephalic trauma.

Materials and Methods

A cross-sectional, retrospective study was conducted. Through convenience sampling, we included patients with cranioencephalic trauma and with suspected vascular injury who were admitted to the Hospital Universitario del Valle between June 2016 and June 2019 and underwent simple CT and digital subtraction angiography. The present study was conducted in accordance with the Declaration of Helsinki, and adhered to the Good Clinical Practice guidelines.

A descriptive analysis was performed. For the continuous variables, measures of central tendency were estimated, and, for the categorical variables, frequencies and percentages were calculated. The distribution of the variables was verified by histograms and box and whisker plots.

A univariate analysis was performed using logistic regression to establish the association between the TC and angiography findings. In addition, a multivariate analysis was performed using logistic regression with stepwise selection and an inclusion probability of 0.1. Statistical analyses were performed with the Stata (StataCorp LLC, College Station, TX, United States) software, version 3.

Results

A total of 138 subjects were identified from the search of the trauma registry databases of the Hospital Universitario del Valle and the angiography service of the institution Hospital Universitario del Valle. A total of 138 subjects were included, and 82% were men ($n = 112$) with an average age of 32.1 ± 16.04 years. The most frequently reported trauma mechanism was gunshot wound, reported in 59% of the cases ($n = 81$), followed by blunt trauma, reported in 36% of the cases ($n = 49$), and sharps injury, reported in 5% of the cases ($n = 7$).

The results of the logistic regression showed an association between temporal fractures and the presence of lesions on angiography (odds ratio [OR]: 2.1; 95% confidence interval [95%CI]: 0.98 to 4.53), and no association regarding the location of bleeding or fractures. Concerning the Glasgow coma scale (►**Fig. 1**), 66 patients (48.18%) presented a Glasgow of 15 on admission, and 23 patients had a Glasgow of 8 or lower on admission (16.79%); on the other hand, 48 patients were admitted with a Glasgow between 9 and 14 (35.1%).

A regression analysis was performed to evaluate the association with venous sinus injury, and a significant relationship with fractures of the temporal base and of the sphenoid bone (►**Table 1**) was found. No statistically significant association was found with pseudoaneurysm. In the

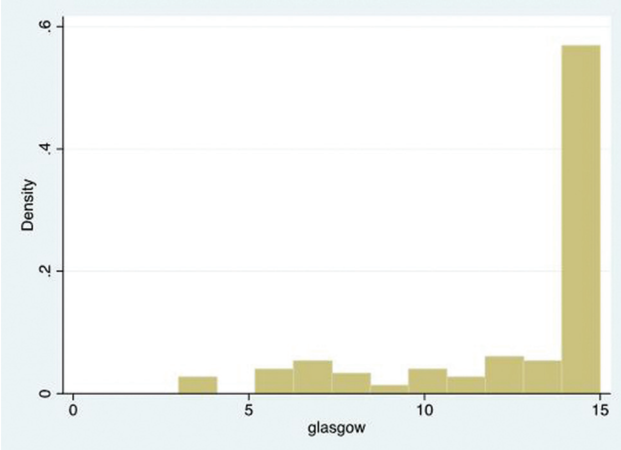


Fig. 1 Distribution of Glasgow scores upon admission.

multivariate analysis to evaluate the association with the incidence of vascular dissection, a relationship was found with temporal base fractures (OR: 4.6; 95%CI: 1.4 to 14.9), but not with sphenoid hemosinus.

Discussion

The present study evaluated different markers on simple cranial CT scans to establish their association with the presence of vascular lesions, and found that temporal base fractures are associated with the diagnosis of arterial dissection and venous sinus lesions. Traumatic pseudoaneurysms are lesions in which all the layers of the vessel are compromised; they are classified as false aneurysms. Pseudoaneurysms generate the formation of a hematoma, which is transformed into a material rich in collagen and presents the appearance of an aneurysmal sac on neuroimaging studies. In contrast, in a true traumatic aneurysm, the adventitia of the vessel is preserved.[9] The clinical manifestations of aneurysms and traumatic pseudoaneurysms might include intracranial bleeding or persisting epistaxis, decreased visual acuity, and headache. There are specific radiological findings on the simple cranial CT scan that enable the suspicion of a vascular lesion, including the presence of projectile fragments near the base of the skull, the presence of a hematoma near the site of entry of the penetrating trauma,[10] and intracranial hemorrhage. The treatment of this condition is usually transcranial or endovascular surgical management.[9]

Regarding arteriovenous fistulas, the most common location is between the internal carotid artery (ICA) and the cavernous sinus.[11] The pathophysiology is based on the transmission of energy and torsional forces to the cavernous ICA at its point of dural fixation to the clinoid process. The compromise is usually unilateral, and the symptoms and signs are generated by the compromise of the venous drainage of the orbit and the increase in intraorbital pressure, which causes proptosis, limitations to extraocular movements, diplopia, chemosis, orbital murmur, and scleral injection.[9] An important and rare complication of fistulas is intracranial hemorrhage secondary to cortical venous

Table 1 Logistic regression for venous sinus injury

Variable	Odds ratio	95% confidence interval	*p*-value
Temporal skull base fracture	4.3	1.6–11.8	0.004
Sphenoid skull base fracture	0.09	0.01–0.72	0.023

hypertension, which is an emergency, and management is usually interventional.[12] Carotid-cavernous fistulas can be classified as direct or indirect; the latter occurs when there is substitution of the dural branches of the external or internal carotid.[11] The Barrow classification establishes that fistulas can be classified as: type A, when they are direct and have high flow without supply from the external carotid; type B, when they have low flow from the meningeal-feeding branches of the internal carotid; type C, when they have low flow and are fed exclusively by the internal carotid; and type D, when they have low flow but are fed by branches of the internal and external carotid.[10]

Vascular injuries secondary to head trauma are associated with complications with a very high percentage of morbidity and mortality, and present a diagnostic challenge because they can be asymptomatic; therefore, it is necessary to include different radiological criteria in the diagnostic process. Among the criteria that help determine the need to perform a vascular study is the Denver scale for closed trauma.[13] It is widely known that the "gold standard" for ruling out a traumatic vascular injury is cerebral angiography with digital subtraction, which has greater diagnostic capacity in the case of pathologies such as aneurysms and pseudoaneurysms.[14] However, the current recommendation is to perform CT angiography with a minimum of 16 channels, a procedure that has decreased the rate of associated infarcts from 15.2% to 3.8%.[13] With this measure, the time between diagnosis and the start of treatment has been shortened, since cranial CT scan is a technique that can be rapidly performed and has great value for determining vascular lesions.[15] This radiodiagnostic method can be implemented as a predictor of intracerebral vascular lesions.[13]

Conclusions

The limitations of the present study lie in its retrospective nature and its limited power due to the sample size. Prospective studies with larger samples could identify additional predictors. Given the results obtained from the present study, it can be concluded that the presence of temporal and sphenoid skull base fracture can predict the finding of venous sinus injury. In addition, fractures of the base of the temporal skull are associated with arterial dissections.

Informed Consent and Patient Details

The authors declare that this report does not contain any personal information that could lead to the identification of the patient(s) and/or volunteers.

Author Contributions

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for authorship.

Funding Sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interests

The authors have no conflict of interests to declare.

References

1 Monson KL, Converse MI, Manley GT. Cerebral blood vessel damage in traumatic brain injury. Clin Biomech (Bristol, Avon) 2019;64:98–113
2 Kobata H. Diagnosis and Treatment of Traumatic Cerebrovascular Injury: Pitfalls in the Management of Neurotrauma. Neurol Med Chir (Tokyo) 2017;57(08):410–417
3 Tunthanathip T, Phuenpathom N, Saehaeng S, Oearsakul T, Sakarunchai I, Kaewborisutsakul A. Traumatic cerebrovascular injury: Prevalence and risk factors. Am J Emerg Med 2020;38(02):182–186
4 Abdalkader U, Kaliaev A, Nguyen T. Endovascular Management of Ruptured Traumatic Middle Meningeal Artery Pseudo aneurysm and Arteriovenous Fistula. J Vasc Endovasc Ther. 2019;4(02):1–4
5 Zheng Y, Lu Z, Shen J, Xu F. Intracranial Pseudoaneurysms: Evaluation and Management. Front Neurol 2020;11:582
6 Amorim RL, Morais BA, Pereira FOC, et al. Evaluation of Head Computed Tomography Assessment of Brain Swelling after Acute Traumatic Brain Injury: A Pilot study. Arq Bras Neurocir Brazilian Neurosurg. 2019;38(04):257–262
7 Alons IME, Goudsmit BFJ, Jellema K, van Walderveen MAA, Wermer MJH, Algra A. Prediction of vascular abnormalities on CT angiography in patients with acute headache. Brain Behav 2018;8(06):e00997
8 Miley JT, Rodriguez GJ, Qureshi AI. Traumatic Intracranial Aneurysm Formation following Closed Head Injury. J Vasc Interv Neurol 2008;1(03):79–82
9 Larsen DW. Traumatic vascular injuries and their management. Neuroimaging Clin N Am 2002;12(02):249–269
10 Guyot LL, Kazmierczak CD, Diaz FG. Vascular injury in neurotrauma. Neurol Res 2001;23(2-3):291–296
11 Torres Zambrano M, Rubio Rodríguez W, Conde Cardona G, et al. Síntomas neurológicos de fístula carotídeo carvenosa: reporte de caso. Acta Neurol Colomb 2017;33(04):274–278
12 Fusco MR, Harrigan MR. Cerebrovascular dissections: a review. Part II: blunt cerebrovascular injury. Neurosurgery 2011;68(02):517–530, discussion 530
13 Brommeland T, Helseth E, Aarhus M, et al. Best practice guidelines for blunt cerebrovascular injury (BCVI). Scand J Trauma Resusc Emerg Med 2018;26(01):90
14 Catapano JS, Lang MJ, Koester SW, et al. Digital subtraction cerebral angiography after negative computed tomography angiography findings in non-traumatic subarachnoid hemorrhage. J Neurointerv Surg 2020;12(05):526–530
15 Mata-Mbemba D, Mugikura S, Nakagawa A, et al. Early CT findings to predict early death in patients with traumatic brain injury: Marshall and Rotterdam CT scoring systems compared in the major academic tertiary care hospital in northeastern Japan. Acad Radiol 2014;21(05):605–611

Study on Outcome Analysis of Transforaminal Interbody Fusion with Transpedicular Screws and Rods in Lumbar Spondylolisthesis and Spondylolysis

Estudo sobre análise de resultados de fusão intersomática transforaminal com parafusos e hastes transpediculares na espondilolistese e espondilólise lombar

Prakash Mahantshetti[1] Prasad Soraganvi[2] Rayadurg Palegar Raghavendra Raju[3]

[1] Department of Neurosurgery, Jawaharlal Nehru Medical College, Belgaum, Karnataka, India
[2] Department of Orthopedics, P.E.S. Institute of Medical Sciences and Research, Kuppam, Andhra Pradesh, India
[3] Department of Orthopedics, MS Naidu Hospital, Vijayawada, Andhra Pradesh, India

Address for correspondence Prakash Mahantshetti, MS, MCh, Department of Neurosurgery, JN Medical College: Jawaharlal Nehru Medical College, R.C Nagar 2nd stage Belagavi, Karnataka- 590006, India (e-mail: drprakashsm@gmail.com).

Arq Bras Neurocir 2022;41(4):e335–e339.

Abstract

Introduction The management of spondylolisthesis and spondylolysis is primarily conservative or surgical. There are various surgical procedures available for spondylolisthesis.

Objective To evaluate the functional outcome and efficacy in patients undergoing transforaminal lumbar interbody fusion with transpedicular screws and rods in symptomatic lumbar spondylolisthesis and spondylolysis.

Methods From 2017 to 2018, a prospective observational study was performed in a tertiary care hospital. The preoperative evaluation was performed both clinically and radiologically. Based on indications, transforaminal interbody fusion was performed. A total sample of 20 patients was included. The primary outcome variables were the visual analogue scale (VAS), the Oswestry Disability Index (ODI), slip percentage, and disc height at follow-up. For the statistical analysis, coGuide (BDSS CORP, Bangalore, Karnataka, India) was used.

Results In 20 participants studied, the mean age was 48.25 ± 5.35 years old. Degenerative spondylolisthesis was seen in 60% of the participants. The majority (70%) of the patients had grade 2 slips. The mean difference of the VAS, the ODI, slip

Keywords
- ► spondylolisthesis
- ► spondylolysis
- ► intervertebral disc degeneration

received
May 30, 2021
accepted
September 6, 2021

DOI https://doi.org/10.1055/s-0041-1740167.
ISSN 0103-5355.

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

percentage, and disc height between the preoperative and postoperative periods was statistically significant ($p < 0.001$). The majority (70%) of the patients had no complications after the procedure.
Conclusions Transforaminal interbody fusion with pedicle screws and rods is a safe, simple procedure and has less morbidity. This procedure also provides better functional outcomes and reduction in symptoms by maintaining the disc height and providing sagittal balance.

Resumo

Introdução O tratamento da espondilolistese e espondilólise é principalmente conservador ou cirúrgico. Existem vários procedimentos cirúrgicos disponíveis para espondilolistese.
Objetivo Avaliar o resultado funcional e a eficácia em pacientes submetidos a fusão intersomática lombar transforaminal com parafusos e hastes transpediculares em espondilolistese e espondilólise lombar sintomática.
Métodos De 2017 a 2018, foi realizado um estudo observacional prospectivo em um hospital terciário. A avaliação pré-operatória foi feita clínica e radiologicamente. Com base nas indicações, a fusão intersomática transforaminal foi feita. Uma amostra total de 20 pacientes foi incluída. As variáveis de desfecho primárias foram a escala visual analógica (EVA), o Oswestry Disability Index (ODI, na sigla em inglês), porcentagem de escorregamento e altura do disco no acompanhamento. Para análise estatística, foi utilizado o coGuide (BDSS CORP, Bangalore, Karnataka, Índia).
Resultados Nos 20 participantes estudados, a média de idade foi de $48,25 \pm 5,35$ anos. Espondilolistese degenerativa foi observada em 60% dos participantes. A maioria (70%) dos pacientes apresentou deslizamentos de grau 2. A diferença média da EVA, do ODI, da porcentagem de escorregamento e da altura do disco entre os períodos pré- e pós-operatório foi estatisticamente significativa ($p < 0,001$). A maioria (70%) dos pacientes não apresentou complicações após o procedimento.
Conclusões A fusão intersomática transforaminal com parafusos pediculares e hastes é um procedimento seguro, simples e de menor morbidade. Este procedimento também fornece melhores resultados funcionais e redução dos sintomas, mantendo a altura do disco e proporcionando equilíbrio sagital.

Palavras-chave
- espondilolistese
- espondilólise
- degeneração do disco intervertebral

Introduction

In the evolution of humans to an upright posture, human beings have developed a pelvis system that acts as a key structure within the locomotor system. During the course of human development, various developmental modifications have happened around the skeleton of the pelvis. These developments have also increased the susceptibility to degeneration.[1] Spondylolisthesis is one such degenerative condition that occurs due to the forward slippage of the cephalad vertebra on a caudal vertebra.[2] It is one of the common causes of lower back pain in the adult population. The treatment of the symptomatic cases is either conservative or surgical.[3] Bone healing, pain relief, and optimization of physical activity are the three major objectives of the management modality. Various surgical interventions are available for management, such as posterior lumbar interbody fusion (PLIF) and anterior lumbar interbody fusion (ALIF).[4,5] In 1982, a technique devised by Harms et al. was termed transforaminal lumbar interbody fusion (TLIF), in which a bone graft filled in a titanium cage was inserted through the transforaminal route.[6] Transforaminal lumbar interbody fusion is one such technique in which the anterior and posterior columns are fused through a posterior approach. The anterior segment is stabilized using a bone graft and spacer, whereas the posterior segment is stabilized using rods, pedicle screws, and bone graft.[2] The main advantage of this technique is that it restores the disc space and maintains the lumbar lordosis and sagittal balance. It provides another advantage of conserving the posterior segment on the opposite side, thereby increasing the surface area for laminal fusion. When compared with other surgical techniques, TLIF has lesser nerve and dual damage and also provides better fusion.[7] In a study by Balasubramanian et al., clinical and radiological correlations were performed and the study showed that 85% of the participants showed good clinical outcome at the end of 1 year.[8] Previously available literature has shown that symptomatic lumbar spondylolisthesis and spondylolysis can be efficiently managed by TLIF.[5,7,9,10] There is a gap in the available literature regarding the functional outcome of the patient in the postoperative period. Hence, the present study was planned to fill in this gap. The present study was performed to evaluate the functional outcome in symptomatic lumbar spondylolisthesis and spondylolysis patients treated by TLIF using transpedicular screws and rods.

Materials and Methods

In a tertiary care hospital, a prospective observational study was performed from 2017 to 2018. Twenty participants were enrolled in the study. Informed written consent forms were signed and baseline clinical examination was done. Clearance of the institutional ethical committee was obtained prior to the start of the study. Data confidentiality was maintained. Baseline clinical and radiological evaluations were done. Patients who had intractable pain, progressive slip, slip $\geq$ 25% on presentation, neurological deficit-claudication, significant gait disturbance, cosmetic or postural disturbance, and significant motion in dynamic X-rays were taken up for transforaminal interbody fusion. Patients $>$20 years old with isolated symptomatic lumbar spondylolisthesis of any grade with or without spinal canal stenosis, as well as patients who were willing to undergo surgery were included in the study. Patients with severe osteoporosis and vertebral pathologies were excluded.

The sample size was calculated with the assumption of an expected mean difference in the outcome before and after intervention of 5.3 and a standard deviation of 4.5 according to the previous study by Reddy et al.[1] The power of the study was kept at 90% with a 5% two-sided α error. The sample size was determined by using the formula as proposed by Kirkwood et al.[11] The required sample size, according to the aforementioned calculation, was 16. To make up for a nonparticipation rate of $\sim$ 30%, 3 participants were added to the sample size. Hence, the total sample size was 19 subjects.

Both anteroposterior and lateral films were taken. When slippage or pars defect was not clear, oblique (45° angled) radiographs were taken. In high-grade spondylolisthesis, the slippage appears as 'invented Napoleon's hat', and in pars defect, the 'Scottie dog' pattern is seen.

Transpedicular Screw Placement

For the entry point into the lumbar pedicle, the Roy-Camille technique was used. In the Roy-Camille method, the location of the entry point is by the intersection of the midtransverse process line and the superior facet midline. These bony landmarks are easily identified during surgery. The entry points were identified under C-Arm guidance, and screws were placed through the pedicle into the body. Monoaxial and polyaxial screws were used for instrumentation. Sacral screws were placed parallel to the sacral endplate with bicortical purchase. Unilateral laminectomy and unilateral facetectomy were performed. Using an intervertebral distractor and a nerve root distractor, the disc was approached through the transforaminal route, and complete discectomy was performed. Endplates were thoroughly scraped. The adequate reduction was attempted by distraction after placing the titanium rod, and the upper body was moved in a cranial and posterior direction by rotatory movements. The spinous process and lamina bone graft were made into small pieces and placed in the interbody space so that they fit snugly in the titanium cages placed in the interbody space. The closure was performed in multiple layers-paraspinal muscle fascia and subcutaneous tissue with Vicryl and skin with Ethilon under a negative suction drain. The preoperative and postoperative comparison was made of the various study parameters.

The visual analogue scale (VAS) and the Oswestry Disability Index (ODI) were the primary outcome measures used. Preoperative measurements were corroborated with postoperative measurements and compared with the effectiveness of the surgery.

Statistical Methods

The primary outcome variables were the VAS, the ODI, slip percentage, and disc height at follow-up. Age, gender, duration of symptoms, complications, etc., were kept as other relevant variables. The description of the data was represented by mean and standard deviation (SD). Statistical significance was considered with $p < 0.05$. coGuide (BDSS CORP, Bangalore, Karnataka, India) version V.1.0 statistical software was used.

Results

Twenty patients were included for the final analysis.

Among the study subjects, the mean age was 48.25 ± 5.35 years old, ranging from 22 59 years old. Regarding the duration of symptoms, 11 (55%) patients had symptoms for $<$36 months and 9 (45%) of them had symptoms for $\geq$36 months; 20 (100%) of them had lower back pain, 14 (70%) had radiculopathy, 7 (35%) had claudication, and 11 (55%) had comorbid conditions. Regarding the level of slippage, 11 (55%) had L5-S1, and 9 (45%) had L4-L5. Regarding the grade of slippage, 14 (70%) had grade 2, and 5 (25%) had grade 3 (►**Table 1**).

Among the study population, the mean preoperative VAS score was 7.50 ± 1.05, and the mean postoperative VAS score was 2.20 ± 1.19. The mean difference in the VAS score between the two periods was statistically significant, ($p < 0.001$). The mean difference for ODI, slip percentage, and disc height between the two periods was statistically significant, with a high preoperative ODI of 59.11 ± 8.65 compared with a postoperative ODI of 33.10 ± 9.69 ($p < 0.001$), (►**Table 2**).

Discussion

The most common spondylolisthesis type among the study participants was degenerative. Although many procedures exist for the management of spondylolisthesis, achieving disc stability and postoperative pain reduction is the main aim of performing a procedure. Transpedicular screw fixation with interbody fusion is one of the procedures with advantages such as high fusion rate, early postoperative mobilization of

Table 1 Descriptive analysis of baseline parameters in the study population ($n = 20$)

Parameter	Summary statistics
Age (years old)	48.25 ± 5.35 (22–59)
Age (years old)	
30–40	01 (5%)
41–50	10 (50%)
51–60	09 (45%)
Gender	
Male	09 (45%)
Female	11 (55%)
Type of spondylolisthesis	
Degenerative	12 (60%)
Isthmic	7 (35%)
Traumatic	1 (05%)
Duration of symptoms (months)	
< 36 months	11 (55%)
≥ 36 months	9 (45%)
Lower back pain - present	20 (100%)
Radiculopathy - present	14 (70%)
Claudication - present	7 (35%)
Comorbid conditions - present	11 (55%)
Level of slip	
L4-L5	09 (45%)
L5-S1	11 (55%)
Grades of slip	
Grade 1	01 (5%)
Grade 2	14 (70%)
Grade 3	05 (25%)
Spacer	
Bone graft	15 (75%)
Titanium cage	05 (25%)
Fusion	
Fusion	18 (90%)
Pseudo arthroses	02 (10%)
Rate of fusion	4.85 ± 2.05 (1–8)
Complications	
Implant related	01 (5%)
Infection	02 (10%)
Others	03 (15%)
No complications	14 (70%)

Table 2 Comparison of outcome parameters between the preoperative and postoperative periods ($n = 20$)

Parameter	Periods		*p-value*
	Preoperative	Postoperative	
VAS	7.50 ± 1.05	2.20 ± 1.19	< **0.001**
ODI	59.11 ± 8.65	33.10 ± 9.69	< **0.001**
Slip percentage	44.65 ± 15.01	18.75 ± 7.52	< **0.001**
Disc height	8.96 ± 0.17	10.69 ± 0.18	< **0.001**

Abbreviations: ODI, Oswestry Disability Index; VAS, visual analogue scale.

the patient, and lack of need for orthoses postoperatively.[1] The foremost findings of the present study were that the mean difference in the VAS between the preoperative and postoperative periods was statistically significant ($p < 0.001$), and that the mean difference in the ODI, slip percentage, and disc height between the preoperative and postoperative period were also statistically significant ($p < 0.001$).

In the present study, most prevalent age group ranged from 41 to 50 years old. Degenerative spondylolisthesis was the most common among the study participants. Similar findings were observed by Reddy et al.[1] in whose study the most commonly affected group was in the range between 40 and 50 years old. In the present study, the most common type of spondylolisthesis was degenerative, followed by isthmic and traumatic. Similar findings were also observed by Soren et al.,[9] in whose study 62.4% of the participants had degenerative spondylolisthesis. In the present study, 55% of the participants had a level of slippage at L5-S1. A similar level of slippage was observed by Vekatesh et al.[1] and Kalichman et al.[10] In these two studies, the slippage level at L5-S1 was due to degenerative spondylolisthesis, whereas in isthmic listhesis the slippage level L4-L5. Invariably, all participants of the present study had lower back pain, similar to other studies.[13,14] In a study by Möller et al.,[15] 62% of the study participants had lower back pain with sciatica. Most commonly, spondylolisthesis presents with two types of symptoms. The back symptoms, like lower back pain, are caused due to mechanical pain, and the patient will feel better with fixation, whereas the leg symptoms, such as sciatica, tingling, and numbness caused due to nerve compression, will respond well to a decompression procedure. Ironically, the back pain of the spondylolisthesis disappears once there occurs spontaneous fusion of the spondylolisthesis segment. The leg symptoms associated with spondylolisthesis is caused due to canal compromise caused due to disc prolapse and also due to ligamentum flavum hypertrophy. The relief of these symptoms can be achieved by wide decompression. In all study participants, wide laminectomy and discectomy were performed to achieve adequate decompression.

Despite the available evidence, the management of lumbar spondylolisthesis remains controversial due to lack of absolute success by any single modality. There are several other techniques, such as anterior interbody fusion (ALIF), extreme lateral interbody fusion (XLIF), and posterolumbar interbody fusion (PLIF). Achieving symptomatic relief from pain, removal of neurological defects, and improving stability remains the main objectives of treatment. Transforaminal lumbar interbody fusion with transpedicular screws and rods has been successful in producing a functional outcome postoperatively. In the present study, there was a statistically significant difference in the VAS, the ODI. slip percentage, and disc height in the preoperative and postoperative periods. This indicates that the operative procedure has addressed the aforementioned objectives. Similar efficacy and functional outcomes have been documented in previous literature.[1,2,13,14] The present adds evidence to support that TLIF with transpedicular screws and rods provides the best functional outcome.

The limitation of the present study was that it was based on a small sample from a single center. Multicentric studies comparing the efficacy of other treatment modalities in the management of spondylolisthesis and spondylolysis are recommended in the future.

Conclusion

Transformational interbody lumbar fusion with transpedicular screws and rods is a safe and effective management option for degenerative spondylolisthesis and spondylosis. It provides a good functional outcome through pain relief and improves quality of life.

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

Acknowledgments
We acknowledge the technical support in data entry, analysis and manuscript editing by “Evidencian Research Associates.”

References

1 Reddy VVR, Chathrapathi H, Amar JFunctional outcome analysis of transforaminal lumbar interbody fusion using transpedicle screws and rods in the management of symptomatic lumbar spondylolisthesis and spondylolysis. Int J Sci Res 2020;9:40–43
2 Premkumar DT, Thirumalaimurugan DP. A study on functional outcome of transforaminal lumbar interbody fusion in spondylolisthesis. Int J Orthop Sci. 2018;4:637–643
3 Beutler WJ, Fredrickson BE, Murtland A, Sweeney CA, Grant WD, Baker D. The natural history of spondylolysis and spondylolisthesis: 45-year follow-up evaluation. Spine (Phila Pa 1976) 2003;28(10):1027–1035, Discussion 1035
4 Schnee CL, Freese A, Ansell LV. Outcome analysis for adults with spondylolisthesis treated with posterolateral fusion and transpedicular screw fixation. J Neurosurg 1997;86(01):56–63
5 Zdeblick TA. A prospective, randomized study of lumbar fusion. Preliminary results. Spine 1993;18(08):983–991
6 Harms J, Rolinger H. [A one-stager procedure in operative treatment of spondylolistheses: dorsal traction-reposition and anterior fusion (author’s transl)]. Z Orthop Ihre Grenzgeb 1982;120 (03):343–347
7 Dehoux E, Fourati E, Madi K, Reddy B, Segal P. Posterolateral versus interbody fusion in isthmic spondylolisthesis: functional results in 52 cases with a minimum follow-up of 6 years. Acta Orthop Belg 2004;70(06):578–582
8 Balasubramanian VA, Douraiswami B, Subramani S. Outcome of transforaminal lumbar interbody fusion in spondylolisthesis-A clinico-radiological correlation. J Orthop 2018;15(02): 359–362
9 Soren A, Waugh TR. Spondylolisthesis and related disorders. A correlative study of 105 patients. Clin Orthop Relat Res 1985; (193):171–177
10 Kalichman L, Kim DH, Li L, Guermazi A, Berkin V, Hunter DJ. Spondylolysis and spondylolisthesis: prevalence and association with low back pain in the adult community-based population. Spine 2009;34(02):199–205
11 BR K. Essentials of medical statistics. 2 ed. London: Blackwell Scientific Publications; 1988:1–513 p.
12 Venkatesh , Chathrapathi HAJ, R R VFunctional outcome analysis of transforaminal lumbar interbody fusion using transpedicle screws and rods in the management of symptomatic lumbar spondylolisthesis and spondylolysis. Int J Sci Res 2020; 9:40–43
13 Yan DL, Pei FX, Li J, Soo CL. Comparative study of PILF and TLIF treatment in adult degenerative spondylolisthesis. Eur Spine J 2008;17(10):1311–1316
14 Yehya A. Tlif Versus Plif In Management Of Low Grade Spondylolisthesis. Alex J Med 2010;46:127–134
15 Möller H, Hedlund R. Instrumented and noninstrumented posterolateral fusion in adult spondylolisthesis–a prospective randomized study: part 2. Spine 2000;25(13):1716–1721

The Learning Curve in Skull Base Surgery Part 1– From Historical-Philosophical Concepts to Microsurgical Lab Training

Gustavo Rassier Isolan[1,2,3] Jander Monteiro[1] Marco Antônio Schlindwein Vaz[1] Joel Lavinsky[1,3,4] Ricardo Lopes de Araújo[5] Giuseppe Santis[1] Eberval Gadelha Figueiredo[6] Viviane Buffon[1,2] Carmem Austrália Paredes Ribas Filho[2] Jurandir Marcondes Ribas Filho[2] Osvaldo Malafaia[2]

[1] The Center for Advanced Neurology and Neurosurgery (CEANNE), Brazil
[2] Evangelical Mackenzie University of Paraná, Bigorrilho, Curitiba, PR, Brazil
[3] The Center for Neurotology and Acoustic Neuroma (CNNA), Porto Alegre, Brazil
[4] Lavinsky Clinic, Porto Alegre, Brazil
[5] Department of Neurological Surgery, Laboratory of Surgical Innovations for Skull Base Microneurosurgery, Weill Cornell Medical College, New York, NY, USA
[6] Department of Neurosurgery, University of São Paulo, São Paulo, SP, Brazil

Address for correspondence Gustavo Rassier Isolan, MD, PhD, CEANNE, Rua Dr Vale 234. Porto Alegre, RS 90560-010, Brazil (e-mail: gustavo.isolan@fempar.edu.br).

Arq Bras Neurocir 2022;41(4):ee340–ee347.

Abstract

The learning curve reflects surgeons' experience in managing several patients with the same disease. In skull base surgery, the professional's place on the curve could be related to the number of times the same procedure was performed. Where does curve begin? What amount of training is necessary prior to its application in surgical settings? What were the results of the first few skull base tumor surgeries performed by a surgeon who goes on to produce excellent results, and how is reflected in the start of their learning curve? The only way for neurosurgeons to improve their results from the start is with prior training in the microsurgery laboratory. This learning technique is essential to maximize the chance of success of a neurosurgical procedures, minimizing the morbidity rate to which patients are subjected by less experienced neurosurgeons. This article is divided in two parts, and its purpose is to show how training in the microsurgical laboratory fits into the construction of knowledge about skull base surgery, based on authors' experience and reflections. This first part discusses the technical, psychological, and philosophical aspects of medical knowledge, primarily addressing those training in skull base surgery, the principles of some selected philosophical currents, and their influence on the development of current medical knowledge.

Keywords
- skull-base
- learning curve
- microsurgical laboratory

This paper, divided in two parts, is a tribute to Professor Evandro de Oliveira, MD, PhD. (1945 - 2021).

received
July 29, 2022
accepted
August 18, 2022

DOI https://doi.org/10.1055/s-0042-1758220.
ISSN 0103-5355.

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

Introduction

The learning curve, as applied to the surgical sciences, could reflect one's experience in managing several patients treated surgically for the same pathology.[1] In skull base surgery, the surgeon's place on the curve could be related to the number of times the same procedure was performed, for example, in treating vestibular schwannoma. Alternatively, the procedure's execution within a subgroup of the disease, or even the surgical approach, such as in the middle fossa, used to treat a small vestibular schwannoma.

We should first consider the ethical challenge encountered at the base of this curve when residents, young surgeons, and even more experienced professionals take on technically challenging procedures that are new to them. Where should this curve begin? What amount of training is necessary prior to its ascent? What were the results of the first few skull base tumor surgeries performed by a surgeon who goes on to produce excellent results, and how should this be reflected in the start of their learning curve?

Similarly, what are the results of young neurosurgeons employing their first extended endoscopic approaches for tumor resection at the anterior skull base? Or the outcome of aneurysm surgeries? How did their first neural or vascular anastomoses go? Or their first petroclival meningiomas? Many more examples could be cited.

However, with regard to a large number of neurosurgical procedures, perhaps the only way for neurosurgeons to improve on their results from the start of their career is training in the microsurgery laboratory.[2–5] This learning technique is essential to maximize the chance of success of a neurosurgical procedure. Furthermore, to minimize the morbidity rate to which patients are subjected to by less experienced neurosurgeons, this dictum should be heeded: "A neurosurgeon's first surgery should commence only after they have completed their 100th corpse dissection." Combined with training in neurosurgical microanatomy, the development of manual dexterity and practice of novel surgical techniques on animal models or in virtual reality are essential to maximize good outcomes.

Moreover, in-depth knowledge of microsurgical anatomy acquired in the laboratory alone is no guarantee of good results for patients and their families. In the training of a skull base surgeon, other areas of knowledge, along with technical training, are the foundation for optimal patient management and should be included in a professional's education.[6]

Surgeons undertaking a procedure for the first time will clearly be further along in their learning curve if they practice on corpses and experimental animals first. Justifying poor performance in surgery by noting that a professional is at the start of their education is unacceptable. Of course, complications arise in surgery and their likelihood, however small, is inherent to any procedure even when performed with the most experienced hands. However, the probability of such complications should be minimized by first attaining a solid knowledge of neurosurgical microanatomy. This paper will discuss examples of this knowledge at length, as well as the education they trace.

This article is divided in two parts. The first part discusses the technical, psychological, and philosophical aspects of medical knowledge, primarily addressing those training in skull base surgery, the principles of some selected philosophical currents, and their influence on the development of current medical knowledge. The second part addresses the foundations of neurosurgical training and their effect on surgery education, proposing a guide to microsurgical laboratory training, not only to understand anatomy but also to develop surgical skills. After this, training in the microsurgery laboratory and the challenges of being a neurosurgical assistant will be explored. Then, regarding cognitive skills, we will address the multidisciplinary aspect and the need for a comprehensive knowledge of the areas related to neurosurgery. As for affective skills, we will discuss the significance of their development and their direct results on patients and colleagues. While this article focuses on the work of neurosurgeons, it could be applied to any medical specialty in skull base surgery, such as ear, nose, and throat (ENT) or head and neck surgery.

Why We Think That Way? The Development of Scientific Knowledge

The type of medicine most widely practiced today is allopathic or conventional medicine. Diseases are considered to be caused by external insults or by dysfunction of an internal organ or system, and treatment is oriented toward their causes and symptoms. Other approaches to dealing with diseases include those that regard it as originating in a mental or spiritual disorder, or from phenomena for which there is no physical or biological explanation. These approaches include homeopathy, traditional Indian medicine and Ayurveda, traditional Chinese medicine and acupuncture, folk medicines, faith healing, shamanism, and intuition.

There is no doubt that the decisions we make today about, for example, the best way to treat a skull base meningioma, have their origins in the 7th century BCE with the pre-Socratic philosophers. This may seem like a useless or tenuous assertion, but they were the first scholars to reject gods and demons in their explanations of reality.

Three philosophers in particular are noteworthy for having built frameworks, which, despite seemingly having no relation with neurosurgery today, are the basis of our professional conduct: René Descartes, Baruch Spinoza, and Immanuel Kant (►**Fig. 1**). One of the world's greatest philosophers, René Descartes, sought the foundation of truth in his works, and "Discourse on the Method" is his proposal. Descartes starts from methodical doubt, which is the simple act of doubting everything; this principle is based on the fact that our ideas come from our senses, and so are uncertain and unstable. Some, however, present themselves to the human spirit, with clarity and stability, and occur to all people in the same way, regardless of how they experience senses, which means they reside in everyone's minds and are innate. The first of these innate ideas is the Self. The statement "I think, therefore I am" leaves us with no doubt about

Fig. 1 René Descartes (1596–1650), Baruch Spinoza (1632–1677), and Immanuel Kant (1724–1804).

our existence. The second is the dual nature of man, that is, the mind-body dualism; for Descartes, the universe consists of "thinking substance," or mind, and matter, the is latter capable of being explained by physical and mathematical laws. Mind and matter are only united in humans. Thus, Descartes proclaims, correct reasoning is to "never accept anything as true if it cannot be seen clearly and distinctly as such." As for the third idea, he proposes to "conduct my thoughts in such order that, by commencing with objects the simplest and easiest to know, I might ascend little by little, and, as it were, step by step, to the knowledge of the more complex." This method is the cornerstone of today's medical knowledge and decision-making in medical practice. Evidence-based medicine can be considered the ultimate refinement of this philosophy. Criticisms of this method, however, are also part of this refinement, which is why they shall be addressed here, when discussing current microsurgical recommendation for vestibular schwannoma management.

The philosophy of Baruch Spinoza is considered a response to Descartes's dualistic philosophy, which made the world impossible to understand, in his opinion. He found out that through Descartes's philosophy it would be impossible to explain the relationship between God and the world, or between the spirit and the body. In response, Spinoza deduced a complete metaphysical system, which presents the world as a perfectly intelligible whole. As irrelevant as this philosophy may seem, we must consider that, when treating a patient, it is not only the Cartesian aspects that are involved, but also an intelligence that is often intuitive and irrational and seems to be closer to reality, where moral and religious factors can influence decisions. Regarding ethics, Spinoza manages to unite three systems of ethics in a harmonious unit. These three systems, according to Will Durant,[7] are the ethics that consider all men to be equally precious, reciprocate evil with good, preach in politics an unlimited democracy (like Christianity and Buddhism), accept the inequality of men, and appreciate the risks of combat and dominance (along with Nietzsche and Machiavelli) and, finally, consider that only the informed and mature minds can judge when love or power should rule. This type of philosophical approach within neurosurgery tends to value the experience of neurosurgeons and their ethics, and not only decision-making based on scientific aspects, as Descartes postulates. This could be exemplified in patients with skull base diseases with a clear indication for surgical treatment, but who have strong negative feelings regarding a procedure in which the surgeons don't feel confident. Sometimes, the best approach is to understand the patients' humanity and reschedule the procedure for later.

A third philosopher who exerts a great deal of influence on the way we practice medicine is Immanuel Kant, whose ideas dominated the 19th century thinking and still inform mature philosophical discourse today. Kant postulated that we have a completely distorted notion of reality because our knowledge is restricted by what we can sense. Therefore, reason and logic are recent constructions originating in a fragile and deceptive part of the self. Science, as we are capable of knowing it, would thus be naïve, as it concerns "things in themselves, in their full external and incorrupt reality,"[7] and not the sensations, perceptions and concepts of those who merely observe phenomena. A definitive concept of reality would, for this reason, be a mere hypothesis from our point of view. Kant asserts that what brings us closer to reality is our moral sense, the inevitable feeling that an act is either right or wrong when confronted with temptation, which is inherent to every human being. This could not come from our sense-based reasoning, but instead must derive from a more vivid and immediate feeling, which suggests a transcendental, physical, and metaphysical perception of a given phenomenon. To answer the question of "what truly exists?", Kant tries to reconcile realism with idealism, and rationalism with empiricism.

Although the Cartesian method is generally accepted as our guide to professional decision-making, in practice, the Kantian viewpoint and its more complex considerations of patients and ourselves should instead guide the practice of medicine. This argument alone should encourage the skull base surgeon in training to go well beyond just technical training.

Learning Curve Growth Patterns

According to Charles Handy, the normal pattern of acquiring knowledge and experience can be seen as a steep upward curve that eventually slows, peaks, and begins to decline (►**Fig. 2A**). The secret to professional and personal success, for Handy, is to start a new curve as the current one descends. As he puts it, "what leads you to success is probably not what will keep you there." Considering the many areas of knowledge we encounter in our lives, such as technical, personal, and emotional knowledge, a single curve could not represent

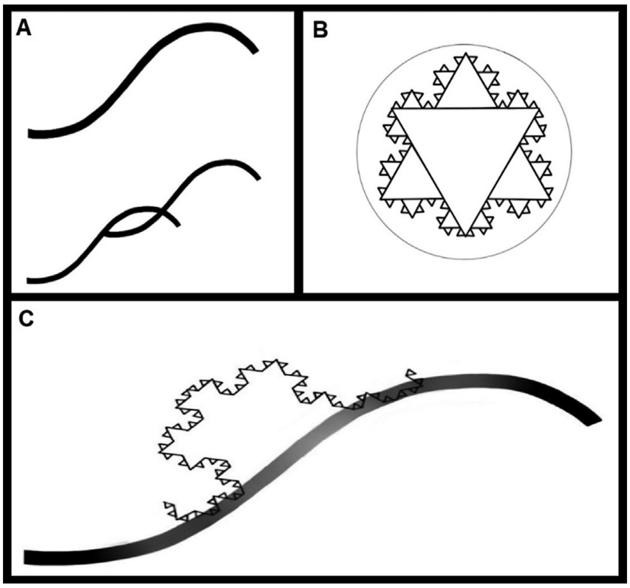


Fig. 2 Learning curves, based on Traynelis[8]: (A) Handy curve; (B) Koch snowflake model; (C) Handy-Koch superposition.

our relation to it all.[6] These infinite aspects of knowledge may create the perspective of a more chaotic pattern, like the Koch snowflake model (►**Fig. 2B**), in which knowledge is represented as a triangle from which each can became a new branch of knowledge, indefinitely. Combining the Handy and Koch models, we can represent an infinite number of curves, with emerging branches, some more or less developed, as the multiple aspects of one's knowledge should be represented (►**Fig. 2C**).

If we consider skull base surgery training, each curve represents the affective, cognitive, and psychomotor knowledge to be developed by neurosurgeons in training. In a more advanced phase of training, surgeons may choose to branch off and seek a subspecialty. Likewise, the path of knowledge they take can branch into new techniques, such as temporal bone drilling or microvascular anastomoses.

Evidence-Based Medicine and Skull Base Surgery

Evidence-based medicine is a recent development, having emerged in Canada in the 1980s. It is based on a decision-making process that relies on the bibliographical analysis of a given subject. A critical evaluation is conducted and externally validated by asking "to what extent do the results published in the literature serve the population I am treating?".

Although there is not yet enough data with a high degree of clinical and epidemiological evidence on which to base most treatments in neurosurgical practice, a critical analysis of class I studies should be undertaken to recommend certain surgical modalities and discard others. For example, microsurgery, embolization, radiosurgery, and surveillance are four possible courses of treatment that are widely accepted by the neurosurgical community and require little analysis to qualify the internal validity of their results. The well-known international subarachnoid aneurysm trial (ISAT) study,[8] which compared embolization versus microsurgery in the treatment of intracranial brain aneurysms, is a class I study, meaning it was prospective, comparative, double-blind, and randomized. However, its internal validity, the results that derive from a large use of neurointervention procedures, cannot be extrapolated to provide external validity over the surgical results, which have historically been excellent. Clearly, we are moving toward a multidisciplinary approach that joins the work of neurosurgeons and interventional radiologists in such a way that debates concerning the selection of one technique among several options are increasingly rare, or maybe redundant. The same is true of radiosurgery increasingly replacing microsurgery in the management of skull base tumors and several other conditions. Therefore, any surgeon training in skull base techniques should be aware that all assertions based on studies must be interpreted with a critical view, and should not be accepted without personal evaluation.

To discuss how to evaluate the best course of treatment for a disease using evidence-based medicine, along with its advantages and criticisms, let's use the following disorder as an example. The management of vestibular schwannomas has become a controversial topic. Although it is met with dogmatic responses in many neurosurgery centers, as well as arbitrary flowcharts and archaic habits of treatment, in some others it prompts a thorough evaluation to determine the best course of treatment in light of clinical and epidemiological evidence, because it is recognized that this disorder raises several questions for which there are still no answers.

In 2017, the Congress of Neurological Surgeons published a series of systematic reviews on vestibular schwannomas,[9–11] and the questions asked were remarkably varied. What is the best surgical approach for preserving facial and vestibulocochlear nerve function? Does the tumor's size influence the choice of approach? Should intracanalicular tumors be resected? Should surgery be the first therapeutic option for patients with type 2 neurofibromatosis (NF2)? Another part of the study addressed issues related to radiosurgery, such as what are the best radiosurgery devices, techniques, and follow-up exams. Similarly, Systematic Review and Evidence-Based Guidelines on Hearing Preservation Outcomes in Patients with Sporadic Vestibular Schwannomas were produced. A large number of studies were evaluated in these works, and their conclusions always noted that there were large amounts evidence available to support decision making.

Increasingly, neurosurgeons choose more conservative management options not because they want the best outcomes for their patients in light of the literature but, often, because they have not developed enough with educational methods before trying to manage certain illnesses.[12] They may lack the necessary perspective that surgical experience should provide. As with skull base diseases, in which intervention procedures and radiosurgery have been increasingly indicated, radiosurgery has been replacing surgery indiscriminately as the first choice of treatment for all patients, even those with vestibular schwannomas or skull base meningiomas. However, this is not always the best option for the patient. Microsurgical technique remains superior to many new technologies and less invasive approaches.[13]

To gain the experience that provides results comparable to those of well-established skull base surgeons, and results that are comparable or superior to those achieved with less invasive techniques, young professionals must have a broad education. This should include, but not be limited to, training in microsurgery and anatomy laboratories, accompanying senior colleagues with recognized expertise and watching their routine before, during, and after surgery, watching surgical videos of the specialties they are pursuing, and, when finally undertaking their first surgeries, having all the necessary resources at their disposal, such as an ultrasonic aspirator, a surgical microscope, and other appropriate microsurgical instruments, followed by intraoperative neurophysiological monitoring.

Data from pioneers in skull base surgery should help motivate the current generation of young physicians to start on a path of improving their skills with training to improve patients' outcomes.[6,14–20] Given the ongoing evolution of neurosurgical science, it is expected that the first cases of a young surgeon should bear results at least similar to those of surgeons with decades of experience. Likewise, many complications encountered by the older generation of surgeons will mostly not be repeated by the younger generation thanks to this evolution.[12] Our work in Brazil illustrates this well. In the past 8 years, all of our vestibular schwannoma patients have been managed by a team composed of an otologist (JL), two neurosurgeons (GRI and FB), and a neurophysiologist. Both surgeons trained for over a year in microsurgical laboratories. In our series of 93 cases of vestibular schwannomas, the main objective was to preserve facial nerve function, and the secondary objective was total resection of the tumor. Following this strategy, facial nerve preservation with complete tumor resection was achieved in all T1, T2, and T3 neurinomas (Hannover classification – ►**Fig. 3**). For some of the T4 tumors, near total resection based on intraoperative neurophysiological changes was chosen instead.

Hearing was preserved in half of the patients with T1 and T2 tumors. We used retrosigmoid approaches with most patients, and translabyrinthine in patients without any

Grade	Tumor
T1	Purely intracanalicular
T2	Intrameatal or extrameatal
T3a	Filling the cerebellopontine cistern
T3b	Reaching the brainstem
T4a	Compression of the brainstem
T4b	Compression of the brainstem with dislocation of the fourth ventricle

Fig. 3 Hannover classification for vestibular schwannomas.

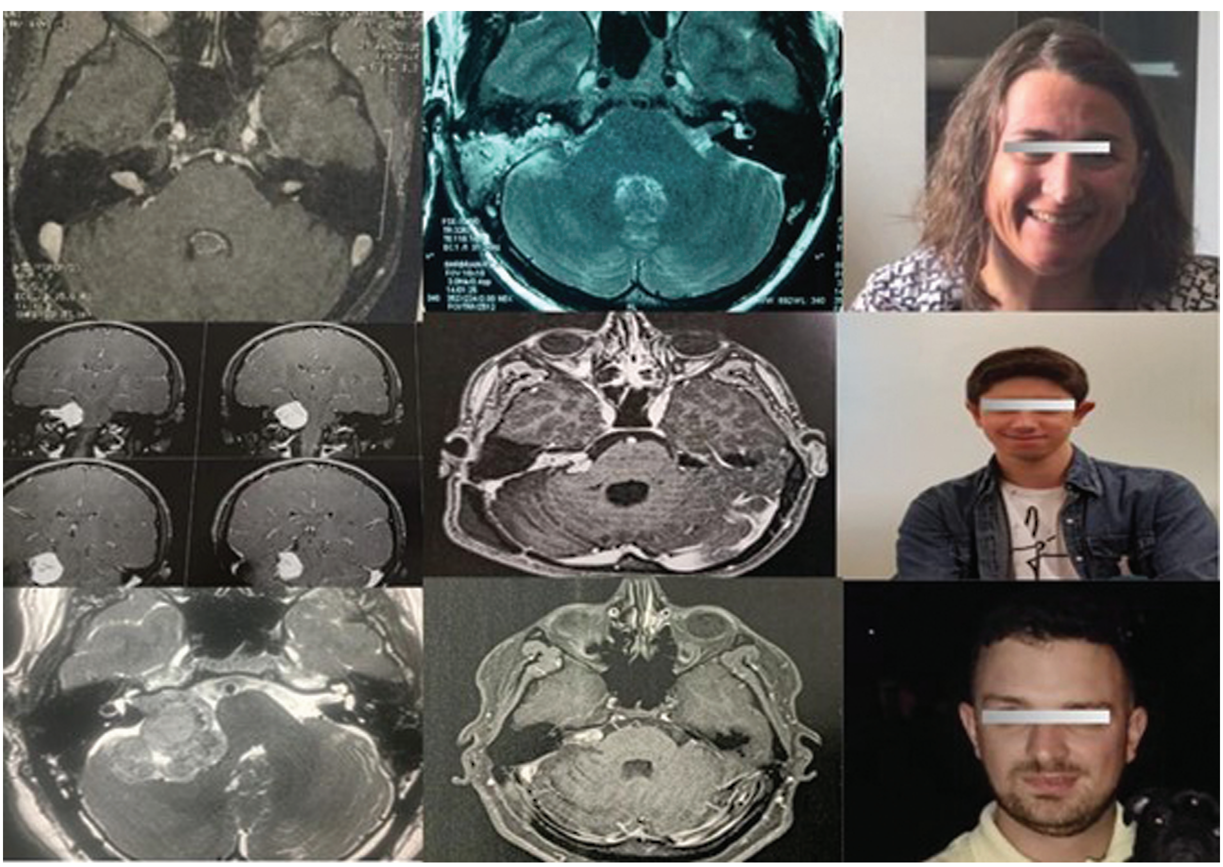


Fig. 4 Pre- and postoperative exams of three cases of vestibular schwannomas, with their respective postoperative preserved facial mimic. The main objective was to preserve facial nerve function, even if some residual tumor must be left, guided by intraoperative neurophysiological monitoring.

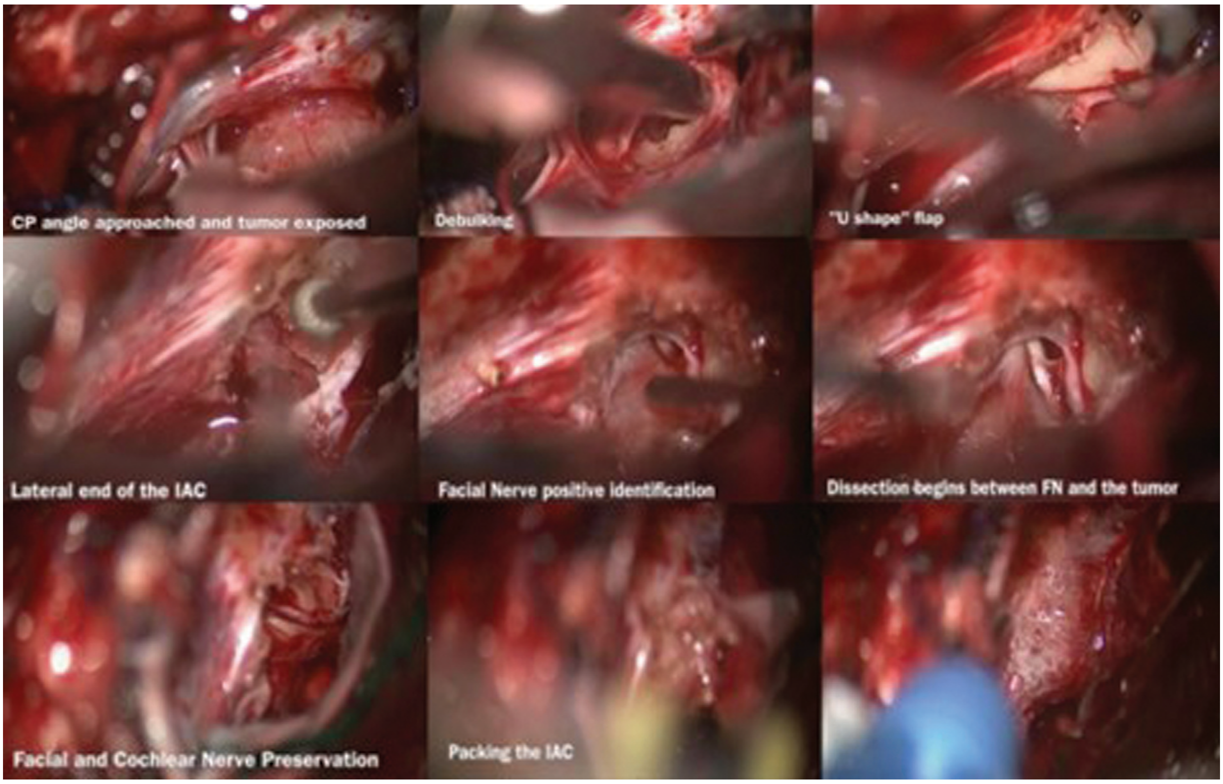


Fig. 5 Step-by-step approach to the internal acoustic canal: applying knowledge from microanatomy laboratory training in the operative room.

viable hearing who had small tumors extending to the fundus of the meatus. For cases that presented with complete facial paralysis, we opted for early facial hypoglossal anastomosis, 3 months after surgery at most. Except for one patient with venous infarction after resection of a T4 tumor, there were no deaths in this series.

So far, our methodology for managing patients with vestibular schwannoma has not grown to statistically significant numbers, and we have no clinical-epidemiological evidence based on prospective randomized studies. However, this work has been highly satisfactory for our patients. Several case series and reports have shown improvement in facial paralysis indexes over the years.[6,12,14–21] While, in our series, we have seen improvement in the extent of tumor resection over the years, the rate and severity of facial paralysis remained low since the beginning. ►**Figs. 4–9** illustrate some cases of cerebellopontine angle tumors in our series. We have been following another 46 patients with serial magnetic resonance imaging (MRI). Most of them are elderly patients with asymptomatic intrameatal tumors.

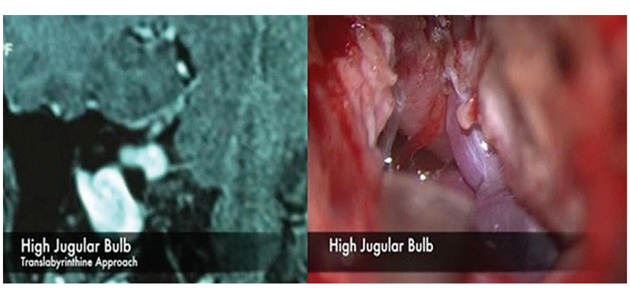


Fig. 6 A case of a high jugular bulb in a cerebellopontine angle approach: the importance of microanatomy knowledge to prevent unexpected situations in surgery.

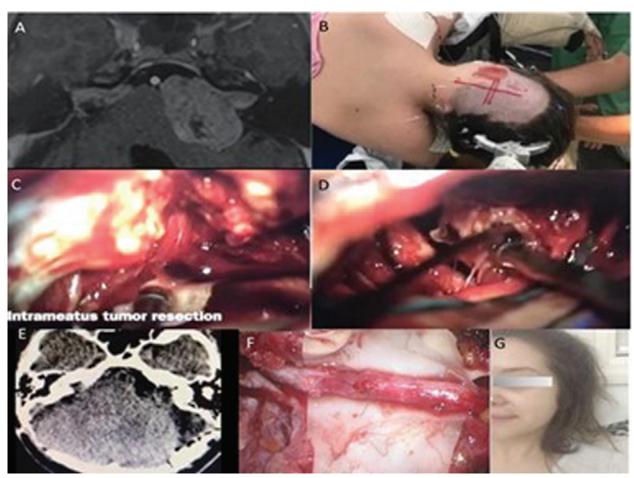


Fig. 7 A case of a grade IVB vestibular schwannoma. (A) Gadolinium-enhanced T1-weighted axial image showing left-sided vestibular schwannoma compressing brainstem and dislocating the fourth ventricle; (B) patient's surgical positioning: ¾ prone position with shoulder retraction; (C) opened internal acoustic canal; (D) tumoral resection; (E) early postoperative computed tomography (CT) scan showing gross total tumor resection and opened internal acoustic canal; (F) intraoperative hypoglossal-facial nerve anastomosis; (G) postoperative facial motricity preservation.

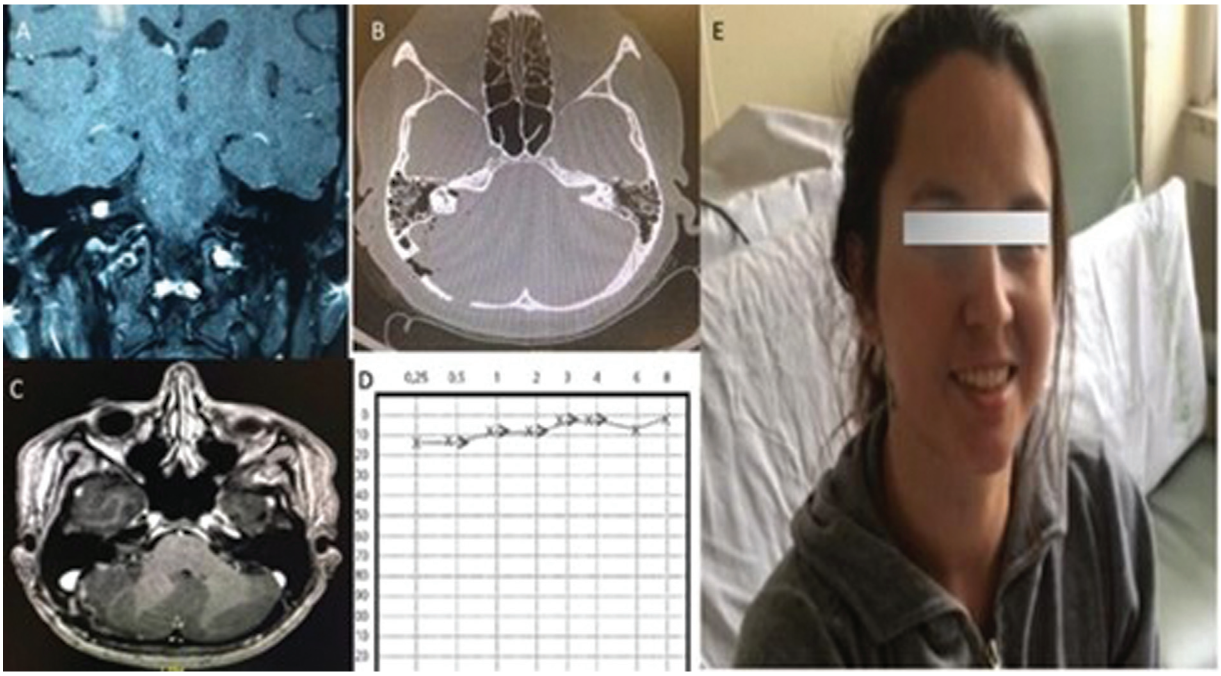


Fig. 8 Intracanalicular vestibular schwannoma (grade I). (A) Gadolinium-enhanced T1-weighted sagittal image showing a small lesion within the internal acoustic canal; (B) early postoperative computed tomography (CT) scan showing the opening of the internal acoustic canal; (C) gadolinium-enhanced T1-weighted axial image showing complete tumoral resection; (D) postoperative audiometry showing hearing preservation; (E) postoperative facial motricity preservation.

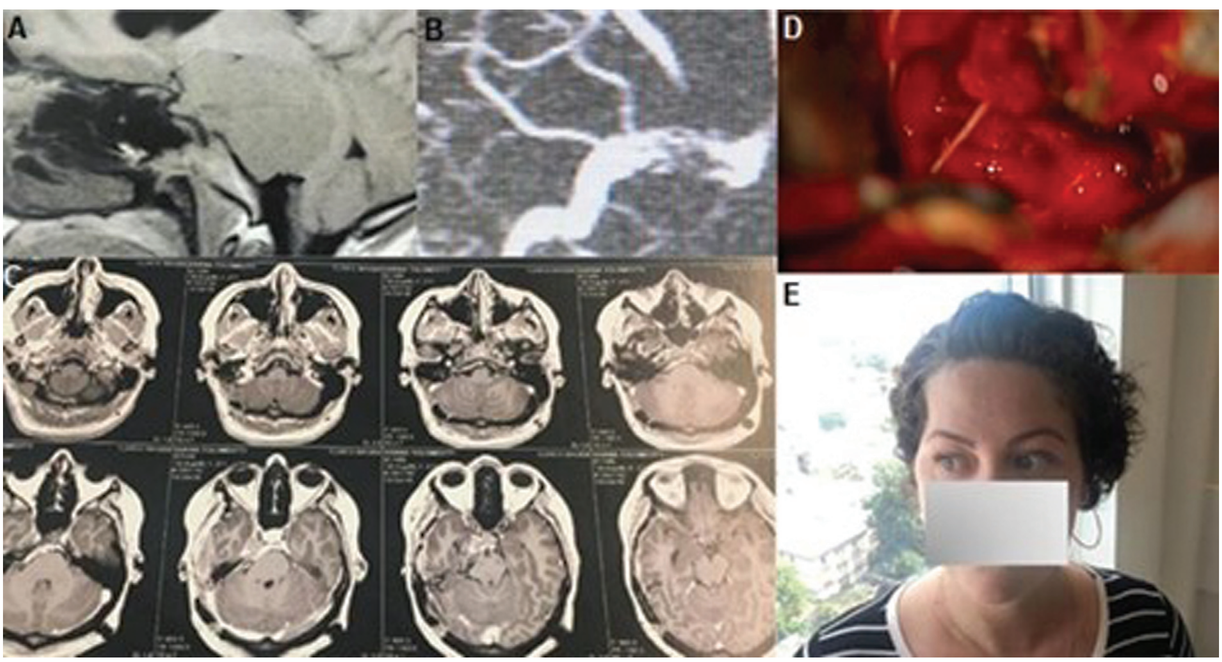


Fig. 9 Sphenopetroclival meningioma. The patient had lower cranial nerves palsies and hemiparesis. (A) Sagital T1-weighted image showing tumor interface with brainstem; (B) brain venography showing Labbé vein in its usual position. Based on that, a posterior petrosal approach was performed; (C) gadolinium enhanced T1-weighted postoperative image, showing near total ressection; (D) intraoperative image showing the IV cranial nerve. Near total resection without ophtalmoparesis was achieved. Residual tumor left in the cavernous sinus; (E) asymptomatic patient in a 6-years follow-up. Annual magnetic resonance imaging (MRI) with no tumor growth.

Final Considerations

In the first part of this article, we’ve tried to briefly demonstrate the construction of western knowledge and the steps that skull base surgeons, in the beginning of their careers, must take when evaluating the medical literature using evidence-based medicine. We emphasize that for uncommon diseases, including most of the skull base ones, the best approach is rarely based on rigid statistical data, but rather on the patients’ expectations and surgeons’ experience, knowledge, and empathy levels at that particular point of their career.

Note

Some small parts of this article were published previously in Portuguese by the senior author, * but with a different focus on the learning curve. Following the Brazilian Association for Technical Standards (ABNT) and copyright rules (lei número 9.610), these parts are identified by quotation marks.

*Isolan GR: A construção do conhecimento pelo jovem neurocirurgião: ética, ciência e a importância do treinamento em laboratório de microcirurgia. J Bras Neurocirurg 20 (3): 314–334, 2009.

Conflict of Interests

The authors have no conflict of interests to declare.

References

1 Wright TP. Factors Affecting the Cost of Airplanes. J Aeronaut Sci 1936;3(04):122–128
2 Yaşargil MG. Microneurosurgery. Vols I, II, and IVB. Georg Thieme VerlagStuttgart1996
3 Yaşargil MG. Reflections of a neurosurgeon. Clin Neurosurg 1988; 34:16–21
4 Yaşargil MG. A legacy of microneurosurgery: memoirs, lessons, and axioms. Neurosurgery 1999;45(05):1025–1092
5 Yaşargil MG, Chandler WF, Jabre AF, Roth P. Neurosurgical horizons. Clin Neurosurg 1988;34:22–41
6 Traynelis VC. The geometry of education: patterns for growth. Clin Neurosurg 2005;52:1–5
7 Durant W. (1996) História da Filosofia. Ed. Nova Cultural, São Paulo
8 Molyneux AJ, Kerr RS, Yu LM, et al; International Subarachnoid Aneurysm Trial (ISAT) Collaborative Group. International subarachnoid aneurysm trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised comparison of effects on survival, dependency, seizures, rebleeding, subgroups, and aneurysm occlusion. Lancet 2005;366(9488):809–817
9 Carlson ML, Vivas EX, McCracken DJ, et al. Congress of Neurological Surgeons Systematic Review and Evidence-Based Guidelines on Hearing Preservation Outcomes in Patients With Sporadic Vestibular Schwannomas. Neurosurgery 2018;82(02):E35–E39
10 Germano IM, Sheehan J, Parish J, et al. Congress of Neurological Surgeons Systematic Review and Evidence-Based Guidelines on the Role of Radiosurgery and Radiation Therapy in the Management of Patients With Vestibular Schwannomas. Neurosurgery 2018;82(02):E49–E51
11 Hadjipanayis CG, Carlson ML, Link MJ, et al. Congress of Neurological Surgeons Systematic Review and Evidence-Based Guidelines on Surgical Resection for the Treatment of Patients With Vestibular Schwannomas. Neurosurgery 2018;82(02):E40–E43
12 Roser F, Tatagiba MS. The first 50s: can we achieve acceptable results in vestibular schwannoma surgery from the beginning? Acta Neurochir (Wien) 2010;152(08):1359–1365
13 Lawton MT, Lang MJ. The future of open vascular neurosurgery: perspectives on cavernous malformations, AVMs, and bypasses for complex aneurysms. J Neurosurg 2019;130(05): 1409–1425
14 Buchman CA, Chen DA, Flannagan P, Wilberger JE, Maroon JC. The learning curve for acoustic tumor surgery. Laryngoscope 1996; 106(11):1406–1411
15 Elsmore AJ, Mendoza ND. The operative learning curve for vestibular schwannoma excision via the retrosigmoid approach. Br J Neurosurg 2002;16(05):448–455
16 Moffat DA, Hardy DG, Grey PL, Baguley DM. The operative learning curve and its effect on facial nerve outcome in vestibular schwannoma surgery. Am J Otol 1996;17(04):643–647
17 Samii M, Gerganov V, Samii A. Improved preservation of hearing and facial nerve function in vestibular schwannoma surgery via the retrosigmoid approach in a series of 200 patients. J Neurosurg 2006;105(04):527–535
18 Samii M, Matthies C. Management of 1000 vestibular schwannomas (acoustic neuromas): hearing function in 1000 tumor resections. Neurosurgery 1997;40(02):248–260, discussion 260–262
19 Samii M, Matthies C. Management of 1000 vestibular schwannomas (acoustic neuromas): surgical management and results with an emphasis on complications and how to avoid them. Neurosurgery 1997;40(01):11–21, discussion 21–23
20 Samii M, Matthies C. Management of 1000 vestibular schwannomas (acoustic neuromas): the facial nerve–preservation and restitution of function. Neurosurgery 1997;40(04):684–694, discussion 694–695
21 Dunn IF, Bi WL, Erkmen K, et al. Medial acoustic neuromas: clinical and surgical implications. J Neurosurg 2014;120(05): 1095–1104

The Learning Curve in Skullbase Surgery Part 2–From the Microsurgical Lab Training to the Operative Room

A Curva de Aprendizado em Cirurgia de Base do Crânio - Do laboratório de microcirurgia à sala cirúrgica

Gustavo Rassier Isolan[1,2,3] Jander Monteiro[1] Marco Antônio Schlindwein Vaz[1] Joel Lavinsky[1,3,4] Ricardo Lopes de Araújo[5] Eberval Gadelha Figueiredo[6] Samir Aler Bark[1,2] José Fernando Polanski[2] Carmem Austrália Paredes Ribas Filho[2] Jurandir Marcondes Ribas Filho[2] Osvaldo Malafaia[2]

[1] Department of neurosurgery, The Center for Advanced Neurology and Neurosurgery (CEANNE), Porto Alegre, RS, Brazil
[2] Department of neurosurgery, Paraná Evangelical Mackenzie University (FEMPAR), Curitiba, PR, Brazil
[3] Department of neurotology, The Center for Neurotology and Acoustic Neuroma (CNNA), Porto Alegre, RS, Brazil
[4] Department of neurotology, Lavinsky Clinic, Porto Alegre, RS, Brazil

Arq Bras Neurocir 2022;41(4):e348–e361.

Address for correspondence Gustavo Rassier Isolan, MD, PhD, CEANNE, Rua Dr Vale 234. Porto Alegre, RS 90560-010, Brazil (e-mail: gustavo.isolan@fempar.edu.br).

[5] Surgical Innovations Laboratory for Skull Base Microneurosurgery, Department of Neurological Surgery, Weill Cornell Medical College, New York, NY, United States
[6] Department of Neurosurgery, Universidade de São Paulo, São Paulo, SP, Brazil

Abstract

In this second part, the authors review and suggest a methodology for studies in skull base surgery and training in microsurgical laboratory, based on their experiences and reflections. Not only are the foundations for the acquisition of microsurgical skills presented, but also what is needed to be an effective skullbase surgeon with good results. The present article reflects in particular the philosophy of professor Evandro de Oliveira and also serves to present to the neurosurgical community a new state-of-the-art laboratory for hands-on courses in Brazil, at the Faculdade Evangélica Mackenzie do Paraná.

Keywords
- skullbase
- learning curve
- microsurgical laboratory

Resumo

Nesta segunda parte, os autores revisam e sugerem uma metodologia para o estudo em cirurgia de base de crânio e treinamento em laboratório de microcirurgia baseado em suas experiencias e reflexões. Não apenas os fundamentos para a aquisição de habilidades microcirúrgicas estão presentes, como também, o que é necessário para ser um eficiente cirurgião de base de crânio com bons resultados. Este artigo reflete, em particular, a filosofia do Professor Evandro de Oliveira, além de servir para apresentar a comunidade neurocirúrgica o novo "estado da arte" em laboratórios de cursos "hands-on" no Brasil, na Faculdade Evangélica Mackenzie do Paraná.

Palavras-chave
- Base de crânio
- Curva de aprendizado
- Laboratório de microcirurgia

This paper, divided in two parts, is a tribute to Professor Evandro de Oliveira, MD, PhD (1945 - 2021).

received
July 29, 2022
accepted
August 18, 2022

DOI https://doi.org/10.1055/s-0042-1758221.
ISSN 0103-5355.

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

Introduction

The second part of the present article addresses the foundations of neurosurgical training and their effect on surgery education and propose a guide to microsurgical laboratory training.

Microsurgical Laboratory Training

Part of Professor M.G. Yasargil's immeasurable contribution to neurosurgery[1–4] is an article reflecting on a life dedicated to neurosurgery.[5] In volume 147 of the 2005 Acta Neurochirurgica magazine, he published an editorial entitled "From the Microsurgical Laboratory to the Operating Theater." It describes the history of the use of the microscope in surgery and neurosurgery and the initial experiences of the author with this technology that revolutionized our concept of the surgical treatment of pathologies of the central nervous system (CNS). As a modern microneurosurgery pioneer, he also provides quite valuable advice for young neurosurgeons. First, a thorough knowledge of neurosurgical microanatomy and its correlation with imaging studies, especially cisterns, parenchymal, and vascular structures, is essential for determining the most appropriate surgical strategy. In addition, modern neuroimaging techniques, such as positron emission tomography (PET), single-photon emission computerized tomography (SPECT), spectroscopy, and molecular biology methods using immunohistochemical markers and molecular analyses have brought great advances to the diagnosis and management of certain groups of CNS diseases. Young skullbase surgeons must be aware of these options and obtain at least a basic knowledge of the indications for using each one. Another topic the professor addresses is that, thanks to microsurgical training and knowledge of the anatomy of the CNS and safe anatomical corridors (►Fig. 1), almost any brain injury can be addressed with a low risk of operative morbidity. He ends the editorial by advising young neurosurgeons to train for at least 1 year in a microsurgery laboratory to develop their knowledge of surgical microanatomy and their facility with a microscope. It must be remembered that, as he also wrote, one limitation of cadaver models is that brain retraction cannot be quantified with them. This is problematic, especially when studying new access routes into deep brain regions. On the other hand, anatomical specimens that are not prepared with formalin have more consistent hardening of the formalized brain tissue. This is especially useful for practicing access to the skullbase.

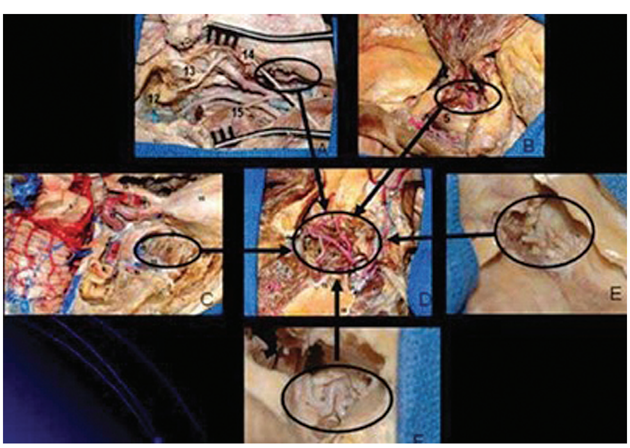


Fig. 1 We can approach the infratemporal fossa from several ways. Mastering microanatomy is fundamental to safe access deep neurovascular structures through the natural corridors of the brain (cisterns).

Fig. 2 Microanatomy laboratories around the world: (A) Skullbase Laboratory at Weill Cornell Brain and Spine Center; (B) Microsurgical Laboratory at the Hospital Beneficência Portuguesa de São Paulo; (C) Dianne and Gazi Yasargil Education Center at the University of Arkansas for Medical Sciences.

There are several microsurgery laboratories in the world today (►Fig. 2). Those who wish to dedicate themselves to skullbase microneurosurgery must be prepared to train in one of these locations. It should also be noted that, as important as the structure and size of the laboratory itself, access to anatomical specimens is essential. Before making this investment of time and money, young neurosurgeons must consider all the obstacles to gaining adequate training. A good way to do this is to talk with colleagues who have trained in one of these locations. It should not be forgotten, however, that as long as a room contains a surgical microscope, microsurgical instruments, and material to dissect or train on, microsurgical training is possible regardless of the location. Manual dexterity is developed with the dissection and microanastomosis of placental vessels (►Fig. 3 and 4), followed by vascular microanastomosis in the internal carotid artery of rats (►Figs. 5–7) and arterial bypass using the femoral artery of guinea pigs, to name a few examples. After all this training the surgeon would be able to perform his/her first bypass (►Fig. 8).

Laboratory Training to Access the Lateral Skullbase

In some microsurgery laboratories, microsurgical dissection exercises can be performed with blocks taken from regions of the skullbase. Temporal bones or skullbase central blocks are

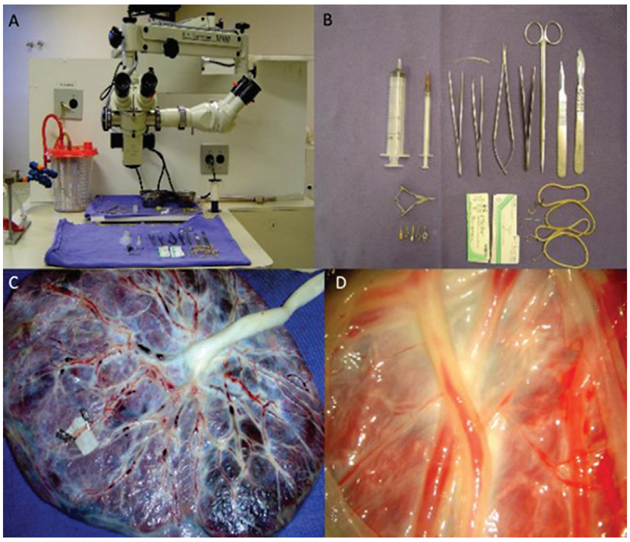


Fig. 3 (A) Desktop sugical microscope for dissection skill training; (B) simple surgical instruments for dissection training; (C) Placenta used for skill training. Notice 2 vascular clips and a microsuture; (D) Placentary vessels: Ideal for microanastomosis training.

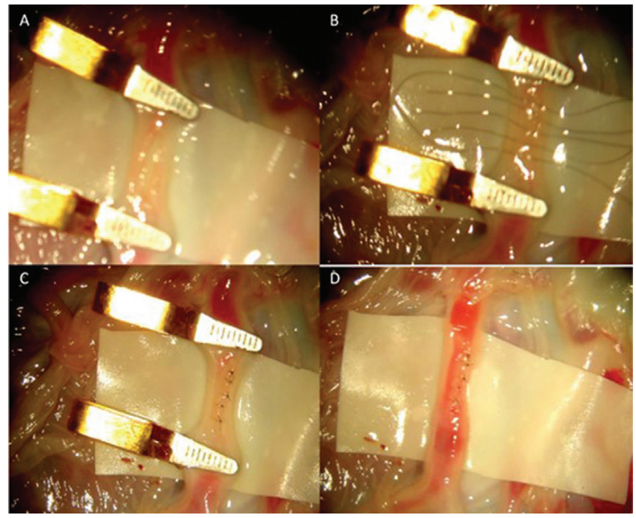


Fig. 4 Suture under microscope step-by-step. (A) dissected vessel with perpendicular incision between distal clips; (B) microsuture of arterial wall being performed; (C) sutured arterial wall; (D) perfused artery.

the most used anatomical preparations for studying the cavernous sinus. Although dissecting these regions is crucial for understanding the three-dimensional anatomy of all the intricate structures, one of the greatest insights that microsurgical laboratory training can provide is an excellent understanding of the relationship of the brain and nerves with the base of the skull as studied for a specific approach.[6–20] Studying the entire head of a corpse not only lets us perform different approaches to the same anatomical region, but also provides us with many neuroimaging insights (►**Fig. 9–11**).[6,20] To maximize training opportunities, such as that every possible access is explored in a single corpse, on the lateral skullbase hands-on access courses we have been providing at the Weill Cornell Medical Center we have been developing the following optimized dissection sequence.

We start the dissections with the cranio-orbito-zygomatic approach (►**Fig. 12**). After the skin incision, we perform a

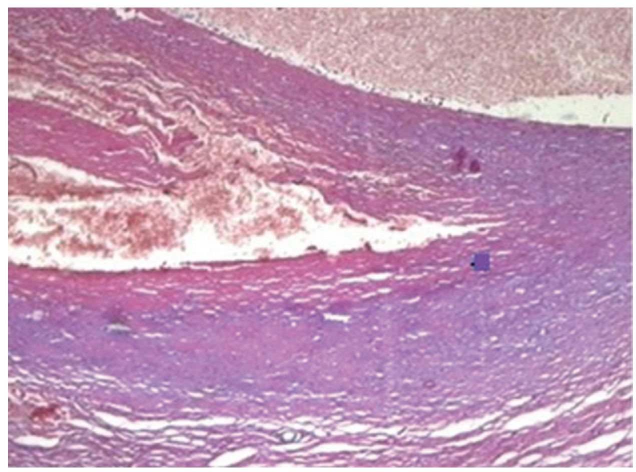


Fig. 6 Histological study of laboratory specimen of previous figure (rat B): blood clot formed within the anastomosed internal carotid artery.

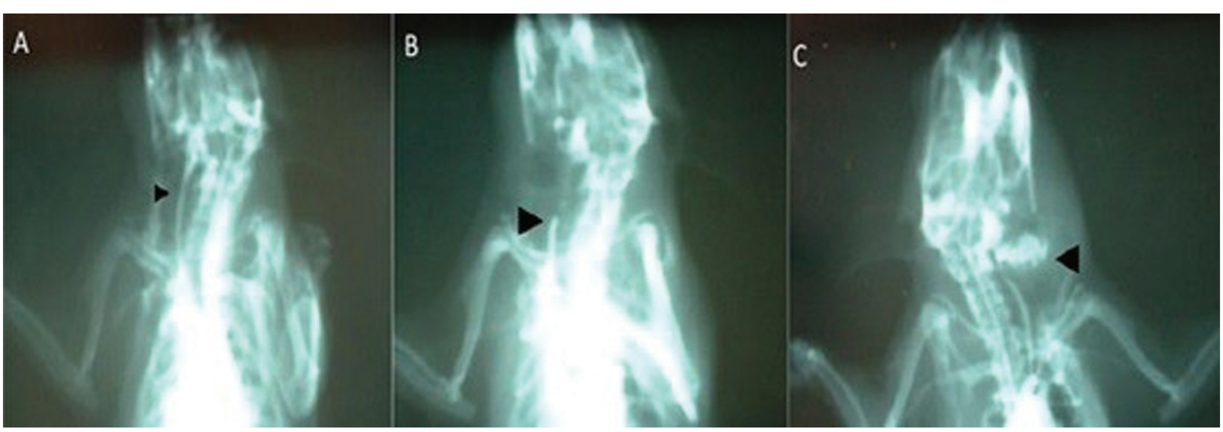


Fig. 5 Postoperative angiography of laboratory specimens; (A) end-to-end anastomosis of internal carotid artery: blood flow reestablished; (B) thrombosis of the microvascular anastomosis and interrupted blood flow; (C) anastomotic pseudoaneurysm formed in the internal carotid artery after microvascular procedure.

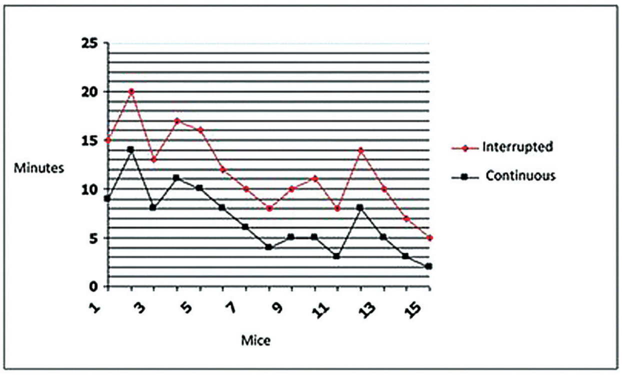


Fig. 7 The result of laboratory training in surgical procedures: less time needed to perform a microanastomosis as more trained becomes the surgeon.

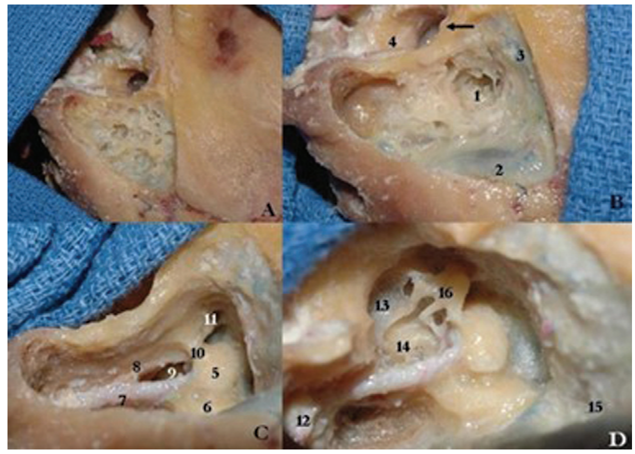


Fig. 9 Anatomical knowledge of the mastoid part of the temporal bone is crucial to perform petrosectomies; 1–mastoid antrum; 2–sigmoid sinus; 3–tegmen mastoideum; 4–external acoustic canal; 5–lateral semicircular canal; 6–posterior semicircular canal; 7–facial nerve; 8–chorda tympani nerve; 9–facial recess; 10–septum osseux; 11–epitympanum; 12–tendon of the posterior belly of the digastric muscle; 13–tympanic membrane; 14–promontory; 15–Citelli's angle; 16–incus.

subfascial dissection of the temporal muscle and expose the zygomatic process of the temporal bone. We use the Cranial-orbit zygomatic (COZ) approach in two pieces on one side of the skull and in three pieces on the other. After the craniotomy, an extradural peeling of the anterior fossa and at the beginning of the middle fossa is performed, exposing the anterior clinoid and part of the cavernous sinus. The clinoid is removed as a single piece, drilling its base. A good exercise in this step is to drill not only at the roof of the optic canal, but also the medial bone at the optic nerve to open the posterior ethmoidal cells. The next exercise is to explore the lateral wall of the cavernous sinus by peeling from anterior to posterior. Cranial nerves III and IV and V1, V2, and V3 branches of the trigeminal nerve are exposed at this stage. The cavernous sinus must be entered either through the

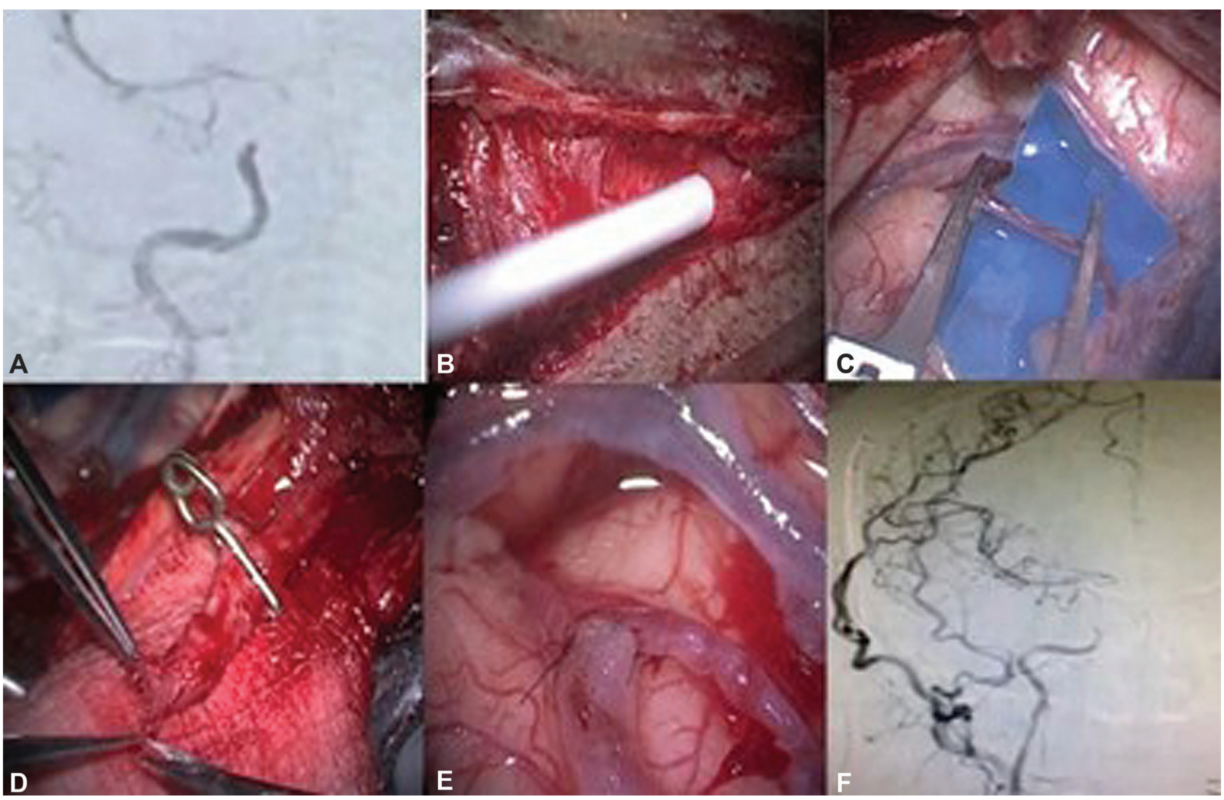


Fig. 8 Microanastomosis of the superficial temporal artery (STA) to the middle cerebral artery (MCA): from laboratory training to the operating room; (A) Preoperative arteriography showing significant occlusion of the internal carotid artery; (B) careful temporal skin incision; (C) checking if the graft measure is compatible with the proposed anastomosis; (D) temporary clip placed in the STA, followed by dissection of the vessel. The surrounding fascia is removed only in the border that will be anastomosed; (E) final aspect of the anastomosis; (F) postoperative arteriography showing significant brain reperfusion.

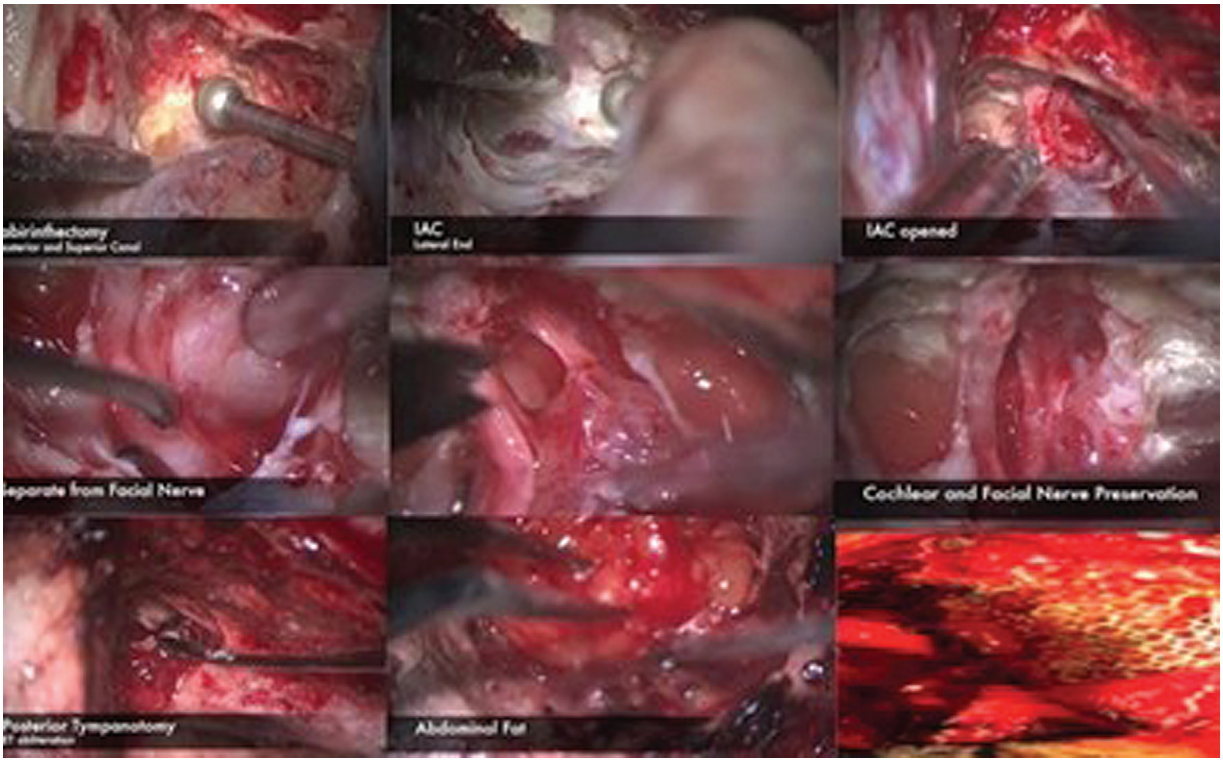


Fig. 10 From microanatomy laboratory training to the operating room: step-by-step mastoid dissection.

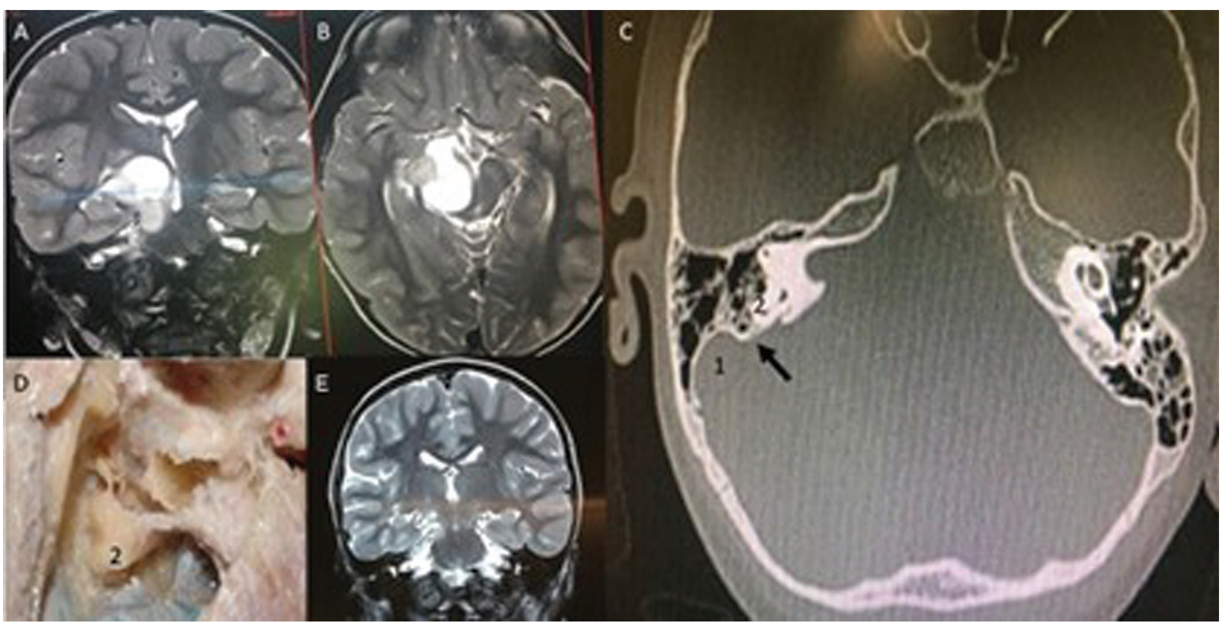


Fig. 11 Thalamic tumor. (A) coronal T2-weighted image showing cystic thalamic tumor; (B) axial T2-weighted image, same tumor; (C) axial computed tomography of the head bone window. A posterior petrosal approach is a possibility. However, in pediatric patients, the space between the sigmoid sinus (1) and the posterior semicircular canal (2) can be too narrow. Based on that, it was performed a transmiddle temporal gyrus approach with near total resection of the lesion and no postoperative deficits; (D) mastoid dissection showing the posterior semicircular canal; (E) coronal T2-weighted postoperative image

supratrochlear or infratrochlear triangles in the lateral wall or through the oculomotor or clinoidal triangles in the upper wall (►**Fig. 13**). Within the cavernous sinus, cranial nerve VI, the internal carotid artery, and the origin of the inferolateral artery and the meningohypophyseal trunk must be visible. After completing this extradural stage, the dura mater is opened in a conventional manner and the Sylvian fissure is dissected. Then, the internal carotid artery, the optic nerve, and the oculomotor nerve can be seen and dissected as far as they extend. This presents an excellent opportunity to continue dissecting the anterior extradural extension of the trigeminal branches and to drill through the anteromedial

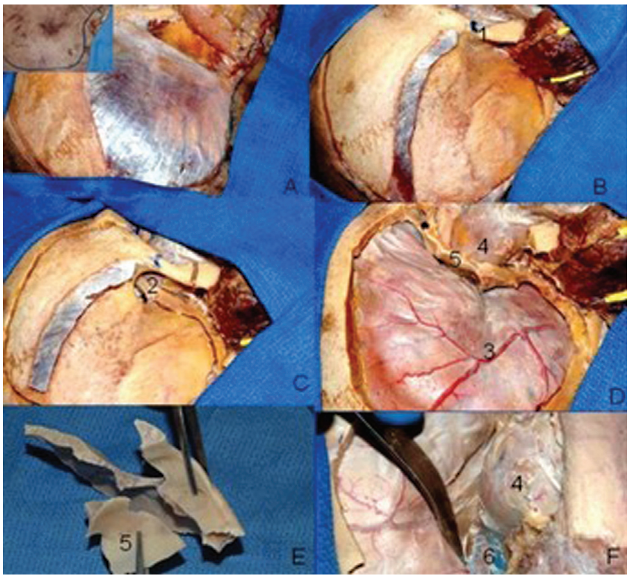


Fig. 12 Cranio-orbital zygomatic approach. (A) skin incision (head rotated to the left); (B) temporal muscle inferiorly mobilized following zygomatic osteotomy; (C) keyhole and craniotomy, bone still in place; (D) bone flap removed; (E) posterior part of the orbital roof removed (later reconstruction); (F) middle fossa dural peeling to expose the cavernous sinus; 1– frontozygomatic suture; 2–orbital roof; 3–middle meningeal artery; 4–periorbita; 5–posterior part of the orbital roof; 6–cavernous sinus.

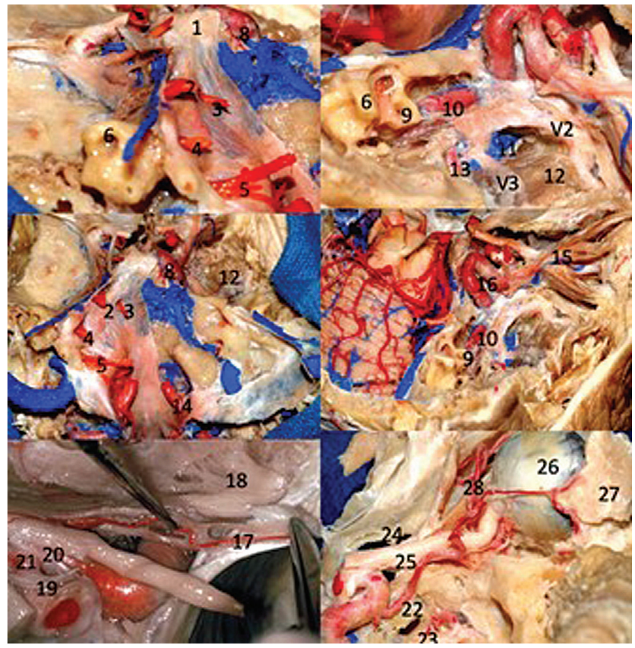


Fig. 13 Cavernous sinus neurovascular relations. 1–dorsum sellae; 2–trigeminal nerve; 3–abducens nerve; 4–facial, vestibular, and trochlear nerves; 5–low cranial nerves; 6–superior semicircular canal; 7–superior petrous sinus; 8–internal carotid artery, cavernous segment; 9–cochlea; 10–internal carotid artery, petrous segment; 11–pterygoid venous plexus; 12–lateral pterygoid muscle, superior head; 13–middle meningeal artery; 14–vertebral artery; 15–oculomotor nerve; 16–internal carotid artery, cavernous segment; 17–marginal tentorial artery (of Bernasconi-Cassinari); 18–Gasser ganglion; 19–distal dural ring; 20–proximal dural ring; 21–internal carotid artery, infraclinoid portion; 22–ophthalmic artery with unusual origin (from the intracavernous segment of the internal carotid artery); 23–sphenoid sinus; 24–ethmoid sinus; 25–optic nerve; 26–ocular globe; 27–lacrimal gland; 28–posterior ethmoidal artery anastomosing with ophthalmic and anterior ethmoidal arteries.

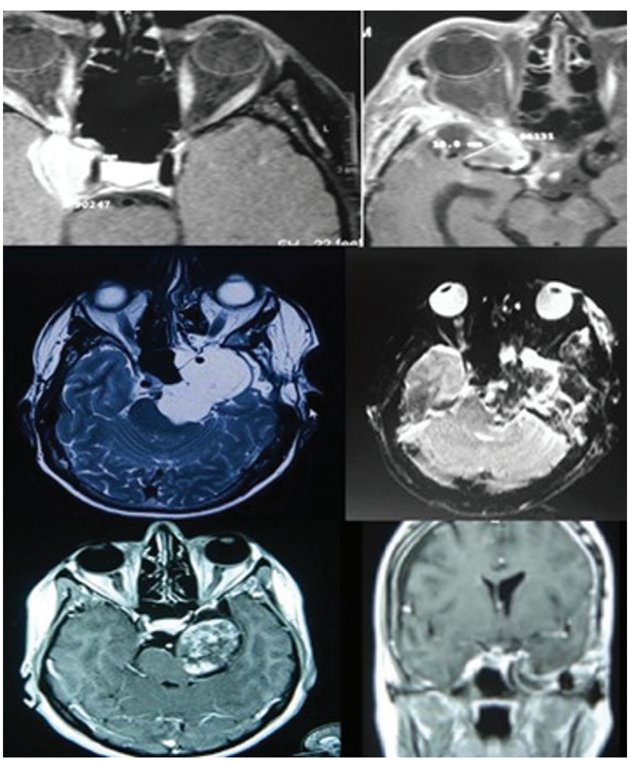


Fig. 14 Examples of cavernous sinus tumors. Preoperative (left) and postoperative (right). Cavernous sinus meningioma (above), cavernous sinus chondrosarcoma (middle), cavernous sinus schwannoma (below).

and anterolateral triangles that are between V1-V2 and V2-V3. This exercise is especially important not only for cavernous sinus tumor resection (►**Fig. 14**) but also for meningiomas in the sphenoid wing (►**Fig. 15**), where there is usually hyperostosis of the pterygoid plate that must be resected. In this intradural area, the posterior clinoid process can be drilled out to observe how it can block the view of the tip of the basilar artery.

After the dura mater is closed, the next exercise is the peeling of the dura mater of the middle fossa, from anterior to posterior, to perform an anterior petrosectomy (►**Fig. 16**). In this step, the head is rotated 90° and an incision is made running posteriorly from the middle of the previous incision. The craniotomy performed in the COZ approach is then extended to the temporal region. The peeling of the middle fossa starts at the level of the external auditory canal and extends anteriorly and medially. The first visible structure should be the middle meningeal artery exiting the spinous foramen. As the trigeminal branches were dissected in the previous approach, at this point the Gasser ganglion is dissected until reaching the petrous apex. In the more posterior region, the greater superficial petrosal nerve (GSPN), the geniculate ganglion, and the superior petrous sinus are exposed (►**Fig. 17**). The arcuate eminence is reached and, in most cases, correspond to the upper

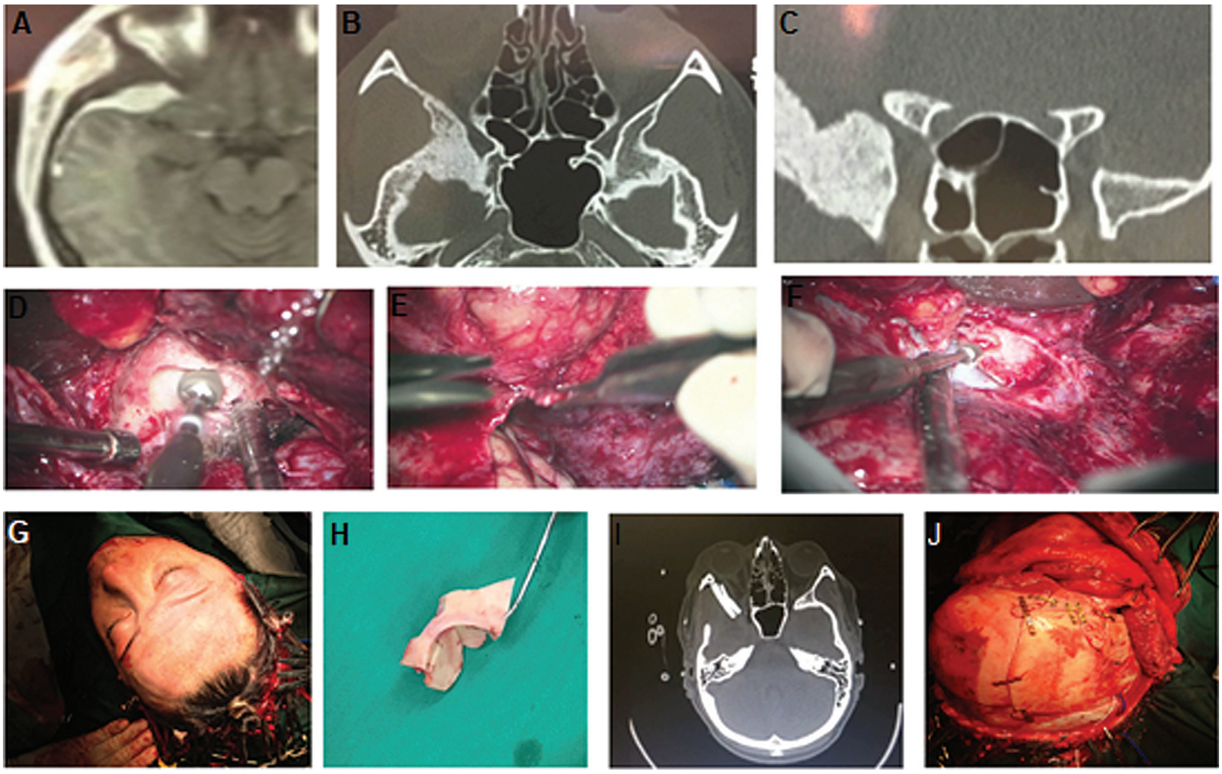


Fig. 15 A multidisciplinary approach is crucial to acquire good results in skullbase surgery. In this case, an en-plaque sphenoid wing meningioma was resected by the neurosurgical team while the cranial and orbital reconstruction was performed by the craniofacial surgery team. (A) magnetic resonance imaging (MRI) showing an en-plaque meningioma; (B) axial computed tomography (CT) scan showing a hyperostosis of the pterygoid plate; (C) coronal CT scan showing large hyperostosis not only of the pterygoid plate but also in the anterior clinoid process; (D) intraoperative view of the hyperostotic anterior clinoid process being drilled; (E) intraoperative view of the reconstruction of the lateral and superior orbital walls; (F) intraoperative view of the cranial reconstruction using the inner table of the parietal bone; (G) patient's position; (H) orbital wall reconstruction with parietal bone flap; (I) postoperative CT scan showing a part of the inner table of the parietal bone that was placed in the lateral wall of the orbit to avoid enophthalmos; (J) final cranial reconstruction.

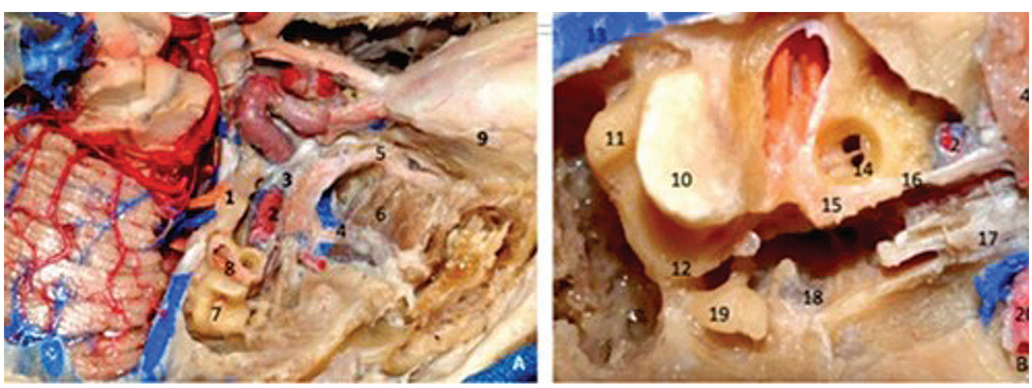


Fig. 16 Anterior petrosectomy performed in a cadaveric specimen. 1–petrous apex; 2–internal carotid artery, petrous segment; 3–petrolingual ligament; 4–V3; 5–V2; 6–lateral pterygoid muscle; 7–otic capsule; 8–internal acoustic canal; 9–orbit; 10–superior semicircular canal; 11–posterior semicircular canal; 12–lateral semicircular canal; 13–superior petrosal sinus; 14–cochlea; 15–geniculate ganglion; 16–greater superficial petrosal nerve (GSPN); 17–chorda tympani nerve; 18–tympanic membrane; 19–incus; 20–middle meningeal artery.

semicircular canal (►**Fig. 18**). The petrous apex is drilled, its lateral limit being the petrous portion of the Internal carotid artery (ICA), its posterior limit being the internal acoustic meatus, its anterior limit V3 and the trigeminal ganglion, and its medial limit being the dura mater of the posterior fossa. Although the petrous apex has no neurovascular structure, it has a varying degree of pneumatization. Special care must be taken not to open the cochlea, which is located at the angle between the internal auditory canal and the GSPN. Studying the middle fossa is important for the treatment of diseases such as superior semicircular canal dehiscence (SSCD) (►**Fig. 18**), petrous apex chondrosarcoma or dermoid cyst (►**Fig. 19**), proximal control of the carotid in its intrapetrous portion, facial nerve or vestibular meatus schwannomas, as well as creating an access corridor for intradural tumors such as petroclival and incisural meningiomas.

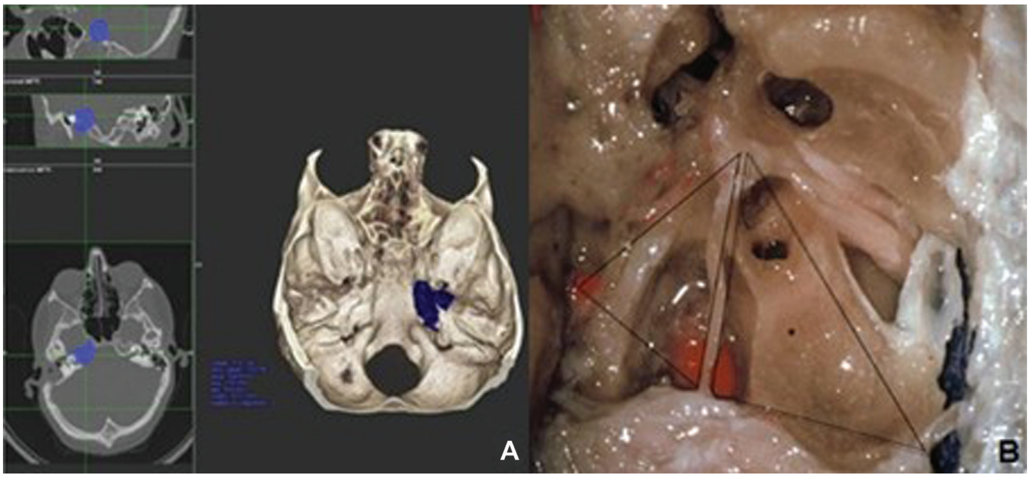


Fig. 17 Middle fossa anatomy. (A) volumetry of the petrosal apex shows the versatility of petrosectomy to reach different portions of the posterior fossa; (B) superior view of the floor of the middle fossa. The bone covering the malleus, internal carotid artery and internal acustic meatus was drilled. To the left, the posterolateral middle fossa triangle (Glasscock's triangle) and, to the right, the posteromedial middle fossa triangle (Kawase's triangle).

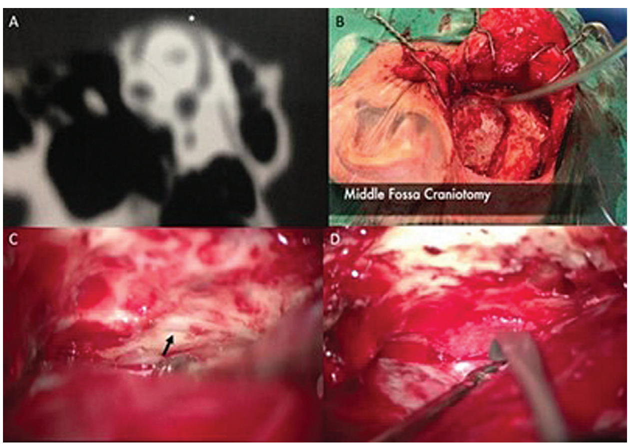


Fig. 18 Middle fossa anatomical knowledge applied to treat a superior semicircular canal dehiscence. (A) axial head bone window computed tomography; (B) middle fossa craniotomy; (C) exposed superior semicircular canal dehiscence (black arrow); (D) surgical repair result.

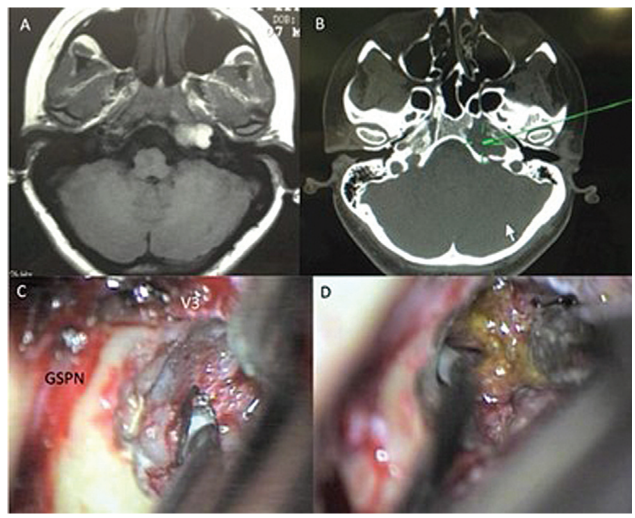


Fig. 19 Cholesterol granuloma of the petrosal apex. (A) axial T1 weighted showing high signal image; (B) axial head bone window computed tomography showing bone erosion of the petrosal apex; (C) intraoperative anterior petrosectomy in-course; (D) exposed tumor.

The next stage is mastoidectomy and labyrinthectomy (►**Fig. 9**). For this, the head is repositioned at a 45° angle and the posterior incision of the anterior petrous approach is extended inferiorly to the cervical region to expose the posterior fossa. After the incision is made, the skin flap is folded anteriorly over the ear. The tip of the mastoid is palpated and a line following the posterior portion of the temporal line is drawn indicating the upper bone limit of the mastoidectomy. The different stages of dissection must be performed as shown in ►**Fig. 9**. After exposing the presigmoid dura mater, the limits of the triangle of Trautmann are identified. This type of laboratory knowledge provides the surgeon great insight and aid in understanding neuroimaging exams to accurately predict what may be found later in the operating room, especially given anatomical variations. At this point in the dissection, a labyrinthectomy should not be performed to avoid reducing the integrity of the internal auditory canal before the next approach, the retrosigmoid. To accomplish this, the bone posterior to the sigmoid sinus is skeletonized and removed, and then the dura mater is opened, and the cisterns explored. In this stage, the three neurovascular complexes of the posterior fossa are identified, and the opening of the internal auditory canal is performed. The next step is to observe from various angles the access that the presigmoid and rectosigmoid approaches provide to the internal acoustic meatus, focusing on its bottom, and to the cistern of the pontocerebellar angle.

The next step is to connect the upper petrous sinus and to section the tentorium, parallel to the petrous part of the temporal bone and toward the incisural space. This exercise is similar to the supra-infratentorial presigmoid approach, also known as posterior petrosectomy. The head is rotated again to view the same anatomical region from different angles and approaches. Even at this stage of dissection, it is

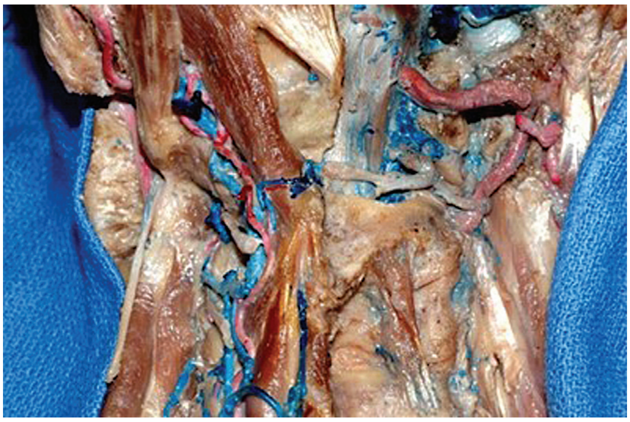


Fig. 20 Anatomical knowledge of the posterior cervical region and the craniocervical junction is important for a safe transcondylar approach.

possible to observe the exposed operative field after resection of the petrous apex and of the presigmoid dura, which is called the "double petrosal approach". The last stage of this review of lateral accesses to the skullbase consists of conducting transcondylar approaches to the craniocervical junction (►**Fig. 20**) and dissecting the jugular foramen as well as the cervical region.

The cadaver head can still be used for endoscopic endonasal approaches and extended endoscopic endonasal approaches.

Laboratory Training to Acquire Microsurgical Skills

Proper training in microvascular techniques requires great concentration and persistence and can be very frustrating at first. The surrounding environment should be calm and, ideally, prevent any kind of interruption. To make the most of this training and diminish physiological tremors, which almost everyone has to some degree, caffeine and nicotine should be avoided 24 hours before training, as any exercises impacting the appendicular muscles. In addition, training should be interrupted for 5 minutes every hour to reduce fatigue.[21–24]

The instruments used for microvascular anastomoses consist of jeweler's micropenets, microscissors, microclamps, a 10-ml syringe with insulin needle and a 90° angled blunt tip, clip holders, number 11 scalpels, retractors, and monofilament nylon threads. 11–0 nylon thread should be used for 0.5 mm diameter vessels, 10–0 for 1.0 mm vessels, and 9–0 for 2.0 mm vessels. The neurosurgeon must be thoroughly familiar with the instruments and the lens system of the surgical microscope and should be able to recognize the magnification that provides the most appropriate visual field: a standard combination is a 12.5x magnification lens on a 200-mm objective, which allows zooming from 4x to 25x. Using binocular vision to work in the center of the visual field is also crucial for good technique.

Placenta Exercises

The placenta has a fetal and a maternal side, and the fetal side has placental vessels that are closely related to the chorionic membrane in much the same way that cerebral vessels are related to the arachnoid membrane. After removing part of the chorionic membrane with microsurgical instruments, arteries and veins can be identified. The former are recognized by three main characteristics: the arteries cross over the veins, have a smaller diameter and a thicker vascular wall.

One of the first exercises to be done is the incision (arteriotomy) and suturing of the arterial wall. After identifying an appropriate artery, microdissection is conducted in the transition between the selected vessel and the placental stroma along a length of $\sim$ 5 cm. Two microclamps are then put in place, first on the proximal and then on the distal end. The next step is to gently separate the tunica externa from the vessel wall, so that the arteriotomy can be made. After that, the arteriotomy is closed with simple sutures. The microclamps are released and the patency of the anastomosed vessel is tested. Another artery is then selected for the next exercise, an end-to-end anastomosis. The steps are the same as in the previous exercise up to the placement of the microclamps, when the microscissors are used to make a single, firm transversal incision through the artery wall, followed by irrigation of the two vascular stumps with saline solution. An end-to-end anastomosis is then performed, in which the first 2 sutures are placed oppositely at the base and the apex of the vessel, that is, at 6 and 12 o'clock positions.

Excess thread is left at the suture for subsequent traction to inspect the pairing of the vessel edges and obtain a symmetrical suture. The next suture locations are to be performed with simple sutures at 9 o'clock, then 7:30 and 10:30 positions on the posterior wall of the vessel. To do this, a 180°4rrrrrt04tg rotation of both clamps has been performed to expose this wall. The next step is to unwind this rotation and suture its anterior wall with simple sutures at 3 o'clock, then 1:30 and 4:30 positions. Finally, the microclamps are removed and this section of the artery is refilled with fluids and the patency of the vessel is verified by observing whether any leaks appear through the suture points.

Experimental Animal Exercises

Every ethical and conscientious society must be concerned with the care and use of any living species. Individuals who work with animals in research, teaching, or laboratory tests should value animal life, consider animals to be sensitive beings, seek to reduce their suffering, and take responsibility to ensure that they are always given excellent care.[21–24] Therefore, it is essential to use techniques that provide, in addition to adequate chemical restraint, anesthetics and analgesics so that the animal does not endure pain to the best of our ability to recognize it.[21–24] Rats are the animal species most commonly used in microsurgical training. After studying the anatomy of the rat and anesthetic techniques for experimental animals, the following exercises can be performed.

The procedure begins by performing a trichotomy of the inguinal and cervical regions. When an angiographic and/or histological study of anastomoses is the goal, typically no tracheostomy is performed, as it is difficult to successfully conduct postoperative procedures on these animals. However, when neither of these are the goal, a tracheostomy is performed, which is, in itself, an excellent microsurgical exercise. This begins with a midline incision from the chin to the sternum, followed by a delicate dissection of the subcutaneous tissue and the placement of retractors at the edges of the incision. The following elements must be recognized: on the midline, the sternohyoid muscle covering the tracheal rings above and bilaterally to the thyroid glands which, when elevated, will allow a view to the triangle formed by the sternohyoid muscle (medial), the sternocleidomastoid (inferolateral) and the omohyoid (superolateral). The carotid artery can be found in this triangle. After making an incision in the sternohyoid muscle, retractors are put in place and the tracheal rings are identified to perform a tracheostomy at the 2nd and 3rd rings. In this way, we obtain a patent airway.

End-to-end Anastomosis

Using opening movements with the microscissors, the carotid artery and the carotid sheath are identified. The rat's carotid artery is usually 1 mm in diameter. At this stage, the vagus nerve must be carefully separated from the carotid artery, avoiding the vagal reflex. Manipulation of the vessels must be minimized to avoid spasm and damage to the vascular wall, and the vessel must always be mobilized by its tunica externa. This is followed by the placement of the distal and proximal microclamps, respectively, and a complete transversal incision to the common carotid artery with the microscissors. It is expected that this should cause a retraction of ~ ⅓ of the vessel. The interiors of both arterial stumps are then irrigated with heparinized saline. The anastomosis is performed as described in the placenta exercises, keeping in mind that the best practice of a microvascular suture is the passage of the needle through all layers of the arterial wall. After the anastomosis is completed, the distal clamp is removed first, and, with a cotton swab, a slight compression is made on the suture site for 2 minutes to wait for platelet aggregation. If there is blood leakage between the sutures, replace the clamp and correct it with another suture. The same procedure is performed again after removal of the proximal clamp.

End-to-side Anastomosis

This type of anastomosis may be arterial or venous and is the most important because it is the most used in neurosurgery. After harvesting the femoral artery from the inguinal area or the internal jugular vein (located in the subcutaneous cellular tissue, lateral to the sternocleidomastoid muscle), two elliptical horizontal incisions are made on the upper surface of the carotid artery, the size of which corresponds to the donor vessel. In the donor segment, a small longitudinal incision of ~ 1 to 1.5 mm is made in one end to split the vessel and increase its diameter. Proceed with anastomosis, suturing both flaps of the donor vessel, starting with the posterior face followed by the anterior face, with 3 to 4 simple sutures on each. Once the exercise is finished, the patency of the anastomosis is verified.

Other Exercises

Several other microanastomosis exercises can be performed on the mouse. In addition to those presented here, end-to-end anastomosis of the femoral artery itself can be performed in the inguinal region, where it has a diameter of 0.5 mm. This is an important exercise that simulates direct cerebral revascularization procedures in children with Moya-Moya. Another exercise consists of performing an end-to-side anastomosis between the left and right carotid arteries, one of which is transposed over the anterior region of the neck for anastomosis with the contralateral artery and connected to its distal surface. Finally, another exercise that can be performed is a laparotomy, which is done by placing the viscera outside the abdominal cavity and then proceeding to anastomose the abdominal aorta. In addition, with the dissection of the membranes surrounding the abdominal vessels, an inflammatory reaction occurs. After 7 days, these membranes become thicker and quite similar to the subarachnoid cisterns at the base of the brain, thus offering more training opportunities. When the main objective is to train for work in deep brain regions, such as when bypassing the superficial temporal artery with the superior cerebellar artery or the occipital artery with the inferior anterior cerebellar artery, place an inverted, 15-cm deep basin with a 4-cm diameter central hole over the rat. The distance between the hole and the carotid artery must be between 6 and 10 cm. Longer instruments must be adapted for this type of training.

The Art of Being a Neurosurgery Assistant

There are many challenges that neurosurgeons-in-training face, such as stressful situations with patients and family members, gaining a complex understanding in treating various diseases and patients under difficult personal circumstances, developing manual skills, confronting careless advisors, finding one's own professional mindset and demeanor, and forming relationships with colleagues both within and beyond one's own specialty. Among all of these, perhaps the greatest challenge is mastering the difficult art of assisting in surgery. It is difficult because, in the anxious rush to acquire psychomotor skills by pursuing any opportunity to train/use them, young neurosurgeons often hinder treatments instead of helping them. Once, when a surgeon was aspirating a skullbase tumor, I saw the aspirator of the assistant enter the surgical field without authorization and begin aspirating another region of the same tumor. The resident must not forget that manual dexterity is only one part of neurosurgical training and can be best acquired in the laboratory.

According to American surgeon Frank Spencer, an operation consists of two areas of activity. The first, which accounts for three-quarters of all significant events during surgery, depends on decision making. The second, accounting for just one quarter of the significant events during surgery, depends on manual dexterity. Lord Moynihan, an English surgeon, mocked his colleagues who overestimated their dexterity in surgery at the expense of other important aspects by saying that they should limit themselves to performing tricks with billiard balls. The great Brazilian surgeon Benedicto Montenegro criticized the honorific phrase often attached to his profession, 'hands of gold'. He considered surgery to be far more mental than manual since much of surgical procedure is based on decision making. Clearly, manual dexterity is key to surgical procedures, but the dictum "the hand does not tremble when the brain does not waver" states very well the relationship of manual and mental labor in the operating room.

Assisting in surgery is a fundamental part of building a solid foundation of experience. The assistant must always focus on two tasks: first, do not cause any disturbance in the operative field, and second, provide exposure. The best assistants are able to work unnoticed. They should speak to communicate only what is essential, and in a way that does not hinder the progress of the surgery. Comments such as "the aneurysm has ruptured" must be withheld when everyone present can clearly see profuse bleeding in the operating field. Trivial conversation and crass comments are unacceptable. Long conversations unrelated to the procedure intrude on the environment and are disrespectful to the patient. Only with understanding and careful observation of what it means to be an assistant will residents in neurosurgery be able to instill similar behavior in their own assistants when they become surgeons. Learning the art of assisting is fundamental to neurosurgical training and establishes good habits of physical and mental control in future surgeons.

Cognition – Clinical and Multidisciplinary Knowledge

Although it may seem redundant, skullbase surgeons in training must never forget that they are, first of all, doctors and not "operators." Excessive focus on the many potential diagnoses for disorders that are treated with neurosurgery may lead us to overlook the neurological, metabolic, and even psychiatric disorders from which a symptom may arise. This can cause the wrong treatment to be selected, and perhaps leave a patient with serious and disabling sequelae. This is especially important at the beginning of the training of a resident physician, when managing complications and handling clinical dilemmas with proper decision-making is a daily necessity.

Students of skullbase surgery should branch out and deepen their neurosurgical abilities, but never at the expense of basic medical knowledge. This knowledge is particularly valuable when you are part of a team of specialized clinicians facing a patient's rapidly declining condition. For example, an elderly patient presenting with sudden confusion and a brain injury caused by cerebrovascular disease, or a tumor previously diagnosed by imaging should be considered, from an investigative point of view, as being in an "acute confusional state" to be examined and evaluated, rather than a "confusional state due to cerebral tumor," because an infectious or metabolic process is more often the cause of this condition. Many such scenarios could be used to illustrate this point, and as a general principle, skullbase surgeons should always remember to initially regard their patients with a clinical mindset.

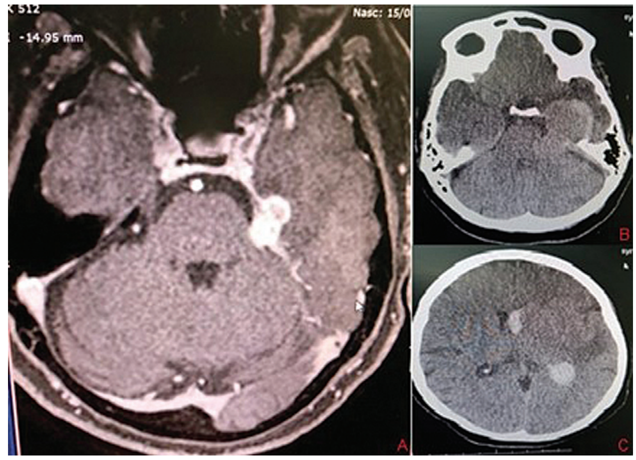


Fig. 21 Illustrative case that shows the importance of a multidisciplinary team. A: Presumed tentorial incisure meningioma, incidental finding. The patient was referred directly to radiotherapy in another hospital, without any neurosurgical evaluation; B: 18 months later, the patient was admitted in the emergency room at our hospital in a coma. Brain computed tomography showed (B) important tumor growth and (C) tumoral hemorrhage. The patient died within 48 hours.

Skullbase surgeons must also develop knowledge of related fields such as neurology, neuroradiology, neuropathology, physiotherapy, speech therapy, and neuropsychology, among others. A doctor training in skullbase surgery should clearly not delve too deeply into these areas, but a little understanding will do much more than simply aid in administering treatment to patients. It will help to foster appreciation and trust among colleagues in these associated fields by allowing a neurosurgeon to "speak the language" and communicate more clearly and directly. This is vital in multidisciplinary teams to avoid wrong treatments (►**Fig. 21**).

Another subject a surgeon should explore is transference and countertransference in relating with patients and their families. A practical understanding of this is especially helpful for anyone treating critically ill and terminal patients as our field is, or course, usually focused on this aspect of care. In a similar way, understanding the psychological stages that terminal neurological patients and their families typically go through – denial and isolation, anger, bargaining, depression, and acceptance – will alleviate the resident's own suffering and foster a surprising amount of learning to humility in facing incurable disease. It will also help them empathize with patients and family members.

Affect – Doubt and Anxieties Surrounding the Doctor-Patient Relationship

Proposed by Professor Roberto Veatch in 1972, the four models of the doctor-patient relationship are: Priestly, Engineering, Collegial, and Contractual.

In molding their professional characters and demeanors, young neurosurgery physicians must be careful to avoid adopting a counterproductive model. The Priestly Model is traditional and is based on the Hippocratic tradition. Here, the doctor assumes a paternalistic attitude toward patients and disregards their wishes. The Engineering Model, unlike the Priestly, places all the decision-making power in the hands of the patients. They are seen as clients procuring a service. The Collegial Model does not differentiate between the roles of doctor and patient in the context of their relationship. This makes the decision-making process highly involved because the physician assumes no authority as a professional, and, instead, power is shared equally. The largest drawback of this model is the loss of purpose for the doctor-patient relationship because it is regarded as a simple relationship between equals who behave as if they possess equal amounts of medical knowledge. Finally, in the Contractual Model, the doctor maintains authority, possess certain skills and knowledge, and assumes responsibility for making technical decisions. Here, patients actively participate in the decision-making process and exercise control as befits their lifestyle and their moral and personal values.

Today, the doctor-patient relationship is no longer guided by the trust of the client and the conscience of the professional. It has become, in many cases, an impersonal contract-for-services in which clients, aware of their rights, demand quality and efficiency in delivery and may become indignant if they perceive any lapses. Even the Code of Hammurabi, established in 1754 BCE, threatened Babylonian physicians with various punishments for injuring their patients. Since then, the doctor-patient relationship has become quite complex and dynamic, particularly in its interpersonal and legal aspects. From the start of training, doctors must be very careful to set aside any personal biases. Ethics and human dignity require us to treat all patients equally, regardless if they have private health insurance, are enrolled in a public healthcare program, or are paying out-of-pocket. This attention to our own feelings and behavior is fundamental to the set of skills we must develop in conducting the doctor-patient relationship. This bond, which has been regarded as almost sacred since the times of Hippocrates, is under threat today. The future success of our profession requires us to address this.[1]

A New "State of Art" Microsurgical Laboratory Training in Brazil

In order to disseminate the culture of microsurgical laboratory training, the southern region of Brazil has since 2022 a modern training center in microsurgical anatomy (►**Fig. 22**). Located in the city of Curitiba, capital of Paraná, at the Universidade Evangélica Mackenzie do Paraná, the microsurgery laboratory has 10 training stations with the most modern medical equipment and another professor's station. In addition, it has modern 3D technology for classes. With an investment of more than 2 million reais, the microsurgical laboratory expects to receive neurosurgeons and otologists from all regions of Brazil not only for its hands-on courses, but also for the development of master's and doctoral research in microsurgical anatomy as part of the postgraduate program in principles of surgery at Paraná Evangelical Mackenzie University (FEMPAR). Being coordinated by the university professors and authors of this article (Isolan G. R. and Bark S. A), the microsurgical anatomy courses will follow the legacy of Professor Evandro de Oliveira's courses and will have a special part dedicated to the correlation of microsurgical anatomy with neuroimaging. Research and thesis in microsurgical anatomy will be guided by professors of neurosurgery and otology at the university and by postgraduate coordinators (Malafaia O. and Filho J. M. R.).

Final Comments

As much as any specialization, skullbase surgery, when conducted with deliberation and sound ethics, is a fascinating and extremely rewarding profession. However, serving our neighbors without being entirely sure that we have chosen the best possible course in light of current knowledge

Fig. 22 Laboratory training at the Universidade Evangélica Mackenzie do Paraná (FEPAR).

Fig. 23 Professor Evandro de Oliveira and his students in the Microsurgery Laboratory at the Hospital Beneficência Portuguesa de São Paulo. More than 5,000 neurosurgeons took Prof. Evandro de Oliveira's microsurgical anatomy courses.

could be a source of unending torment for us. For resident physicians who want to surgically treat pathologies as challenging as brain aneurysms and skullbase tumors, at least 1 year of microsurgical laboratory training is essential. Depending on the subspecialization, they should complement their training in institutions anywhere in the world that are well-regarded for their expertise with specific pathologies.

Understanding that our knowledge is built not only with Cartesian principles, like evidence-based medicine, but also with feelings regarding the social and personal situation of our patients is paramount. Following a rational step-by-step skullbase dissection in the laboratory to achieve the best utility of the cadaveric head, as well as to develop surgical skills performing vascular techniques in placentas and experimental animals is crucial in the skullbase surgeon education.

Anxiety and concern about results are the most powerful resources neurosurgeons have in guiding their conduct in a course of treatment. Approaching each case individually, as if it were their first, benefits the patient. However obvious this may seem, it must be said: the patient should be esteemed above any technique or the gaining of any experience.

Accompanying one of the greatest living icons of neurosurgery, one of the author's (Isolan G. R.) realized that several times, after concluding various surgical procedures that he already possessed a great deal of experience with, he would exclaim: "This was the most difficult case I have ever had." This was the greatest lesson, albeit unintentional, that we have ever received. Every patient is unique and deserves our full attention. We deserve the capacity to give our full attention, and also to reap the personal rewards of it, together with our patients. Always striving for that capacity for attention, for knowledge and skill, is the key.

Finally, Prof. Evandro de Oliveira's legacy will echo in eternity.[25] His school represents what state-of-the-art microsurgery is for most of our patients: simply the best treatment option (►**Fig. 23**).

Note

Some small parts of the present article were published previously in Portuguese by the senior author in a previous article*, but with a focus on the learning. Following ABNT (Brazilian Association for Technical Standards) and copyright rules (law number 9,610), these parts are identified by quotation marks.

*Isolan GR. A construção do conhecimento pelo jovem neurocirurgião: ética, ciência e a importância do treinamento em laboratório de microcirurgia. J Bras Neurocirurg 20 (3): 314–334

Conflict of Interests

The authors have no conflict of interests to declare.

References

1 Yaşargil MG. Microneurosurgery. Vols I, II, and IVB. Georg Thieme VerlagStuttgart1996

2 Yaşargil MG. Reflections of a neurosurgeon. Clin Neurosurg 1988; 34:16–21

3 Yaşargil MG. A legacy of microneurosurgery: memoirs, lessons, and axioms. Neurosurgery 1999;45(05):1025–1092

4 Yaşargil MG, Chandler WF, Jabre AF, Roth P. Neurosurgical horizons. Clin Neurosurg 1988;34:22–41

5 Yaşargil MG. From the microsurgical laboratory to the operating theatre. Acta Neurochir (Wien) 2005;147(05):465–468

6 Adams Pérez J, Rassier Isolan G, Pires de Aguiar PH, Antunes AM. Volumetry and analysis of anatomical variants of the anterior portion of the petrous apex outlined by the kawase triangle using computed tomography. J Neurol Surg B Skull Base 2014;75(03): 147–151. Doi: 10.1055/s-0033-1356491

7 Anichini G, Evins AI, Boeris D, Stieg PE, Bernardo A. Three-dimensional endoscope-assisted surgical approach to the foramen magnum and craniovertebral junction: minimizing bone resection with the aid of the endoscope. World Neurosurg 2014;82(06):e797–e805. Doi: 10.1016/j.wneu.2014.05.031

8 Bernardo A. Virtual Reality and Simulation in Neurosurgical Training. World Neurosurg 2017;106:1015–1029

9 Bernardo A, Boeris D, Evins AI, Anichini G, Stieg PE. A combined dual-port endoscope-assisted pre- and retrosigmoid approach to the cerebellopontine angle: an extensive anatomo-surgical study. Neurosurg Rev 2014;37(04):597–608. Doi: 10.1007/s10143-014-0552-8

10 Bernardo A, Evins AI, Mattogno PP, Quiroga M, Zacharia BE. The Orbit as Seen Through Different Surgical Windows: Extensive Anatomosurgical Study. World Neurosurg 2017;106:1030–1046

11 Bernardo A, Evins AI, Visca A, Stieg PE. The intracranial facial nerve as seen through different surgical windows: an extensive anatomosurgical study. Neurosurgery 2013; 72(2, Suppl Operative): ons194–ons207, discussion ons207

12 Cavalcanti DD, Morais BA, Figueiredo EG, Spetzler RF, Preul MC. Accessing the Anterior Mesencephalic Zone: Orbitozygomatic Versus Subtemporal Approach. World Neurosurg 2018;119: e818–e824

13 Cohen MA, Evins AI, Lapadula G, Arko L, Stieg PE, Bernardo A. The rectus capitis lateralis and the condylar triangle: important landmarks in posterior and lateral approaches to the jugular foramen. J Neurosurg 2017;127(06):1398–1406. Doi: 10.3171/2016.9.JNS16723

14 da Silva SA, Yamaki VN, Solla DJF, et al. Pterional, Pretemporal, and Orbitozygomatic Approaches: Anatomic and Comparative Study. World Neurosurg 2019;121:e398–e403

15 Fukuda H, Evins AI, Burrell JC, Iwasaki K, Stieg PE, Bernardo A. The Meningo-Orbital Band: Microsurgical Anatomy and Surgical Detachment of the Membranous Structures through a Frontotemporal Craniotomy with Removal of the Anterior Clinoid Process. J Neurol Surg B Skull Base 2014;75(02):125–132

16 Isolan GR, Krayenbühl N, de Oliveira E, Al-Mefty O. Microsurgical Anatomy of the Cavernous Sinus: Measurements of the Triangles in and around It. Skull Base 2007;17(06):357–367

17 Isolan GR, Rowe R, Al-Mefty O. Microanatomy and surgical approaches to the infratemporal fossa: an anaglyphic three-dimensional stereoscopic printing study. Skull Base 2007;17 (05):285–302. Doi: 10.1055/s-2007-985193

18 Krayenbühl N, Isolan GR, Hafez A, Yaşargil MG. The relationship of the fronto-temporal branches of the facial nerve to the fascias of the temporal region: a literature review applied to practical anatomical dissection. Neurosurg Rev 2007;30(01):8–15, discussion 15 . Doi: 10.1007/s10143-006-0053-5

19 Oliveira LM, Figueiredo EG. Simulation Training Methods in Neurological Surgery. Asian J Neurosurg 2019;14(02):364–370. Doi: 10.4103/ajns.AJNS_269_18

20 Santos FP, Longo MG, May GG, Isolan GR. Computed Tomography Evaluation of the Correspondence Between the Arcuate Eminence and the Superior Semicircular Canal. World Neurosurg 2018;111: e261–e266. Doi: 10.1016/j.wneu.2017.12.030

21 Andersen ML, D'Almeida V, Ko GM, et al. 2004Princípios Éticos e Práticos do Uso de Animais de Experimentação. UNIFESPSão Paulo

22 Fish R, Brown MJ, Danneman DJ, Karas AZ. 2008Anesthesia and analgesia in laboratory animals. ElsevierSan Diego

23 Isolan GR, Santis-isolan Paola MB, Dobrowolski S, Giotti M. Considerações Técnicas no Treinamento de Anastomoses Microvasculares em Laboratório de Microcirurgia: Technical Considerations. Jbnc 2018;21(01):8–17

24 Serafin D, Georgiade NG. 1986A laboratory manual of microsurgery. Division of Plastic, Reconstructive Surgery and Maxillofacial Surgery, Duke University Medical Center,. Durham North Carolina

25 Vaz MAS, Monteiro JM, Tzu WH, et al. Professor Evandro de Oliveira, a guiding light in skull base surgery and vascular neurosurgery. Surg Neurol Int 2022;13:229

Chronic Traumatic Encephalopathy in Sports Practice: A Literature Review

Encefalopatia traumática crônica na prática de esportes: Uma revisão da literatura

Luiz Henrique Salamoni Abad[1] Ruan Teixeira Lessa[2] Francielle Bianca Moreira de Mesquita[2] Vitória Leite Silva[2] Marcelo Ribeiro Cesar[2] Tayná Beato Ferreira[2] Ana Julia Rodrigues da Costa[2] Thales Nascimento Buzan[3] Nathália Barbosa do Espírito Santo Mendes[1]

[1] Neurosurgery, Monte Sinai Hospital in Juiz de Fora, MG, Brazil
[2] Faculty of Medicine (FAME), Presidente Antônio Carlos University Center (UNIPAC-JF), Juiz de Fora, MG, Brazil
[3] Federal University of Juiz de Fora (UFJF), Juiz de Fora, MG, Brazil

Address for correspondence Ruan Teixeira Lessa, medical student, Avenida Rio Branco, 4335, ap. 403 – Alto dos Passos, Juiz de Fora, MG, 36026-500, Brazil (e-mail: ruan.t.l@hotmail.com).

Arq Bras Neurocir 2022;41(4):e362–e367.

Abstract

Chronic traumatic encephalopathy (CTE) is a neurodegenerative syndrome caused by repetitive and cumulative head trauma. Due to the widespread practice of contact and collision sports, a discussion of the long-term repercussions of repeated head trauma is imperative. The present literature review, performed through the SciELO, PUBMED, and BVS-Bireme databases, includes studies conducted since the year 2000, which established the relationship between CTE and the practice of sports. The diagnosis of CTE was notably present in individuals practicing sports that involve repeated traumatic brain injuries. The noticeable changes triggered by CTE include a series of clinical and neuropathological manifestations that can help in the differentiation from other tauopathies.

Keywords

- traumatic brain injuries
- brain concussion
- chronic traumatic encephalopathy
- tauopathies

Resumo

A encefalopatia traumática crônica (ETC) é uma síndrome neurodegenerativa causada por traumatismo craniano repetitivo e cumulativo. Com a prática disseminada de esportes de contato, torna-se importante discutir as repercussões a longo prazo de traumatismos cranianos repetidos. A presente revisão da literatura, executada através das bases de dados SciELO, PUBMED e BVS-Bireme, inclui estudos realizados desde o ano de 2000 que estabeleceram a relação entre a ETC e a prática de esportes. O diagnóstico de ETC esteve notadamente presente em indivíduos praticantes de esportes que envolvem repetidas lesões cerebrais traumáticas. As alterações perceptíveis desencadeadas pela ETC incluem uma série de manifestações clínicas e neuropatológicas, que podem auxiliar na diferenciação de outras tauopatias.

Palavras-chave

- lesões cerebrais traumáticas
- concussão cerebral
- encefalopatia traumática crônica
- tauopatias

received
June 5, 2021
accepted
April 25, 2022

DOI https://doi.org/10.1055/s-0042-1749350.
ISSN 0103-5355.

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

Introduction

Traumatic brain injury is a proven risk factor for neurodegenerative diseases, including chronic traumatic encephalopathy (CTE).[1] Chronic traumatic encephalopathy was first described in boxers under the name "punch-drunk syndrome", in 1928, by the pathologist and examiner Harrison Martland,[2] later renamed as "pugilistic dementia" (Millspaugh, 1937),[3] and, finally, as CTE (Critchley, 1957).[4] It is characterized as a neurodegenerative tauopathy caused by repetitive and cumulative head trauma or traumatic brain injury (TBI).[5–7] Besides the classical description in boxers, other sport activities, such as muay thay, Chinese boxing, mixed martial arts, wrestling, hurdling, lacrosse, rugby, field hockey, and soccer and football, in particular, have been described as potential causes of TBIs and, consequently, risk factors for the development of CTE.[6,8,9]

Epidemiological studies show that trauma is one of the main causes of morbidity and mortality, ranking third in general mortality in Brazil, with greater severity when considering TBI, whether from contact and collision sports or accidents. Traumatic brain injury can be related with intracranial hemorrhages, hematomas, carotid or vertebral dissection, concussions, and diffuse axonal lesions.[10]

Between 1965 and 2019, research from Europe, the United States, New Zealand, and Australia has found that up to one third of all causes of TBI are sport-related. Furthermore, the occurrence of trauma ranged from 3.5 to 31.5 per 100,000 in studies analyzing those individuals who attended hospitals after TBI, whereas, in the community, it ranged 170 per 100,000, according to the population of the countries.[11] In time, it is important to highlight that concussion is very common when related with contact and collision sports, such as in the United States, where 1.6 to 3.8 million sports-related concussions occur annually.[12]

Chronic traumatic encephalopathy is a neurodegenerative syndrome caused by single, episodic, or repetitive blunt force impacts to the head and transfer of acceleration/deceleration forces to the brain. It presents itself clinically as a syndrome composed of mood disorders and behavioral/cognitive impairment, with or without a sensory-motor disease.[13] Furthermore, it is related to the widespread deposition of hyperphosphorylated tau protein (p-tau) in the form of neurofibrillary tangles (NFTs)[14] in the sulci and perivascular spaces[12] with preferential involvement of the superficial cortical layers and a propensity for sulcal depths.[6,15]

The occurrence of CTE has demonstrated significant importance within the scientific context, with regard to its development and specificities inherent to the etiology. In addition, its health implications with differential value to other diseases evoke the need for more thorough studies in this matter.

Therefore, this article aims to clarify, through a literature review, the existing correlation between chronic traumatic encephalopathy and the practice of sports, as well as its main aspects for a differential diagnosis. Additionally, this paper aims to establish a threshold that distinguishes CTE from other pathologies that have similar clinical outcomes.

Material and Methods

This review article was developed based on a data survey found in the literature. The related bibliographic searches were published in the period between 2000 and 2020 in the following scientific databases: SciELO, PUBMED, and BVS-Bireme.

The descriptors used in the medical subject headings (MeSH) and *Descritores em Ciência da Saúde* (DeSC) were: *chronic traumatic encephalopathy*, *traumatic brain injury*, and *trauma in athletes*. Their respective correspondents in Brazilian Portuguese were also consulted. Subsequently, the studies that met the following inclusion criteria were distinguished as such: electronic bibliographies compatible with the descriptors listed above; chronology from the year 2000 on; books; full texts and theses; abstracts; original articles, review articles, and case reports in the aforementioned medical scientific databases. We decided to exclude studies that did not establish a relationship between CTE and the practice of sports, and, in order to guarantee an adequate theoretical basis for the evolution and discussion of the theme, only the studies considered most significant were analyzed.

From this point, 375 manuscripts were found and, after applying the inclusion criteria, 234 were accounted for. By reading the titles and abstracts, 168 texts were eliminated and 66 of them were analyzed and read in their entirety. Thus, 35 references were considered for this review and 8 duplicates were discarded. In the end, 27 sources were included as proper bibliographic references, which present original scientific properties as well as relevance to the approach of this work.

Results and Discussion

Given what was analyzed, there was significant correlation between the diagnosis of CTE and its connection to sports practitioners, or even in cases of repeated traumatic brain injuries.

Thus, from an analysis of postmortem brains donated and obtained from a cohort of 85 individuals with a history of repetitive mild traumatic brain injury, approved by the Boston University School of Medicine, it was found that 80 were athletes, and 22 of these were athletes and military veterans. Of these 85, evidence of CTE was found in 68 individuals. It is worth noting that all (68) those with evidence of CTE were males aged between 17 to 98 years old, 51 (75%) of whom had the confirmed diagnosis and 7 (10.3% of all cases with evidence of CTE) had Alzheimer disease (►**Table 1**), ranging from focal comorbidity in stages I to III to inclusions and generalized neuritis in stage IV[14] (►**Table 2**).

In contrast, in the review study by McKee et al.,[12] it was observed that of 51 neuropathologically confirmed cases of CTE, 46 (90%) occurred in athletes. The first symptoms were noticed between 25 to 76 years old ($M = 42.8$, $SD = 12.7$). One third were symptomatic at the time of retirement from the sport, and half were symptomatic within 4 years of cessation of practice (►**Table 1**).

Table 1 Diagnostic correlation of chronic traumatic encephalopathy with the practice of sports in identified studies

Source	Type of study	N sample	Age group	Diagnosis
McKee et al.[14]	Cohort (autopsy)	80 athletes (22 of whom were also military veterans)	Between 17 and 98 years old (average of 59.5 years old)	Of the 68 cases with evidence of CTE: 51 (75%) - CTE; 8 (12%) - Motor neuron disease; 7 (10.3%) - Alzheimer disease; 11 (16%) - Lewy body disease; 4 (6%) - Frontotemporal lobar degeneration
McKee et al.[12]	Review	51, of whom: 46 (90%) were athletes (39 boxers [85%], 5 football players [11%], 1 professional wrestler and 1 soccer player).	Between 23 and 91 years old	100% - CTE
Montenigro.[16]	Review	202 (141 boxers, 54 football players, 5 ice hockey players and 2 professional wrestlers)		83 - definite CTE, 90 - probable CTE, and 29 - possible CTE.

Table 2 Symptomatology characteristic of chronic traumatic encephalopathy according to stages I to IV of the disease

Stages of CTE	Symptoms
I	Headache, loss of attention and concentration.[14,18]
II	Depression, explosiveness, and short-term memory loss.[14,18]
III	Executive dysfunction and cognitive impairment.[14,18]
IV	Dementia, difficulty finding words, and aggression.[14,18]

Abbreviations: CTE, chronic traumatic encephalopathy.

Similarly, in another review, 202 cases from 20 publication series, 4 books and 1 medical dissertation[16] were analyzed. The Jordan criteria[17] were considered, which are: definite CTE (any neurological process consistent with clinical presentation of CTE in conjunction with pathological confirmation), probable CTE (any neurological process characterized by two or more of the following conditions: cognitive and/or behavioral impairment; cerebellar dysfunction; pyramidal tract disease or extrapyramidal disease; clinically distinguishable from any known disease process consistent with the clinical description of CTE), possible CTE (any neurological process that is consistent with the clinical description of CTE, but can potentially be explained by other known neurological disorders).[17] Thus, in this study, 83 of the cases would have definite CTE; 90, probable CTE, and 29, possible CTE[16] (►**Table 1**).

However, Montenegro et al.[16] point out new diagnostic criteria, such as: a behavioral/mood variant, a cognitive variant, a mixed variant, and dementia (traumatic encephalopathy syndrome). The progressive, stable, and unknown course modifiers are used to describe the clinical course, and if specific motor signs are evident, the modifier with motor characteristics will be added. The selection of the general

Table 3 Diagnostic characterization of the pathophysiological impairment of chronic traumatic encephalopathy at the clinical, neuroimaging, and neuropathological levels

Level	Alterations
Clinical	Memory disorders; behavioral and personality changes; parkinsonism; speech and gait abnormalities[6,12,18]
Neuroimaging	Atrophy of the cerebral hemispheres, medial temporal lobe, thalamus, mammillary bodies, and brainstem; ventricular dilatation; and a fenestrated septum pellucidum cavum[6,12,18]
Neuropathological	Extensive tau-immunoreactive and astrocytic neurofibrillary tangles; and spindle-shaped neurites throughout the brain[6,12,18]

criteria was based on the literature reviewed by the authors and was designed to favor sensitivity over specificity.[13]

The noticeable changes triggered by CTE involve a series of clinical, encephalic, and microscopic manifestations, which are characteristics that can help in differentiating it from other tauopathies (►**Table 3**).

Pathophysiology

The definitive encephalic lesion, which is established after TBI, is a result of the different densities between the encephalon and the cranial box, thus, when submitted to the same inertial forces, they respond unequally. This mismatch of movements can promote rupture of cerebral veins that flow into the dural sinuses, as well as the impact and laceration of the parenchyma against the rigid structures of the skull. In addition to this mechanism, as the central region of the brain is relatively fixed due to the presence of the brainstem, the peripheral regions of the brain and cerebellum tend to present a greater amplitude of displacement. Therefore, this difference in the extent of movements between the central and peripheral regions of the brain generates stretching of axons and cerebral blood vessels, which can result in anything from temporary dysfunction to rupture of these structures.[18,19]

The alterations are of macro and microscopic character. Macroscopically, modifications of the septum pellucidum are found, with the presence of fenestrations and a large *cavum*, associated with cerebellar atrophy. On the other hand, microscopically, there is loss of cerebellar Purkinje cells, degeneration, and loss of substantia nigra cells, presence of neurofibrillary tangles (NFTs), which are aggregates of tau polymers, neuropil threads and glial tangles (GTs).[10,12,18]

During a traumatic event, there is a shear deformation in the brain and spinal cord, causing transitory or permanent lengthening of axons. Traumatic axonal injury's outcomes are changes in axonal membrane permeability; ionic changes, including great calcium influx and release of caspases and calpains that can trigger phosphorylation of tau; unfolding; truncation and aggregation, as well as cytoskeletal breakdown with dissolution of microtubules and neurofilaments.[6,20]

Immediately after a biomechanical injury to the brain, there is an abrupt and indiscriminate release of neurotransmitters and uncontrolled ion fluxes. In this regard, the binding of excitatory transmitters, such as glutamate, to the N-methyl-D-aspartate (NMDA) receptor conditions additional neuronal depolarization with potassium efflux and calcium influx. These ionic changes promote acute and subacute changes in cellular physiology.[21]

In the acute deformation, the effort to restore the neuronal membrane potential, the sodium-potassium ($Na+$- $K+$) pump, is beyond normal. Therefore, it requires increasing amounts of adenosine triphosphate (ATP), causing a dramatic jump in glucose metabolism. This "hypermetabolism" occurs in the scenario of decreased cerebral blood flow, and the disparity between glucose supply and demand triggers a cellular energy crisis. The resulting energy shortage is a likely mechanism of post-concussive vulnerability, making the brain less able to respond adequately to a second injury and, thus, leading to prolonged deficits.[21]

After the initial period of accelerated glucose utilization, the affected brain enters a period of depressed metabolism. As such, persistent increases in calcium can impair mitochondrial oxidative metabolism and worsen the energy crisis. In addition, unchecked calcium accumulation can also directly activate pathways leading to cell death, and thus intra-axonal calcium flux disrupts neurofilaments and microtubules, impairing post-traumatic neural connectivity. There are other changes, such as: lactic acid generation, decreased intracellular magnesium, free radical production, inflammatory responses, and altered neurotransmission.[21]

Modifications in neurotransmitters are present in the glutamatergic system through glutamate and NMDA binding, in which long-term potentiation, a measurement of plasticity dependent on this receptor, may be persistently impaired in the hippocampus. Meanwhile, there are impairments to the adrenergic and cholinergic systems, such as early changes in choline acetyltransferase activity and neuronal loss in the forebrain, a triggering factor for learning and memory deficits. The loss of hilar neurons, producers of γ-aminobutyric acid (GABAergic), can compromise the normal inhibition of the hippocampal dentate granule cells. This loss may predispose the traumatized brain to the subsequent development of seizures.[20]

Furthermore, nitric oxide (NO) is produced by the increase in intracellular calcium concentration associated to cellular aggression mechanisms present in trauma. In TBI, its action may be divided into three phases. First, NO seems to act preserving the cerebral blood flow (CBF) in its first 30 minutes. In a second phase, there is a depletion of NO accompanied by a decrease of CBF between 30 minutes and 6 hours. Lastly, NO increases again after 6 hours. In this last phase, the accumulation of this oxide affects the endothelium, causing a potent vasodilation and increase in vascular permeability. The combination of these actions leads to increased CBF, cerebrospinal fluid pressure, and cerebral edema.[22]

Therefore, repeated injuries in collision and contact sport practitioners over a period of time can lead to significant anatomical or behavioral impairment. Traumas can be characterized by concussions, which occasionally lead the brain tissue to a state of progressive deterioration by overstimulation of the injured brain. Thus, the pathophysiology has an impact on the possible apparent signs and symptoms that can lead to CTE.[20]

Clinical Aspects

Individuals with CTE may develop a variety of clinical symptoms and secondary illnesses; and many of these are insidious. These include mood and behavioral impairment, such as the manifestation of depression, anxiety, apathy, paranoia, psychotic symptoms, suicidality, explosiveness, violent amnesia, drowsiness, dizziness, altered level of consciousness, slowness to answer questions or follow directions. There are also changes in cognition, with impaired memory, executive dysfunction, loss of attention, and dementia.[12,16,23,24]

Likewise, some physical or somatic signs and symptoms can be observed, such as: blurred vision, decreased performance, diplopia, fatigue, headache, dizziness, nausea, vomiting, incoordination, tinnitus, seizures, difficulty speaking (incoherence), stray and glassy eyes, seeing bright spots, and vertigo.[12,16,24] Less commonly, eye abnormalities, such as ptosis; and in motor functioning, such as the appearance of Parkinsonism features: ataxia and dysarthria, dysgraphia, bradykinesia, tremor, rigidity, gait disturbances, falls, and even Parkinson itself.[12,16,24]

Following a large systematic review of 47 studies, done by McKee AC et al.,[12] that sought to evaluate the long-term effects of sports-related concussion in 46 retired athletes, the mean age of onset was found to be 42.8 years old. Notwithstanding one third of the athletes was symptomatic at that time, the onset roughly occurred around 8 years after retirement. Among the main symptoms noted were major mood disturbances in 30% of the athletes and movement abnormalities (such as Parkinson and slow gait) in 42%.[12]

Therefore, there is social instability, irregular behavior, memory loss, and early symptoms of Parkinson disease in the early affective and psychological disorders. In the later stages, CTE can be clinically confused with Alzheimer disease or frontotemporal lobar degeneration (FTD), as well as general cognitive dysfunction progressing to dementia.[6,14]

Diagnosis Criteria

As previously described, CTE is a progressive neurodegeneration characterized by widespread deposition of hyperphosphorylated tau protein (p-tau) as NFTs, and in late stages it can be clinically confused with other dementia diseases such as Alzheimer disease (AD), frontotemporal lobar degeneration (FTD), and Parkinson disease.[23,24]

Within the vast information present in the literature, it is important to list the topics that guide the laboratory diagnosis of CTE: prominent perivascular distribution of astrocytic tangles (AS) and NFTs; irregular cortical distribution of immunoreactive NFTs to p-tau and AS with a predilection for the depth of the cerebral sulci; subpial and periventricular groups of AS in the cerebral cortex, diencephalon, basal ganglia and brainstem and NFTs located preferentially in superficial layers. Besides the presence of NFTs in the mamillary body, typical of CTE, likewise in the substantia nigra, in a severe stage; and absence of β-amyloid peptide deposits. Regarding macroscopy, there is generalized atrophy of the cerebral cortex, medial temporal lobe, diencephalon and mamillary bodies with enlarged ventricles.[8,25]

Differential Diagnosis

Precisely because it is a dementia, CTE requires differentiation from other syndromes of the same spectrum, as mentioned above: AD, Parkinson disease, and FTD. In order to expose such differences, the following milestones for each pathology are found bellow.

Alzheimer Disease

The criteria for AD were based on the presence of β-amyloid protein plaques and p-tau ENFs. The nature, pattern, and distribution of p-tau neurofibrillary degeneration in CTE are distinct from AD, which denotes diffuse cortical presence of NFTs and absence of pathological perivascular neurofibrillary clustering. Furthermore, there is a widespread cortical distribution of p-tau pathology without accumulation in the sulcal depths, and the subpial region in the depth of the sulcus does not demonstrate AEs positive for p-tau.

Furthermore, there is a notable element of presence of abundant β-amyloid plaques and intercalated NFTs, along with moderate neurofibrillary alteration in the compact substantia nigra typical of severe AD; and absence of AEs or NFTs in the mamillary body in the disease.[14,26]

Parkinson Disease and Lewy Body Dementia

The Parkinsonian diagnosis is made based on the presence of positive Lewy bodies with positive alpha-synuclein predominantly in the brainstem, a laboratory finding absent in CTE. The existence of these bodies may also signal another type of dementia, the Lewy body dementia, which evolves intracytoplasmic aggregation of spherical elements and eosinophilic infiltrate that are, again, elements that are not aggregated to CTE.[14,27]

Frontotemporal Lobar Degeneration

The diagnosis of FTD is based on the predominant involvement of the frontal and temporal cortices and characteristic immunohistochemistry for p-tau and measured by cytoplasmic and intranuclear neuronal inclusions positive for TAR 43 DNA-binding protein, showing some relation with CTE and being presented in the scope of differential diagnoses. Additionally, dystrophic neurites and glial cytoplasmic inclusions are visualized in the superficial layers of the cerebral cortex and dentate gyrus. The differential of FTD includes progressive supranuclear palsy, corticobasal degeneration, and Pick disease, patterns that are absent in CTE.[25,27]

Conclusion

In summary, the relationship established between the genesis of CTE and the practice of sports, especially of contact and collision sports, is clear since repetitive traumas predispose to an array of metabolic, ionic, cellular, and synaptic disorders that may provoke the pathophysiological cascade of CTE. Furthermore, similarities and significant differences have been noted between CTE and other dementia diseases, such as Alzheimer and Parkinson, aiming to present a differential diagnosis.

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

References

1 Arena JD, Smith DH, Lee EB, et al. Tau immunophenotypes in chronic traumatic encephalopathy recapitulate those of ageing and Alzheimer's disease. Brain 2020;143(05):1572–1587
2 Martland H. Soco bêbado. J Am Med Assoc 1928;91:1103–1107
3 Millspaugh JA. Dementia pugilistica. U S Nav Med Bull 1937; 35:297–303
4 Critchley M. Medical aspects of boxing, particularly from a neurological standpoint. BMJ 1957;1(5015):357–362
5 Ling H, Kara E, Revesz T, et al. Concomitant progressive supranuclear palsy and chronic traumatic encephalopathy in a boxer. Acta Neuropathol Commun 2014;2(01):24
6 Gavett BE, Stern RA, McKee AC. Chronic traumatic encephalopathy: a potential late effect of sport-related concussive and subconcussive head trauma. Clin Sports Med 2011;30(01):179–188, xi
7 Nascimento LES, Rocha WN, Sanches TP. A importância dos exames de imagem na detecção precoce de demência pugilística. UNILUS Ensino e Pesquisa 2016;13(30):249
8 Areza-Fegyveres R, Caramelli P, Nitrini R. Encefalopatia traumática crônica do boxeador (dementia pugilistica). Rev Psiq Clín 2005;32(01):17–26
9 Ortiz MI, Cánovas GM. Conmoción cerebral asociado a un traumatismo craneoencefálico en los deportista. Medwave 2013;13 (01):e5617
10 Damiani D, Laudanna N, Barril C, Sanches R, Borelli NC, Damiani D. Encefalopatias: etiologia, fisiopatologia e manuseio clínico de algumas das principais formas de apresentação da doença. Rev Bras Clin Med 2013;1(11):67–74

11 Theadom A, Mahon S, Hume P, et al. Incidence of Sports-Related Traumatic Brain Injury of All Severities: A Systematic Review. Neuroepidemiology 2020;54(02):192–199

12 McKee AC, Cantu RC, Nowinski CJ, et al. Chronic traumatic encephalopathy in athletes: progressive tauopathy after repetitive head injury. J Neuropathol Exp Neurol 2009;68(07):709–735

13 Omalu B. Chronic traumatic encephalopathy. Prog Neurol Surg 2014;28:38–49

14 McKee AC, Stern RA, Nowinski CJ, et al. The spectrum of disease in chronic traumatic encephalopathy. Brain 2013;136(Pt 1):43–64

15 Fesharaki-Zadeh A. Chronic Traumatic Encephalopathy: A Brief Overview. Front Neurol 2019;10:713

16 Montenigro PH, Baugh CM, Daneshvar DH, et al. Clinical subtypes of chronic traumatic encephalopathy: literature review and proposed research diagnostic criteria for traumatic encephalopathy syndrome. Alzheimers Res Ther 2014;6(05):68

17 Jordan BD. The clinical spectrum of sport-related traumatic brain injury. Nat Rev Neurol 2013;9(04):222–230

18 Aldag M, Armstrong RC, Bandak F, et al. The Biological Basis of Chronic Traumatic Encephalopathy following Blast Injury: A Literature Review. J Neurotrauma 2017;34(S1):S26–S43

19 Andrade AFD, Paiva WS, Amorim RLOD, Figueiredo EG, Neto ER, Teixeira MJ. Mecanismos de lesão cerebral no traumatismo cranioencefálico. AMB Rev Assoc Med Bras 2020;55(01):75–81

20 Giza CC, Hovda DA. The neurometabolic cascade of concussion. J Athl Train 2001;36(03):228–235

21 Cantu RC. Neurologic Athletic Head and Spine Injuries. WB Saunders Company; 2000:80–100

22 Cherian L, Hlatky R, Robertson CS. Nitric oxide in traumatic brain injury. Brain Pathol 2004;14(02):195–201

23 Omalu BI, DeKosky ST, Minster RL, Kamboh MI, Hamilton RL, Wecht CH. Chronic traumatic encephalopathy in a National Football League player. Neurosurgery 2005;57(01):128–134, discussion 128–134

24 Koga S, Dickson DW, Bieniek KF. Chronic traumatic encephalopathy pathology in multiple system atrophy. J Neuropathol Exp Neurol 2016;75(10):963–970

25 Sparks P, Lawrence T, Hinze S. Neuroimaging in the Diagnosis of Chronic Traumatic Encephalopathy: A Systematic Review. Clin J Sport Med 2020;30(Suppl 1)S1–S10

26 Omalu BI, DeKosky ST, Hamilton RL, et al. Chronic traumatic encephalopathy in a national football league player: part II. Neurosurgery 2006;59(05):1086–1092, discussion 1092–1093

27 Victoroff J. Traumatic encephalopathy: review and provisional research diagnostic criteria. NeuroRehabilitation 2013;32(02): 211–224

Falcotentorial Meningiomas: Optimal Surgical Planning and Intraoperative Challenges - Case Report and a Review

Luiz Severo Bem Junior[1] Pedro Lukas do Rêgo Aquino[2] Luiz Euripedes Almondes Santana Lemos[1] Maria Améllia do Rêgo Aquino[3] Marcelo Moraes Valença[4] Hildo Rocha Cirne de Azevedo Filho[1]

[1] Department of Neurological Surgery, Hospital Da Restauração, Recife, PE, Brazil
[2] Facuty of Medical Sciences, Universidade de Pernambuco, Recife, PE, Brazil
[3] Faculty of Medical Sciences, Universidade Federal de Pernambuco, Recife, PE, Brazil
[4] Neurosurgery Department, Hospital das Clínicas, Universidade Federal de Pernambuco, Recife, PE, Brazil

Address for correspondence Luiz Severo Bem Junior, MD, Neuroscience Post-Graduate Program, Federal University of Pernambuco, Av. Prof. Moraes Rego, 1235 - Cidade Universitária, Recife - PE, Zipcode: 50670-901, Recife, Brazil (e-mail: luizseverobemjunior@gmail.com).

Arq Bras Neurocir 2022;41(4):e368–e374.

Abstract

Meningiomas arising from the falcotentorial junction are rare, and the selection of the optimal surgical approach is essential. We report a falcotentorial meningioma (FTM) case approached by occipitotranstentorial resection and subtotal tumor resection presenting a satisfactory clinical outcome. The present review sought to reveal the current knowledge regarding the clinical presentation, radiological imaging, and the microsurgical anatomy of FTMs as a form of improving the surgical approach. The selection of the optimal surgical approach is essential for the safe and effective removal of an FTM. Preoperative imaging analysis should identify the anatomical relations of the tumor and guide toward the least disruptive route that preserves the neurovascular structures.

Keywords
- falcotentorial meningioma
- occipital transtentorial approach
- pineal region meningioma
- outcome

Introduction

Among pineal region tumors, meningiomas are a rare entity, corresponding to between 2 and 8% of pineal tumors and to 1% of all intracranial meningiomas.[1–3] Guttmann[4] described the first pineal meningioma in 1930. In 1937, Araki[5] published two cases successfully treated with a posterior transcallosal approach. These tumors originate from the posterior portion of the velum interpositum or falcotentorial union.[3] Falcotentorial meningiomas (FTMs), as with other pineal region tumors, are prevalent in females.[3] These tumors present a different relationship with vital neuroanatomical structures; therefore, it is essential to decide on the ideal surgical approach.[1] It is often difficult to discriminate between FTM and velum interpositum meningiomas, even after significant advances in neuroimaging.[3] However, arterial irrigation is the main difference between these two groups of tumors. The tentorial branches of the meningohypophyseal trunk usually supply FTMs, while branches of the posterior choroidal arteries 4 to 7 irrigate velum interpositum meningiomas. The surgical treatment of these tumors is not well-established in literature, since there are two main controversial issues. First, concerning validating criteria for selection of the optimal surgical approach, and second,

received October 10, 2020
accepted July 30, 2021

DOI https://doi.org/10.1055/s-0041-1740593.
ISSN 0103-5355.

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

whether the main infiltrated venous structures can be sacrificed to obtain a radical resection of the tumor or if they should be preserved.[6]

The present review sought to reveal the current knowledge regarding the clinical presentation and radiological imaging of FTMs as a form of improving the surgical approach.

Classification

Falcotentorial meningiomas represent a subgroup of tentorial meningiomas originated from the dura mater junction depending on the posterior cerebral falx and on the convergence of both tentorial folds, projecting anterosuperiorly, inferiorly, or posteriorly depending on their growth pattern.[3] Regarding their classification, the pineal region meningioma group included FTMs with anterosuperior and inferior extension and velum interpositum meningiomas.[1] Yasargil et al. made one of the first tumor descriptions and eight types of tentorial meningiomas (with types T3 and T8 being falcotentorial) were identified.[7] In 1995, Asari et al. described the classification systems for FMTs based on tumor projection that classifies the tumors as anterior, superior, posterior, and inferior types.[8] In 2008, Bassiouni et al. classified FMTs according to tumor base location and included four types (►**Table 1**):

Type I. Type I includes tumors between both dural leaves of the cerebral falx, immediately superior to the junction of the vein of Galen with the straight sinus. In the description by Asari et al., this tumor corresponds to the anterior type.[7]

Type II. Type II originates close to junction of the vein of Galen with the straight sinus, underneath the anterior edge of the tentorium. In the description by Asari et al., this type corresponds to an inferior type.[7]

Type III. Type III is the lateralized type; therefore, it includes tumors with a dural origin in a paramedian location of one of the tentorial leaves and has a medial growing pattern toward the vein of Galen.[7]

Type IV. This type includes tumors from dural adhesion in the falcotentorial junction along the straight sinus with a posterior direction and, as described by Asari et al., it corresponds to the posterior type.[7]

On the other hand, velum interpositum meningiomas are related to the posterior portion of the double pia mater layer that covers the posterior wall of the third ventricle.[9]

Clinical Presentation

Falcotentorial meningiomas occur mostly in patients between 42 and 56 years old, similar to the posterior fossa meningiomas (44.4 years old).[10,11] Previous studies revealed headaches as the most common symptom in pineal region meningiomas (present in 60 to 100% of the cases), followed by ataxia (43 to 62%), personality changes and bradypsychia (37 to 46%), and homonymous hemianopia (20 to 46%).[6]

Ataxia is the most frequent late symptom in type I and II tumors.[6] Personality changes and bradypsychia were mostly associated in obstructive hydrocephalus cases.[6] Nevertheless, bilateral visual acuity deterioration due to progressive papilledema and the subsequent atrophy of the optic nerve is extremely rare.[8,12] Hearing impairment has been occasionally reported in patients with FTM, which improves after surgical removal.[6] The clinical symptoms of meningioma have a propensity to occur insidiously due to their slow growth, thereby explaining the diagnosis delay to ∼ 25 months, on average.[3]

Some authors consider the presence of alterations in ocular supraversion (Parinaud syndrome) or oculomotor cranial nerve alterations as an important differential diagnosis because this feature presents a considerably lower rate (10%) in pineal region meningiomas than in other neoplasms in the same location.[13,14]

Surgical Anatomy

Falcotentorial meningiomas present their vascular blood supply originating from the internal carotid artery (ICA), the external carotid artery (ECA), or the posterior cerebral artery (PCA).[15] ►**Table 2** summarizes the blood supply and their distal branches.

Regarding surgical treatment, understanding the relationship between meningiomas of the pineal region and the deep venous system is decisive for better results. Invasive tumor degree or the permeability of the vein of Galen and the straight sinus and the displacement of these vessels are relevant points in view of the mass effect of the tumor.[7,15]

Occlusion and invasion of the vein of Galen and of the straight sinus were described in preoperative angiographic studies; consequently, the development of a secondary collateral venous drainage is frequently found.[8,10,29] It can be explained due to the fact that the posterior half of the vein

Table 1 Bassiouni Falcotentorial Meningioma Classification[7]

Type of Meningioma	Origin	Venous displacement	Surgical approach
FTM type I	Posterior cerebral falx	Inferior	Occipital transtentorial
FTM type II	Inferior margin falcotentorial	Superior	Supracerebellar infratentorial
FTM type III	Paramedian tentorial	Superomedial	Paramedian supracerebellar infratentorial/Occipito transtentorial
		Inferomedial	
FTM type IV	Tentorial toward straight sinus	Contralateral	Occiptotranstentorial

Abbreviation: FTM, falcotentorial meningioma.

Table 2 Arterial supply and branches of falcotentorial meningiomas

Arterial supply	Distal Branches
ICA	Anterior choroidal artery branches
	Posterior branches from meningohypophyseal trunk
	Middle meningeal artery branches from external carotid artery
ECA	Ophthalmic artery branches
	Middle meningeal artery branches
PCA	Medial choroidal branches
	Lateral choroidal branches

Abbreviations: ECA, external carotid artery; ICA, internal carotid artery; PCA, posterior cerebral artery.

of Galen and the anterior half of the straight sinus are mostly the first vessels affected by meningiomas and are not related to the growth direction of the tumor.

Identifying vessel occlusion and the secondary collateral venous drainage is essential to evaluate the optimal surgical planning for FTMs.[8,10] Many authors have proposed that the displacement of the deep venous system due to the direction of tumor growth is the most important characteristic when deciding the surgical approach.[1,2,6,7] Therefore, Type I FTMs displace the venous complex inferiorly, type II superiorly, type III medially (supero/inferomedial), and type IV to the contralateral side of the meningioma.[6]

Imaging Assessment

Magnetic Resonance Imaging (MRI): Falcotentorial meningiomas are identified as a homogeneous mass, predominantly oval, with homogeneous enhancement after the administration of gadolinium-T1 contrast.[27] In T1 sequences, they are usually hypo/isointense and iso/hyperintense in T2 sequences. Peritumoral edema was observed in 85% of the patients in a case series, whereas obstructive hydrocephalus, mainly revealed in infratentorial lesions, was observed in ~ 32%. In this study, the average diameter of the lesion was 52 mm.[30]

In the preoperative period, knowledge about the patency of the rectal sinus and the displacement of the Galen vein and internal cerebral veins are fundamental to optimal surgical planning, and MRI can provide this information.[6]

Furthermore, MRI is more accurate in enabling the visualization of the straight sinus and the vein of Galen when compared with conventional angiography, since it was able to identify these structures in ~ 20% of the patients.[6]

Cerebral Angiography: Currently, some authors do not indicate cerebral angiography routinely in FTMs because angiomagnetic resonance has advanced in the last years.[6] The direction of the displacement of the medial choroidal artery is one of the most important angiographic features that can be used to differentiate FTMs from other pineal masses.[5,8,31,32] Therefore, medial choroidal artery displaces anteriorly in FTMs and superior and posteriorly in the other pineal tumors.[5,32]

Surgical Approach

The objective of the surgical treatment of FTMs is to achieve a macroscopically complete resection of the lesion, to relieve or solve the neurologic/clinical symptoms, and to acquire a tissue sample for a definitive diagnosis. Therefore, the recommendation to perform an intraoperative biopsy is established, paving the way to obtaining a differential diagnosis from other pineal tumors (for example, germinoma) for which the management may be different, aiming a partial resection after adjuvant therapy.[33]

Classically, preoperative artery embolization is an important adjuvant treatment for meningiomas. However, most FTMs present a short artery caliber, which can difficult preoperative artery embolization.[15]

The anatomical relation between the tumor and the deep venous complex of Galen is the most crucial factor when choosing the surgical approach. Five surgical approaches are described for these tumors:

Transtentorial/Transfalcine Occipital Approach. This is the most frequently used approach for pineal meningiomas. It was first described by Poppen 1968 and was improved afterwards by Jamieson in 1971.[34,35] This approach is more specifically advised in type I and IV FTMs, which originate from the posterior falx immediately above the junction of vein of Galen and the straight sinus. In this location, the growth of the tumor displaces posterior and inferiorly the deep venous complex (►**Table 2**).

The occipital interhemispheric approach is used to reach tumors with a mostly supratentorial and a smaller infratentorial extension. The transfalcine/transtentorial route is used for the removal of the contralateral supratentorial/ infratentorial component. The occipital lobe is also gravity-dependent positioned bearing the largest component of the tumor.

This surgical approach is performed with the patient in a prone or three-quarters prone position with the side of the approach depending on the lateralization of the tumor, avoiding excessive occipital retraction (►**Fig. 1A**).[28]

However, this surgical approach has some disadvantages, such as an increased risk of visual cortex damage (due to

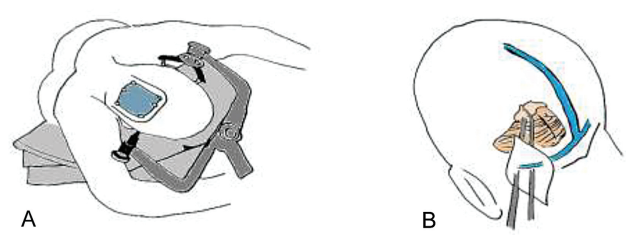


Fig. 1 A. The three-quarter prone position in the transtentorial/ transfalcine occipital approach. B. Surgical view of the supracerebellar infratentorial approach. The schematic illustration belongs to the authors.

cortex retraction), possible trochlear nerve damage at the tentorial opening, and a limitation of the contralateral view of the tumor margin.[28,34,36–38]

Supracerebellar infra-tentorial approach: This is the second most frequently used approach for pineal meningiomas and was the first surgical approach described for these tumors, being reported by Krause et al. in 1913.[39] This approach is recommended for type II and III FTMs according to the Bassiouni classification. It uses the space between the upper surface of the cerebellum and the tentacle (►**Fig. 1B**). Regarding the position of the patient, the sitting position promotes greater cerebral relaxation, but is inappropriate for patients with cardiac comorbidities. Thus, surgery with the patient in a semiseated position seems to be promising in recent studies.[19,33,40,41] A suboccipital craniotomy is performed and centered on the torcula, with a consequent exposure of the two transverse sinuses and retraction of the cerebellum. Currently, some studies suggest that a supracerebellar infratentorial approach could be difficult in patients presenting a steep tentacle and, in these cases, the occipital transtentorial/transfalcine approach seems to be better.[42,43]

Occipital bitranstentorial/falcine approach: This approach was first described by Sekhar et al. in 2002.[15,44] This surgical approach is recommended particularly for large pineal tumors with supra- and infratentorial extension or for those with a significant lateral extension. This technique can be described as a modification of the occipital transtentorial approach, with the division of the falx and the bilateral tentorium. An important advantage of this approach is the better exposition of the contralateral quadrigeminal region.[45]

Anterior interhemispheric trans-splenial approach: This approach was recently described by Yağmurlu et al. and examined cadaveric heads. This surgical approach has several advantages and provides an effective surgery, particularly for patients with supratentorial pineal region tumors with superior extension; for tentorial tumors that displace the deep venous system inferiorly; or for those that originate from the splenium of the corpus callosum.[26] Hendricks et al. described that the anterior interhemispheric approach provides the safest route for accessing the largest portion of the tumor while protecting the deep venous system; however, in this case, the tumor was subtotally removed because of the adherence along the vein of Galen (►**Table 3**).[26]

Posterior interhemispheric retrocallosal transfalcine approach: In 2016, Liu et al. reported this surgical approach using endoscopic assistance to resect a superiorly positioned FTM. In this study, the Galen vein complex was preserved.[18] Lopez-Gonzales et al. described two cases using this approach and achieved a subtotal and a total resection in those cases, respectively[20] (►**Table 3**). However, further studies about this technique are still required.

Adjuvant Radiosurgery

Adjuvant treatments for FTMs are based on histopathological grades and surgical resections. The surgical resection margins are classified using the Simpson classification.[17] Adjuvant radiosurgery is recommended for high-grade histopathological tumor lesions and tumors without Simpson I resection.[43]

Complications and Prognosis

Despite surgical techniques and neuroimaging advances, risks and complications are inherent to FTM procedures, in view of the depth of the location and relationships to important vascular structures. Currently, the attempt to perform a radical tumor resection is not well-established in the literature.[16] Considering that aggressive resections are related to high morbidity rates, a conservative strategy, with subtotal resections, seems to be beneficial in most cases, decreasing a severe neurological deficit rate. The adherence or invasion into the brainstem or the deep venous system by the tumor is an essential factor for a subtotal resection.[16] Surgical mortality was reported in up to 23% of patients, and morbidity, with permanent neurological damage, was recorded in up to 50%. Homonymous hemianopia is the most frequent postoperative deficit.[16] In addition, transient deficits related to the deviation from the conjugated gaze (Parinaud syndrome) and diplopia, being justified by manipulation during the resection of the structure of the dorsal midbrain, such as the collicular plate. This deficit is mostly reversible a few days after the surgery, especially if the arachnoid plan is respected. Permanent cortical amaurosis has been described as a possible surgical complication related to prolonged occipital lobe retraction time.[16] Hemiparesis, hemidysesthesia, tetraparesis, neglectsyndrome, and postoperative intraventricular hemorrhage were described in the literature.[16,43] Our patient developed superior temporal homonymous quadrantanopia in the immediate postoperative period, permanently, without other neurological symptoms. ►**Table 3** summarizes the most relevant reports in the literature from the past 10 years, focusing on the surgical approach, outcomes, and complications.

Conclusion

The selection of an optimal surgical approach is essential for the safe and effective removal of an FTM. Preoperative imaging analysis should identify the anatomical relations of the tumor and guide the least disruptive route that preserves the neurovascular structures.

Ethical Approval
For this type of study, formal consent is not required.

Informed Consent
The authors state that the patient his given their written informed consent for publication of data and images.

Previous Presentation
None.

Disclosure of Funding and Financial Support
None.

Table 3 Review of the most relevant reports in literature from the past 10 years

Study	Number of patients	Approaches (%)	Outcome	Morbidity or complication
Okada et al., 2020[16]	4	Parieto-occipital interhemispheric transfalcine, transbitentorial approach	GTR	none
Hendricks et al., 2019[17]	1	Anterior interhemispheric	STR	ns
Lopez-Gonzales et al., 2019[18]	2	Retractorless interhemispheric	GTR in two times (1/2)	none
			STR (1/2)	
Zhao et al., 2019[19]	17	SCIT (4/17)	GTR (12/17)	Permanent visual field deficits (2/17)
		O-TT (4/17)		Transient visual field deficits (4/17)
		AITS (3/17)	STR (5/17)	Hemiparesis (2/17)
		PVT (1/17)		Hemidysesthesia (1/17)
		Torcular (2/17)		Cerebellar hematoma (1/17)
Garcia et al., 2019[20]	2	SCIT (1/2)	GTR (2/2)	none
		Parieto-occipital interhemispheric (1/2)		
Mendez-Rosito, 2019[21]	1	SCIT	GTR	none
Talacchi et al., 2018[22]	16	Occipital (5/16)	GTR (8/16)	Hematoma (2/16)
		Parieto-occipital (5/16)		Hydrocephalus (1/16)
		Occipitosuboccipital (3/16)	STR (8/16)	Pleural effusion (1/16)
				Tracheostomy (1/16)
		Suboccipital (3/16)		Tetraparesis (1/16)
				Cranial nerve deficit (1/16)
Couldwell, 2017[23]	1	Occipital interhemispheric	GTR	ns
Gomes et al., 2017[24]	1	Posterior interhemispheric	ns	Neglectsyndrome
Hong et al., 2017[25]	11	Bioccipital transtentorial (1/11)	GTR (10/11)	Occipitocerebellar hemorrhage (1/11)
		O-TT (4/11)		
		Occipital (4/11)	STR (1/11)	
		Occipitoparietal (2/11)		Transient visualfield deficit (1/11)
Liu et al., 2016[26]	1	Posterior interhemispheric retrocallosal transfalcine	STR	none
Liu, 2016[18]	1	Combined bi-occipital suboccipital transsinus transtentorial	STR	ns
Nowak et al., 2014[27]	4	O-TT (4/4)	GTR (3/4)	Temporary homonymous hemianopsia (4/4)
				Upward-gaze palsy (1/4)
			STR (1/4)	Postoperative intraventricular hemorrhage (1/4)
Bahari et al., 2014[20]	2	O-TT (2/2)	STR (2/2)	none
Qiu et al., 2014[28]	15	O-TT (15/15)	GTR (11/15)	Homonymous hemianopia (2/15)
			STR (4/15)	Parinaud syndrome (1/15)
				Dipoplia (1/15)

Abbreviations: AITS, anterior interhemispheric trans-splenial; GTR, gross total resection (Simpson I and II); ns, not specified; O-TT, occipital transtentorial/transfalcine; PTV, parietal transventricular; STR, subtotal resection (Simpson III and IV).

Contributions of the Authors

1. Bem Junior L. S.: Conceptualization, data curation, formal analysis, visualization, writing, reviewing, and editing.
2. Aquino P. L. R.: Data curation, writing of the original draft, reviewing and editing.
3. Lemos L. E. A. S.: Data curation, writing of the original draft, reviewing and editing.
4. Aquino M. A. R.: Data curation, writing, reviewing, and editing.
5. Valença M. M.: Conceptualization, writing, reviewing, and editing, supervision.
6. Azevedo Filho H. R. C.: Conceptualization, writing, reviewing, and editing, supervision.

Funding
None.

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

Acknowledgments
The present research was carried out at the Hospital da Restauração, Recife, state of Pernambuco, Brazil. We thank our colleagues from the Hospital da Restauração who provided insight and expertise that greatly assisted in the research. We are also grateful to the advanced neurosurgery support unit (ANSU) from the Hospital da Restauração for all the care provided in the postoperative period of the patient.

References

1 Behari S, Das KK, Kumar A, et al. Large/giant meningiomas of posterior third ventricular region: falcotentorial or velum interpositum? Neurol India 2014;62(03):290–295. Doi: 10.4103/0028-3886.136934
2 Hong CK, Hong JB, Park H, et al. Surgical treatment for falcotentorial meningiomas. Yonsei Med J 2016;57(04):1022–1028. Doi: 10.3349/ymj.2016.57.4.1022
3 Yaşar S, Kırık A. Surgical Management of Giant Intracranial Meningiomas. Eurasian J Med 2021;53(02):73–78
4 Guttmann E. Zur pathologie und Klinik der Meningiome. Z Gesamte Neurol Psychiatr 1930;123:606–625
5 Ito J, Kadekaru T, Hayano M, Kurita I, Okada K, Yoshida Y. Meningioma in the tela choroidea of the third ventricle: CT and angiographic correlations. Neuroradiology 1981;21(04):207–211. Doi: 10.1007/BF00367342
6 Bassiouni H, Asgari S, König HJ, Stolke D. Meningiomas of the falcotentorial junction: selection of the surgical approach according to the tumor type. Surg Neurol 2008;69(04):339–349, discussion 349. Doi: 10.1016/j.surneu.2007.02.029
7 Sekhar LN, Goel A. Combined supratentorial and infratentorial approach to large pineal-region meningioma. Surg Neurol 1992;37(03):197–201. Doi: 10.1016/0090-3019(92)90230-k
8 Asari S, Maeshiro T, Tomita S, et al. Meningiomas arising from the falcotentorial junction. Clinical features, neuroimaging studies, and surgical treatment. J Neurosurg 1995;82(05):726–738. Doi: 10.3171/jns.1995.82.5.0726
9 Tubbs RS, Louis RG Jr, Wartmann CT, et al. The velum interpositum revisited and redefined. Surg Radiol Anat 2008;30(02):131–135. Doi: 10.1007/s00276-007-0293-2
10 Quinones-Hinojosa A, Chang EF, McDermott MW. Falcotentorial meningiomas: clinical, neuroimaging, and surgical features in six patients. Neurosurg Focus 2003;14(06):e11. Doi: 10.3171/foc.2003.14.6.11
11 Roberti F, Sekhar LN, Kalavakonda C, Wright DC. Posterior fossa meningiomas: surgical experience in 161 cases. Surg Neurol 2001;56(01):8–20, discussion 20–21. Doi: 10.1016/s0090-3019(01)00479-7
12 Raco A, Agrillo A, Ruggeri A, Gagliardi FM, Cantore G. Surgical options in the management of falcotentorial meningiomas: report of 13 cases. Surg Neurol 2004;61(02):157–164, discussion 164. Doi: 10.1016/S0090-3019(03)00573-1
13 Sung DI, Harisiadis L, Chang CH. Midline pineal tumors and suprasellar germinomas: highly curable by irradiation. Radiology 1978;128(03):745–751. Doi: 10.1148/128.3.745
14 Piatt JH Jr, Campbell GA. Pineal region meningioma: report of two cases and literature review. Neurosurgery 1983;12(04):369–376. Doi: 10.1227/00006123-198304000-00002
15 Quiñones-Hinojosa A, Chang EF, Chaichana KL, McDermott MW. Surgical considerations in the management of falcotentorial meningiomas: advantages of the bilateral occipital transtentorial/transfalcine craniotomy for large tumors. Neurosurgery 2009;64(5, Suppl 2):260–268, discussion 268. Doi: 10.1227/01.NEU.0000344642.98597.A7
16 Okada T, Miyahara K, Tanino S, et al. Parieto-Occipital Interhemispheric Transfalcine, Trans-Bitentorial Approach for Radical Resection of Falcotentorial Meningiomas. J Neurol Surg A Cent Eur Neurosurg 2020;81(04):355–361
17 Hendricks BK, Spetzler RF. Right Anterior Parasagittal Craniotomy and Interhemispheric Approach for Resection of a Falcontentorial Junction Meningioma: 2-Dimensional Operative Video. Oper Neurosurg (Hagerstown) 2019;17(06):E237–E238. Doi: 10.1093/ons/opz258
18 Lopez-Gonzalez MA, Jaeger A, Kaplan B, et al. Retractorless interhemispheric transtentorial approach for large lesions in the posterior incisural space. Surg Neurol Int 2019;10:130. Doi: 10.25259/SNI-117-2019
19 Zhao X, Belykh E, Przybylowski CJ, et al. Surgical treatment of falcotentorial meningiomas: a retrospective review of a single-institution experience. J Neurosurg 2019 (August):1–12. Doi: 10.3171/2019.4.JNS19208
20 Blasco García de Andoain G, Delgado-Fernández J, Penanes Cuesta JR, Gil-Simoes R, Frade-Porto N, Sánchez MP. Meningiomas Originated at the Falcotentorial Region: Analysis of Topographic and Diagnostic Features Guiding an Optimal Surgical Planning. World Neurosurg 2019;123:e723–e733. Doi: 10.1016/j.wneu.2018.12.013
21 Mendez-Rosito D. The Supra/Infra Transtentorial Transfalcine Approach for the Removal of a Falcotentorial Meningioma: 2-Dimensional Video. Oper Neurosurg (Hagerstown) 2019;16(06):E166–E167
22 Shukla D, Behari S, Jaiswal AK, Banerji D, Tyagi I, Jain VK. Tentorial meningiomas: operative nuances and perioperative management dilemmas. Acta Neurochir (Wien) 2009;151(09):1037–1051
23 Couldwell WT. Left occipital craniotomy for resection of falcotentorial meningioma. Neurosurg Focus 2017;43(VideoSuppl2):V9
24 Gomes D, Fonseca M, Garrotes M, et al. Corpus callosum and neglect syndrome: Clinical findings after meningioma removal and anatomical review. J Neurosci Rural Pract. Medknow Publications 2017;8(01):101–106
25 Larson JJ, Tew JM Jr, Wiot JG, de Courten-Myers GM. Association of meningiomas with dural "tails"; surgical significance. Acta Neurochir (Wien) 1992;114(1-2):59–63
26 Liu JK, Cohen MA. Endoscopic-assisted posterior interhemispheric retrocallosal transfalcine approach for microsurgical resection of a pineal region falcotentorial meningioma: operative video and

technical nuances. Neurosurg Focus 2016;40Video(Suppl 1):2016.1, 15453
27 Nowak A, Dziedzic T, Czernicki T, Kunert P, Marchel A. Falcotentorial and velum interpositum meningiomas: two distinct entities of the pineal region. Neurol Neurochir Pol 2014;48(06):397–402
28 Qiu B, Wang Y, Ou S, Guo Z, Wang Y. The unilateral occipital transtentorial approach for pineal region meningiomas: a report of 15 cases. Int J Neurosci 2014;124(10):741–747. Doi: 10.3109/00207454.2013.878341
29 Goto T, Ohata K, Morino M, et al. Falcotentorial meningioma: surgical outcome in 14 patients. J Neurosurg 2006;104(01): 47–53. Doi: 10.3171/jns.2006.104.1.47
30 Talacchi A, Biroli A, Hasanbelliu A, Locatelli F. Surgical Management of Medial Tentorial Meningioma: Falcotentorial and Torcular. World Neurosurg 2018;115:e437–e447. Doi: 10.1016/j.wneu.2018.04.066
31 Okami N, Kawamata T, Hori T, Takakura K. Surgical treatment of falcotentorial meningioma. J Clin Neurosci 2001;8(Suppl 1):15––18. Doi: 10.1054/jocn.2001.0870
32 Carey JP, Fisher RG, Pelofsky S. Tentorial meningiomas. Surg Neurol 1975;3(01):41–44
33 Lozier AP, Bruce JN. Meningiomas of the velum interpositum: surgical considerations. Neurosurg Focus 2003;15(01):E11. Doi: 10.3171/foc.2003.15.1.11
34 Poppen JL. The right occipital approach to a pinealoma. J Neurosurg 1966;25(06):706–710. Doi: 10.3171/jns.1966.25.6.0706
35 Jamieson KG. Excision of pineal tumors. J Neurosurg 1971;35(05): 550–553. Doi: 10.3171/jns.1971.35.5.0550
36 Reid WS, Clark WK. Comparison of the infratentorial and transtentorial approaches to the pineal region. Neurosurgery 1978;3 (01):1–8. Doi: 10.1227/00006123-197807000-00001
37 Maselli G, De Paulis D, Ricci A, Galzio RJ. Posterior cranial fossa tumors: Results and prognostic factors in a consecutive series of 14 operated patients by occipital transtentorial approach. Surg Neurol Int 2012;3(01):85. Doi: 10.4103/2152-7806.99911
38 Zaidi HA, Elhadi AM, Lei T, Preul MC, Little AS, Nakaji P. Minimally Invasive Endoscopic Supracerebellar-Infratentorial Surgery of the Pineal Region: Anatomical Comparison of Four Variant Approaches. World Neurosurg 2015;84(02):257–266. Doi: 10.1016/j.wneu.2015.03.009
39 Quest DO, Kleriga E. Microsurgical anatomy of the pineal region. Neurosurgery 1980;6(04):385–390. Doi: 10.1227/00006123-198004000-00006
40 Sonabend AM, Bowden S, Bruce JN. Microsurgical resection of pineal region tumors. J Neurooncol 2016;130(02):351–366
41 Stein BM. The infratentorial supracerebellar approach to pineal lesions. J Neurosurg 1971;35(02):197–202. Doi: 10.3171/jns.1971.35.2.0197
42 Hart MG, Santarius T, Kirollos RW. How I do it–pineal surgery: supracerebellar infratentorial versus occipital transtentorial. Acta Neurochir (Wien) 2013;155(03):463–467. Doi: 10.1007/s00701-012-1589-5
43 Soffar H, Alsawy MF. Assessment of necessity of neuronavigation in localization of calvarial extra-axial lesions in the setting of limited resources. Chin Neurosurg J 2021;7(01):35
44 Gusmão S, Oliveira MM, Arantes A, Ulhoa TH, Morato EG. Occipital bi-transtentorial/falcine approach for falcotentorial meningioma: case report. Arq Neuropsiquiatr 2006;64(01):136–138. Doi: 10.1590/S0004-282X2006000100029
45 Yağmurlu K, Zaidi HA, Kalani MYS, Rhoton AL, Preul MC, Spetzler RF. Anterior interhemispheric transsplenial approach to pineal region tumors: anatomical study and illustrative case. J Neurosurg 2018;128(01):182–192. Doi: 10.3171/2016.9.JNS16279

Recurrence of Anaplastic Large Cell Lymphoma in the Frontal Lobe After Eleven Years of the Initial Diagnosis: Histopathological Findings and Prognosis

Recorrência de linfoma anaplásico de grandes células no lobo frontal onze anos após o diagnóstico inicial: Achados histopatológicos e prognóstico

Eduardo Cambruzzi[1,2,3,4] Nelson Pires Ferreira[2] Marcelo Paglioli Ferreira[2] Guilherme Gago[2] João Pedro Pattussi Bertinatti[2]

[1] Medicine Faculty, Department of Histology and Pathology, Universidade Federal do Rio Grande do Sul, Porto Alegre, Rio Grande do Sul, Brazil
[2] Departamento de Patologia, Hospital Santa Rita, Santa Casa da Misericórdia de Porto Alegre, Porto Alegre, Rio Grande do Sul, Brazil
[3] Grupo Hospitalar Conceição, Porto Alegre, Rio Grande do Sul, Brazil
[4] Hemodynamics Department, Instituto de Cardiologia, Fundação Universitária de Cardiologia, Porto Alegre, Rio Grande do Sul, Brazil

Address for correspondence Eduardo Cambruzzi, PhD, Departamento de Patologia, Hospital Santa Rita, Santa Casa da Misericórdia de Porto Alegre, Rua Sarmento Leite 187, 2° andar, Porto Alegre, Rio Grande do Sul–RS, Brazil (e-mail: dudacambruzzi@yahoo.com.br).

Arq Bras Neurocir 2022;41(4):e375–e378.

Abstract

Anaplastic large cell lymphoma (ALCL) is a rare, high-grade, T-cell neoplasm classified into cutaneous primary, systemic primary ALK-positive (ALK^+), systemic primary ALK-negative, or breast-implant associated. Secondary involvement of the central nervous system (CNS) by systemic primary ALK^+ ALCL is a rare occurrence. We present a case of CNS involvement by ALK^+ ALCL eleven years after diagnosis of the primary tumor in the thoracic vertebra. The anatomopathological examination confirmed the diagnosis of ALK^+ ALCL. A brief review of the treatment and the clinical and pathological aspects is presented.

Keywords
- anaplastic large cell lymphoma
- central nervous system
- pathology
- immuno-histochemistry
- prognosis

Resumo

O linfoma anaplásico de grandes células (LAGC) corresponde a uma neoplasia de alto grau rara, com imunofenótipo T, que podendo ser dividido em primário cutâneo, primário sistêmico ALK positivo (ALK^+), primário sistêmico ALK negativo, e associado a próteses mamárias. Acometimento secundário do sistema nervoso central (SNC) por LAGC primário sistêmico ALK^+ é uma rara entidade. Os autores apresentam um caso de acometimento do SNC por LAGC ALK^+ onze anos após o diagnóstico do tumor primário em vértebra torácica. O exame anatomopatológico confirmou o diagnóstico de LAGC ALK^+. Fez-se também uma breve revisão de aspectos clínicos e patológicos e tratamento.

Palavras-chave
- linfoma anaplásico de grandes células
- sistema nervoso central
- patologia
- imuno-histoquímica
- prognóstico

received June 10, 2021
accepted April 25, 2022

DOI https://doi.org/10.1055/s-0042-1749375.
ISSN 0103-5355.

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

Introduction

ALK-positive anaplastic large cell lymphoma (ALK$^+$ ALCL) is a single entity defined by the World Health Organization (WHO) as a T-cell lymphoma composed of generally large, pleomorphic lymphoid cells with abundant cytoplasm, chromosomal translocation involving the *ALK* gene, and ALK and CD30 expression on surface membranes. Upon microscopic examination, the most common pattern is large cells with eccentric, horseshoe-shaped nuclei. However, there is great morphological variation, with reports of the following patterns: small cells, lymphohistiocytic, Hodgkin-like, multinucleated giant cells, and fusocellular. Anaplastic large cell lymphoma accounts for about 3% of non-Hodgkin lymphomas in adults, and for 10% to 20% of lymphomas in children.[1] The clinical presentation is generally characterized by advanced stages (III or IV) and associated with B symptoms. Lymph node and extranodal involvement are common, including sites such as the skin, bones, soft tissues, lungs, and liver. Involvement of the bone marrow occurs in about 30% of the cases analyzed by immunohistochemistry.[2] Primary involvement of visceral and central nervous systems (CNS) is rare, and CNS metastasis is even rarer.

We herein report a case of ALK$^+$ ALCL involving the thoracic vertebra in a pediatric patient, with subsequent emergence of the same pathology in the right frontal lobe after eleven years of remission.

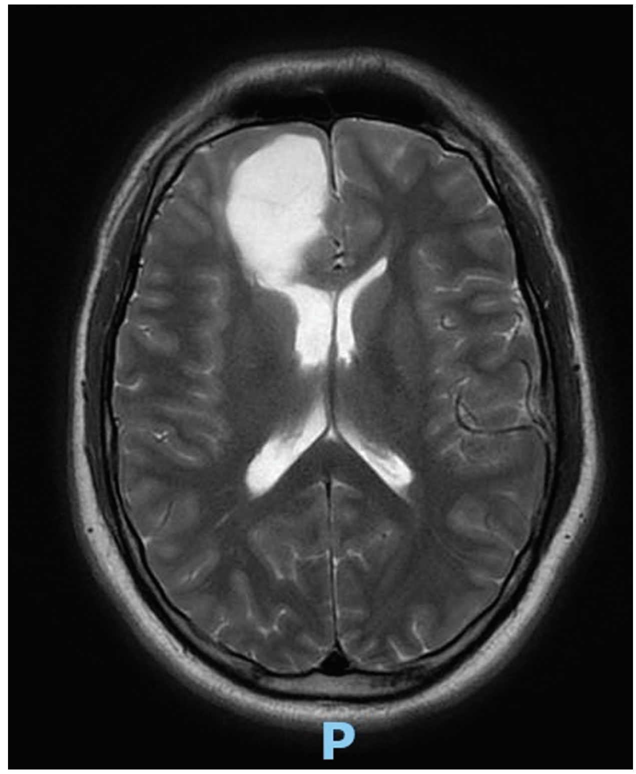


Fig. 1 Axial magnetic resonance imaging (MRI) scan showing an expansive fronto-basal tumor.

Case Report

An 18-year-old patient presented to the hospital with nausea and vomiting followed by five generalized tonic-clonic seizures lasting 30 minutes, associated with salivation, tongue biting, and urinary incontinence, without recovery between the seizures. The patient was medicated with five ampoules of phenytoin and transferred to the reference hospital, with no further abnormalities on the neurological examination. A review of the medical records revealed a history of anaplastic lymphoma of the twelfth thoracic vertebra treated with chemotherapy. Eleven months of clinical follow-up showed no disease recurrence or involvement of the bone marrow, liver, spleen, tonsils, skin, or CNS. The patient underwent regular follow-up with the neurosurgery team for progressive vertebral collapse. Brain computed tomography (CT) scans of the last 8 years revealed the presence of an extensive area of encephalomalacia in the right frontal lobe, without significant changes between evaluations. During the current hospitalization, a magnetic resonance imaging (MRI) scan of the CNS (►**Figs. 1** and **2**) was requested, which identified an expansive fronto-basal lesion on the right side, with marked low signal on fluid-attenuated inversion recovery (FLAIR) sequences and T1, hyperintense on FLAIR in the periphery, and a solid portion of blood-brain barrier breakdown near the lower anterior brain portion. The lesion measured about 4.8×3.3 cm in its largest diameters, and the solid portion with contrast enhancement measured about 1.3 cm in the largest diameter, which was suggestive of primary glial neoplasm. The patient underwent surgical intervention, with resection of the mural nodule, drainage of the cystic area via opening of the nodule/ventricle wall, and successful resolution of cerebrospinal fluid fistula, being discharged with outpatient follow-up. The anatomopathological examination revealed a poorly-differentiated malignant neoplasm compromising the CNS parenchyma, consisting of medium-sized round cells arranged in solid groups (►**Figs. 3** and **4**) or in a perivascular pattern, with moderate mitotic index and areas of necrosis. The immunohistochemical examination showed that the neoplasm was positive for cluster determinant 2 (CD2), cluster

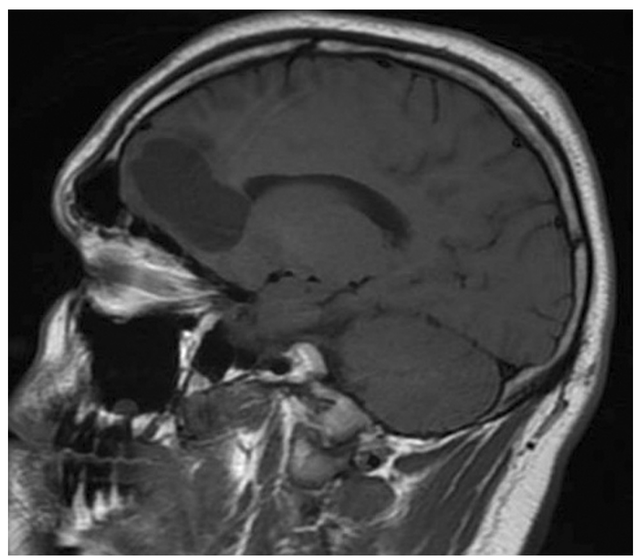


Fig. 2 Sagittal MRI scan showing an expansive fronto-basal tumor.

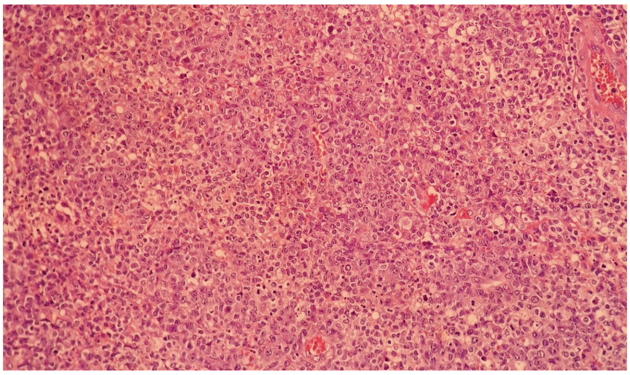


Fig. 3 A poorly-differentiated malignant neoplasm compromising the CNS parenchyma; hematoxylin-eosin, magnification: 200x.

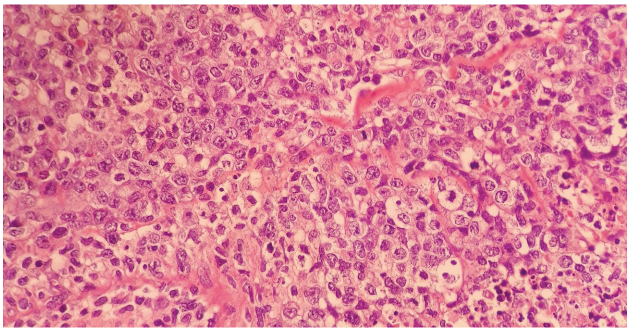


Fig. 4 A poorly-differentiated malignant neoplasm consisting of intermediate-sized round cells arranged in solid groups; hematoxylin-eosin, magnification: 400x.

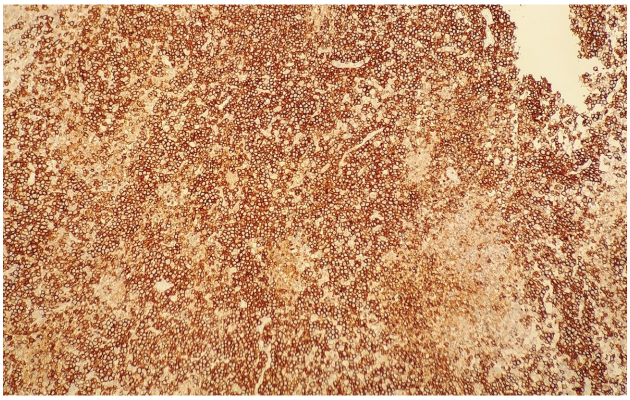


Fig. 5 Anaplastic large cell lymphoma showing positive immunoexpression for CD30; Ventana System, 40x.

determinant 3 (CD3), cluster determinant 5 (CD5), cluster determinant 30 (CD30) (►**Fig. 5**), anaplastic lymphoma kinase (ALK) (►**Fig. 6**), epithelial membrane antigen (EMA), perforin, and granzyme B, enabling the diagnosis of ALK^+ ALCL involving the cerebral parenchyma. The proliferative index of the neoplasm was of about 90%, as estimated by Ki-67 expression (►**Fig. 7**). The patient was referred to chemotherapy.

Discussion

Involvement of the brain parenchyma in cases of ALK^+ ALCL is a rare event, with few reports of primary involvement[3–7] and even fewer of secondary involvement.[8–10] One study[11] analyzed the ALCL99 database, which comprises data on 618 patients with confirmed CNS biopsy between 1999 and 2017, involving 175 centers across 11 European countries and Japan. Central nervous system relapse was observed in 26 patients, 5 of whom had CNS disease at diagnosis. There was a mean interval of 8 months between the initial diagnosis and CNS relapse, with only 3 patients presenting relapse after 5 years; the latest relapse occurred 130.7 months after the initial diagnosis. We herein report the case of a patient who presented relapse in brain parenchyma 134 months after the initial diagnosis, becoming the latest case of relapse of ALK^+ ALCL described in the literature.

The low incidence of CNS relapses can be explained by the effectiveness of the initial treatment and by the neoplasm's low tropism for the CNS. Central nervous system relapse is more common in patients who had the disease in this topography at the initial diagnosis, as well as in the case of bone marrow involvement or presence of peripheral blasts.[11] Patients with these risk factors could benefit from a more aggressive CNS prophylaxis.[11]

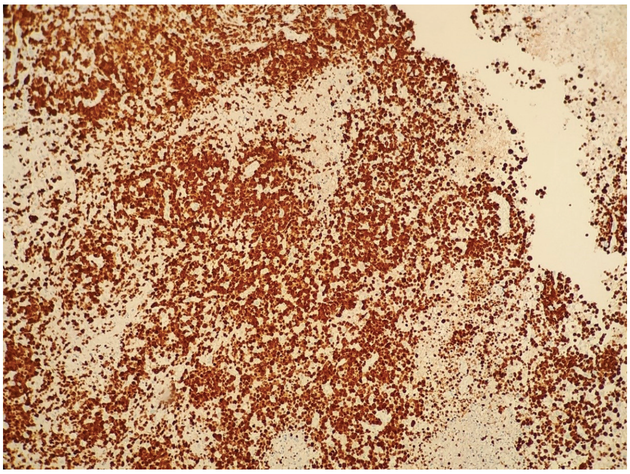


Fig. 6 Anaplastic large cell lymphoma showing positive immunoexpression for ALK; Ventana System (Ventana Medical Systems, Tucson, AZ, United States), magnification: 40x.

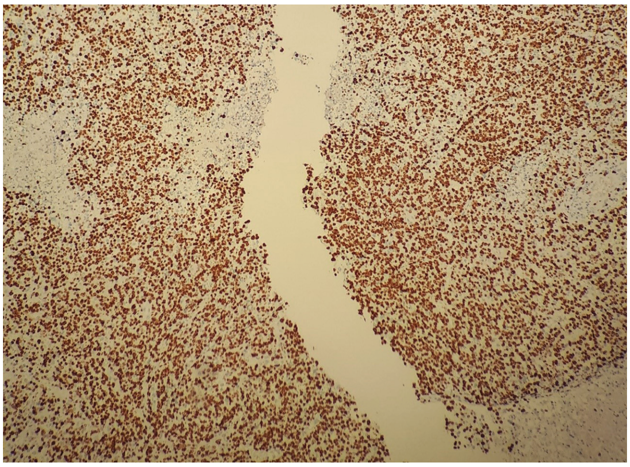


Fig. 7 Anaplastic large cell lymphoma showing a high proliferative index (of about 90%, estimated by Ki-67 expression); Ventana System, magnification: 40x.

As reported, however, our patient did not have the indicated risk factors and had undergone a long asymptomatic period, raising the hypothesis of primary ALCL of the CNS or presence of viable neoplastic cells in the encephalomalacic area identified in CT scans in the initial years of follow-up, which were located at the same topographic site of the current neoplasm.

There is little agreement on the most appropriate therapeutic approach for CNS relapses. The most common treatment options include high-dose chemotherapy, autologous stem-cell transplantation, radiotherapy, and, recently, brentuximab vedotin (anti-CD30 drug).[12,13] ALK-inhibiting drugs, such as crizotinib, ceritinib, and alectinib, were shown to promote long-lasting responses in patients with refractory and/or relapsed ALK^{+} ALCL. A clinical trial[14] used alectinib to treat ten patients, including children and older adults, with refractory/relapsed ALK^{+} ALCL; positive response was observed in eight out of the ten patients, and complete response, in six. Based on these results, in February 2020, Japan approved the use of this drug for refractory/relapsed ALK^{+} ALCL. Most clinical trials, however, exclude patients with CNS disease, explaining the lack of data on treatment efficacy in such cases. Vinblastine demonstrated good efficacy in relapsed ALCL, but there are few reports of the drug's efficacy when the tumor is located in the CNS, given the poor penetration of the blood-brain barrier. In fact, some patients had isolated CNS relapse despite their excellent systemic response.[15,16]

New data on CNS penetration of second- and third-generation ALK inhibitors are emerging from studies on adults with ALK^{+} non-small cell lung carcinoma. Reports[17,18] suggest that alectinib is superior to other ALK inhibitors with regard to CNS penetration (the penetration rates of crizotinib and alectinib were of 0.26% and 86% respectively[19]). Ceritinib, another ALK inhibitor, showed a rate of response of 75% in ALCL patients.[20] According to the International ALCL99 trial,[11] the 3-year survival rate of patients with CNS relapse is of 48.7%, suggesting that the goal of novel treatments should be to achieve complete cure.

In summary, we conclude that isolated CNS recurrence can arise even after more than a decade of the diagnosis and clinical remission of systemic ALK^{+} ALCL without primary CNS involvement. The need for prolonged follow-up becomes evident. Promising medications have emerged, and others are still in development; however, given the current heterogeneity in therapeutic approaches to the CNS relapse of ALCL, it is essential that new studies and strategies be developed.

Funding Statement
The authors declare that they have received no funding regarding the performance of the present study.

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

References

1 Stein H, Foss HD, Dürkop H, et al. CD30(+) anaplastic large cell lymphoma: a review of its histopathologic, genetic, and clinical features. Blood 2000;96(12):3681–3695
2 Fraga M, Brousset P, Schlaifer D, et al. Bone marrow involvement in anaplastic large cell lymphoma. Immunohistochemical detection of minimal disease and its prognostic significance. Am J Clin Pathol 1995;103(01):82–89
3 Dong X, Li J, Huo N, et al. Primary central nervous system ALK-positive anaplastic large cell lymphoma in an adult: A rare case report. Medicine (Baltimore) 2016;95(49):e5534
4 Rupani A, Modi C, Desai S, Rege J. Primary anaplastic large cell lymphoma of central nervous system–a case report. J Postgrad Med 2005;51(04):326–327
5 Vivekanandan S, Dickinson P, Bessell E, O'Connor S. An unusual case of primary anaplastic large cell central nervous system lymphoma: an 8-year success story. BMJ Case Rep 2011;2011;. Doi: 10.1136/bcr.11.2010.3550
6 Feng S, Chen Q, Chen J, Zheng P, Ma K, Tan B. Primary anaplastic large cell lymphoma of the central nervous system in a child: A case report. Medicine (Baltimore) 2020;99(29):e21115
7 Fujisawa E, Shibayama H, Mitobe F, Katada F, Sato S, Fukutake T. A case of primary central nervous system anaplastic lymphoma kinase positive anaplastic large cell lymphoma manifested as a unilateral pachymeningits. Rinsho Shinkeigaku 2017;57(11):705–710
8 Mori T, Sugita K, Kimura K, et al. Isolated central nervous system (CNS) relapse in a case of childhood systemic anaplastic large cell lymphoma without initial CNS involvement. J Pediatr Hematol Oncol 2003;25(12):975–977
9 Wang CX, Wang H, Li J, et al. Brain metastasis of ALK positive anaplastic large cell lymphoma after a long-term disease free survival in an old adult. Int J Clin Exp Pathol 2014;7(03):1182–1187
10 Raffa EH, Branson HM, Ngan B, Alexander S, Abla O. Central nervous system relapse in a child with anaplastic large cell lymphoma: potential for new therapeutic strategies. Cancer Rep (Hoboken) 2021;4(05):e1377
11 Del Baldo G, Abbas R, Woessmann W, et al. Neuro-meningeal relapse in anaplastic large-cell lymphoma: incidence, risk factors and prognosis - a report from the European intergroup for childhood non-Hodgkin lymphoma. Br J Haematol 2021;192(06):1039–1048
12 Pro B, Advani R, Brice P, et al. Brentuximab vedotin (SGN-35) in patients with relapsed or refractory systemic anaplastic large-cell lymphoma: results of a phase II study. J Clin Oncol 2012;30(18): 2190–2196
13 Pro B, Advani R, Brice P, et al. Five-year results of brentuximab vedotin in patients with relapsed or refractory systemic anaplastic large cell lymphoma. Blood 2017;130(25):2709–2717
14 Fukano R, Mori T, Sekimizu M, et al. Alectinib for relapsed or refractory anaplastic lymphoma kinase-positive anaplastic large cell lymphoma: An open-label phase II trial. Cancer Sci 2020;111(12):4540–4547
15 Ruf S, Hebart H, Hjalgrim LL, et al. CNS progression during vinblastine or targeted therapies for high-risk relapsed ALK-positive anaplastic large cell lymphoma: A case series. Pediatr Blood Cancer 2018;65(06):e27003
16 Abid MB, Wang S, Loi HY, Poon LM. ALK-negative anaplastic large cell lymphoma with CNS involvement needs more than just brentuximab vedotin. Ann Hematol 2016;95(10):1725–1726
17 Central nervous system relapse of systemic ALK-rearranged anaplastic large cell lymphoma treated with alectinib
18 Yang J, Li J, Gu WY, et al. Central nervous system relapse in a pediatric anaplastic large cell lymphoma patient with CLTC/ALK translocation treated with alectinib: A case report. World J Clin Cases 2020;8(09):1685–1692
19 Wrona A. Management of CNS disease in ALK-positive non-small cell lung cancer: Is whole brain radiotherapy still needed? Cancer Radiother 2019;23(05):432–438
20 Schulte JH, Moreno L, Ziegler DS, et al. Final analysis of phase I study of ceritinib in pediatric patients with malignancies harboring activated anaplastic lymphoma kinase (ALK). Journal of Clinical Oncology 2020;38:10505

Pilocytic Astrocytoma of the Cerebellopontine Angle with cerebrospinal fluid Spread in an Adult: A Case Report

Astrocitoma pilocítico no ângulo pontocerebelar com disseminação liquórica em paciente adulto: Relato de caso

Erhan Bıyıklı[1] Meltem Kursun[1] Tuba Oguzsoy[2] Suheyla Bozkurt[2] Fatih Bayraklı[3]

[1] Department of Radiology, Faculty of Medicine, Marmara University, Istanbul, Turkey
[2] Department of Pathology, Faculty of Medicine, Marmara University, Istanbul, Turkey
[3] Department of Neurosurgery, Faculty of Medicine, Marmara University, Istanbul, Turkey

Address for correspondence Erhan Bıyıklı, MD, Department of Radiology, Faculty of Medicine, Marmara University, Muhsin Yazicioglu ST 34899 Pendik, Istanbul, Turkey (e-mail: biyiklierhan@hotmail.com).

Arq Bras Neurocir 2022;41(4):e379–e381.

Abstract

Introduction Pilocytic astrocytoma of the cerebellopontine angle (CPA) is uncommon, and its spread to the cerebrospinal fluid (CSF) at the time of diagnosis has not been reported in the literature.
Case Presentation We report the case of a 33-year-old man with multifocal pilocytic astrocytoma diagnosed by magnetic resonance imaging (MRI) and confirmed by histopathological examination, and present the radiological and histopathological findings.
Conclusion In the case herein reported, we observed spread of the pilocytic astrocytoma of the CPA to the CSF at the initial diagnosis, and early detection by MRI is very important regarding the treatment modality and prognosis.

Keywords
► cerebellopontine angle
► pilocytic astrocytoma
► vestibular schwannoma

Resumo

Introdução O astrocitoma pilocítico no ângulo pontocerebelar (APC) é incomum, e sua disseminação liquórica no momento do diagnóstico não foi relatada na literatura.
Apresentação do Caso Relatamos o caso de um homem de 33 anos com astrocitoma pilocítico multifocal diagnosticado por ressonância magnética (RM) e confirmado por exame histopatológico, e apresentamos os achados radiológicos e histopatológicos.
Conclusão No caso relatado, observou-se disseminação liquórica de astrocitoma pilocítico no APC no diagnóstico inicial, e a detecção precoce por RM é muito importante para a modalidade de tratamento e o prognóstico.

Palavras-chave
► ângulo pontocerebelar
► astrocitoma pilocítico
► schwannoma vestibular

received
January 22, 2022
accepted
April 25, 2022

DOI https://doi.org/10.1055/s-0042-1749374.
ISSN 0103-5355.

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

Introduction

Tumors of the cerebellopontine angle (CPA) comprise 6% to 10% of intracranial neoplasms. The most common CPA neoplasms are those of the vestibular schwannoma. Pilocytic astrocytomas (PAs) are low-grade astrocytomas that occur more often in children and young adults, mostly near the midline, usually arising from the cerebellum, the optic chiasm, and the hypothalamic region. They are seldom seen within the CPA.[1] In the literature, they are often the exophytic extension of the primary brainstem or cerebellar PAs at this location. Reports of primary extra-axial PA are extremely rare. Primary spread to the cerebrospinal fluid (CSF) is seen mostly observed in cases of ependymoma, germ-cell tumors, and high-grade glial tumors. According to the classification pf the World Health Organization (WHO), PAs are classified as grade-1 gliomas. However, though uncommon, PAs may spread to the CSF.[2]

We present a case of CSF spread of a PA of the CPA in an adult.

Case Presentation

A 33-year-old male patient was admitted to our neurosurgery department with complaints of dizziness, tinnitus, and mild headache that had started in the previous year. His medical and family histories were non-contributory. Upon physical examination, he was normotensive and his distal upper extremity pulse and heart rate were normal. The presence of neurofibromatosis stigma was not observed. No abnormal finding was revealed in the neurological examination. The routine laboratory findings were normal. The hematologic tests were negative for all rheumatologic and autoimmune disorders.

A brain magnetic resonance imaging (MRI) scan revealed a lesion measuring 5 × 3 × 2.5 cm in the left CPA, which was predominantly hypointense on T1 and hyperintense on T2-fluid-attenuated inversion recovery (FLAIR) weighted images. A CSF cleft between the mass and the brainstem suggested an extra-axial origin of the tumor. The mass was characterized by heterogeneous patchy enhancement and composed of both solid and cystic components (►Fig. 1). There was mild mass effect on the left side of the brainstem structure and on the fourth ventricle, without apparent signal abnormality. No diffusion restriction and peritumoral edema were detected. An axial three-dimensional (3D) constructive interference in steady state (CISS) sequence revealed a large hypointense filling defect within the left CPA with extension into the widened left internal auditory canal (IAC). Upon the initial examination, there were additional tumors located in the right Meckel cave and prepontine cistern, but no enhancement was observed in these lesions (►Fig. 1).

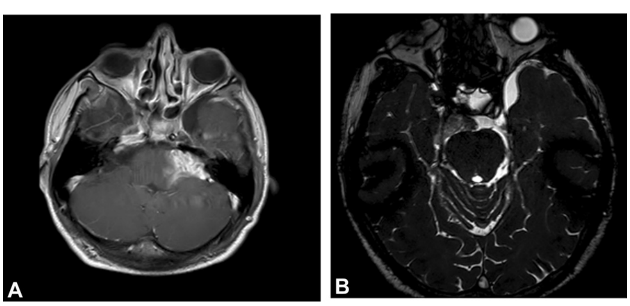


Fig. 1 Axial gadolinium-enhanced T1 weighted image (A) showing a patchy contrast-enhanced lesion on the left CPA with mild mass effect of the adjacent brainstem structure. Axial 3D CISS sequence (B) showing a large hypointense mass in the prepontine cistern.

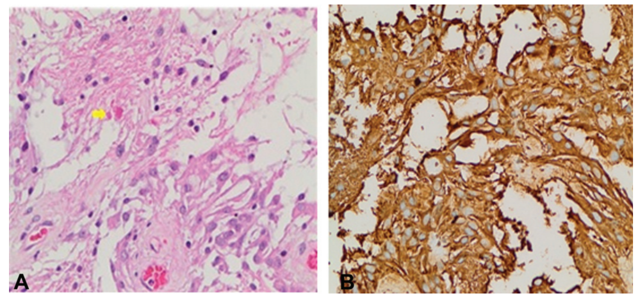


Fig. 2 Perivascular arrangement of elongated bipolar glial cells and microcyst and eosinophilic granular bodies (yellow arrow) in fibrillary background (A) (hematoxylin and eosin staining, 20× original magnification). Strong cytoplasmic GFAP immunoreactivity in neoplastic glial cells (B) (GFAP immunostaining, 40× original magnification).

The patient subsequently underwent surgical resection via the left suboccipital retrosigmoid approach. A gelatinous, yellowish-white, encapsulated, and normovascular tumor was identified in the CPA. Subtotal resection was performed because the tumor was attached to the left facial and vestibulocochlear nerves.

The histopathological evaluation showed a glial tumor composed of bipolar elongated neoplastic glial cells arranged around perivascular areas, resembling pseudorosettes. There were mulberry-shaped eosinophilic granular bodies and loose myxoid microcystic areas in the fibrillary background. Microvascular proliferation, mitosis, necrosis and microcalcification were absent. Immunohistochemical staining revealed immunopositivity for glial fibrillary acidic protein (GFAP), Olig2 and S100, and immunonegativity for epithelial membrane antigen (EMA) (►Fig. 2). The Ki 67 proliferative index was lower than 2%. A final diagnosis of PA (WHO grade I) was made. But the remote lesions were not histologically confirmed as PAs.

The patient was discharged after the surgery and recovered without any significant complications. Adjuvant irradiation treatment and regular follow-up with brain MRI scans were recommended because of the residual tumor mass in the CPA.

Discussion

Gliomas of the CPA are rare entities in adults, and are often the exophytic extension of the primary brainstem or of cerebellar gliomas.[3] In the case herein reported, the primary lesion was located at the CPA and did not have any intra-axial component on preoperative imaging. Intraoperatively, these findings were confirmed by the absence of adherence of the tumor capsule to the brainstem or cerebellum and by the presence of a clear boundary between them.

To date, less than 50 cases of primary extra-axial CPA gliomas have been reported in the literature. Although PAs are low-grade tumors, they have been documented to spread to other parts of central nervous system. Spread to the CSF of a PA of the CPA at the time of diagnosis (the case herein reported) is the first such case reported in the literature.

Preoperative neuroimaging studies suggested the diagnosis of cystic CPA schwannoma with the involvement of the IAC.

In the literature, spread has been defined as a leptomeningeal spread or a tumor found at sites other than that of the primary disease location on MRI. Primary CSF dissemination is mostly observed in cases of ependymoma, germ-cell tumors, and high-grade glial tumors. The spread of Pas to the CSF is uncommon and usually occurs after interventional procedures. The detection of spread during the primary diagnosis, as in the case herein reported, is extremely rare. The mechanism of the CSF spread of the PA is not clear. According to the literature, PA spread to the CSF is facilitated by its proximity to locations such as the ventricular system and basal cisterns. Although this type of spread usually follows the normal CSF flow, in the present case it was in the opposite direction. Mamelak et al.[4] reported that hypothalamic tumors are more prone to spread. But in the present case, the primary tumor was located in the CPA. The case reported by Dutta et al.[1] is similar to the one herein reported because of the size and imaging findings of the primary tumor, but it differs from our case due to the absence of evidence of CSF spread.

The origin of extra-axial gliomas of the CPA is still uncertain. Several theories have been suggested. One theory is that gliomas in this location arise from adjacent anatomical structures, such as the medial velum of the lateral recess of fourth ventricle. Another theory is that the tumor originates primarily in the transformation of heterotopic neuroglial cell nests in the leptomeninges covering the proximal cranial nerves.[1,3,5] In the current case, there was no history of intraparenchymal glioma and no intraoperative evidence of an anatomic association to the lateral recess of the fourth ventricle. We believe that the tumor most probably originates from neuroglial cells.

Conclusion

Pilocytic astrocytoma with CSF spread is a rare entity; therefore, the appropriate therapy for these patients is poorly defined. Mamelak et al. showed that surgery of the primary tumor is the preferred treatment modality for PAs that present spread. It has been documented that total surgical resection results in satisfactory tumor treatment with excellent outcomes and minor morbidity.[4] Pilocytic astrocytoma should be kept in mind in the differential diagnosis of unusual CPA tumors with atypical imaging findings. The possibility of spread of these tumors to another location should always be considered, and, after the primary treatment, radiological follow-up should be performed for the early diagnosis of the spread.

Consent to Participate

The patient herein described has given written consent regarding the inclusion of material pertaining to his case. The patient acknowledges that he cannot be identified through the paper. The authors have fully anonymized the patient.

Consent for Publication

The patient signed an informed consent form regarding the publication of his data.

Availability of Data and Material

The datasets analyzed in the current study are available from the corresponding author upon reasonable request.

Author's Contribution

Dr. Biyikli, Dr. Kursun, and Dr. Bozkurt conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the final manuscript. Dr. Biyikli, Dr. Kursun, Dr. Oguzsoy, Dr. Bozkurt, and Dr. Bayrakli designed the data collection instruments, collected data, carried out the initial analyses, and revised and critically reviewed the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Funding

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

Conflict of Interests

The authors have no conflict of interests to declare.

References

1 Dutta G, Singh D, Singh H, Sachdeva D, Kumar V, Chaturvedi A. Pilocytic astrocytoma of the cerebellopontine angle mimicking vestibular schwannoma: report of a rare entity. Br J Neurosurg 2020;34(01):107–109
2 Redhu R, Nadkarni TD. Multicompartmental cerebrospinal fluid dissemination of cerebellar pilocytic astrocytoma at presentation. J Clin Neurosci 2011;18(10):1412–1414
3 Francesco F, Maurizio I, Stefano C, Marina S, Ugo S, Massimo S. Trigeminal nerve root entry zone pilocytic astrocytoma in an adult: a rare case of an extraparenchymal tumor. J Neurooncol 2010;97(02):285–290
4 Mamelak AN, Prados MD, Obana WG, Cogen PH, Edwards MSB. Treatment options and prognosis for multicentric juvenile pilocytic astrocytoma. J Neurosurg 1994;81(01):24–30
5 Mirone G, Schiabello L, Chibbaro S, Bouazza S, George B. Pediatric primary pilocytic astrocytoma of the cerebellopontine angle: a case report. Childs Nerv Syst 2009;25(02):247–251

Spontaneous Anal Extrusion of Ventriculoperitoneal Shunt Catheter: Case Report

Extrusão anal espontânea de catéter de derivação ventriculoperitoneal: Relato de caso

Lívio Pereira de Macêdo[1] Arlindo Ugulino Netto[1] Kauê Franke[1] Pierre Vansant Oliveira Eugenio[2] Lucas Ribeiro de Moraes Freitas[2] Victor Ribeiro Xavier Costa[3] Eduardo Vieira de Carvalho Júnior[1] Igor Vilela Faquini[1] Nivaldo S. Almeida[1] Hildo Rocha Cirne Azevedo-Filho[1]

[1] Department of Neurosurgery, Hospital da Restauração, Recife, Pernambuco, Brazil
[2] Centro de Ciências Médicas, Universidade Federal da Paraíba, João Pessoa, Paraíba, Brazil
[3] Faculdade de Ciências Médicas da Paraíba, João Pessoa, Paraíba, Brazil

Address for correspondence Lívio Pereira de Macêdo, MD, Departmento de Neurocirurgia, Hospital da Restauração, Rua João Fernandes Vieira 544, Boa Vista, Recife, PE, 50050-200, Brasil (e-mail: livio21@gmail.com).

Arq Bras Neurocir 2022;41(4):e382–e385.

Abstract

Background Ventriculoperitoneal shunt (VPS) has become the standard treatment for congenital hydrocephalus. In the neurosurgical practice, it is a common procedure which usually results in low rates of complication. However, some serious complications can occur, including infections, intestinal perforation, and even death.

Case Description A 19-year-old, female, asymptomatic patient, with a history of appendectomy and revision of the VPS 6 years before, presented spontaneous transanal extrusion of the catheter. Abdominal radiographs and tomography scans showed perforation of the descending colon without peritonitis, with expulsion of the distal tip of the catheter through the anus. The patient underwent removal of the proximal part of the VPS and installation of an external ventricular drain (EVD). On the second postoperative day, there was spontaneous elimination of the distal portion of the catheter, dispensing any additional surgical procedures. With antimicrobial prophylaxis and the contralateral VPS performed, the patient evolved without further complications until discharge. Diverging from cases reported in the literature, the patient in question did not present any abdominal manifestations.

Conclusion Intestinal perforation by VPS may be asymptomatic until anal extrusion occurs. However, the early approach should avoid infections, which are associated with increased mortality. Removing only the proximal catheter, together with antimicrobial prophylaxis, can be an effective, safe and less invasive alternative to manage this complication of VPS.

Keywords
- ventriculoperitoneal shunt
- intestinal perforation
- hydrocephalus

received
January 8, 2022
accepted
April 6, 2022

DOI https://doi.org/10.1055/s-0042-1748848.
ISSN 0103-5355.

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

Introduction

Ventriculoperitoneal shunt (VPS) has become the standard treatment for congenital hydrocephalus since its introduction into the neurosurgical practice in the 1950s.[1]

Although uncommon, several abdominal complications resulting from VPS have been described, including fibrous entrapment of the catheter, blocking or twisting of the distal tube, extrusion by surgical incision, or migration of the shunt to a cavity other than the peritoneal one.[2] Intestinal perforation presents an incidence of 0.1% to 1% of the cases of catheter displacement, which can lead to infections, meningitis, seizures, fever and increased intracranial pressure, as well as abdominal manifestations, such as intestinal obstructions associated with adhesions, inflammatory pseudocysts and ascites.[3] Despite the low incidence, when perforation is associated with infections, it is related to a mortality of up to 15%.[4]

The aim of the present study is to report an unusual case of an adult patient with intestinal perforation and spontaneous extrusion of the VPS catheter through the anus.

Case Report

A 19-year-old female patient underwent a VPS implant at the age of 2 due to congenital hydrocephalus. Over time, it evolved with a delay in neuropsychomotor development and bed restriction. At the age of 13, she underwent an open appendectomy, evolving in the postoperative period with obstruction and infection of the implant site of the VPS, and a shunt review was performed.

Six years later, when the patient was aged 19 years, her caregiver noticed exposure of the distal end of the VPS catheter through the patient's anus (►**Fig. 1**), which motivated her return to the neurosurgery service. Upon physical examination, the tip of the extruded VPS catheter was found 5 cm from the anal margin, without dripping cerebrospinal fluid (CSF). Signs of phlogistic skin were detected in the cervical path of the VPS, but she did not have fever, abdominal distension, pain on palpation of the abdomen, ascites, vomiting or headache, and peritonitis or encephalitis were ruled out.

An abdominal computed tomography (CT) scan showed that the catheter path had no evidence of knots or pneumoperitoneum. Moreover, this image showed the peritoneal

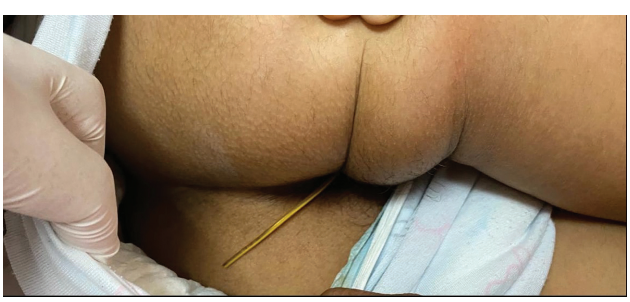


Fig. 1 Exposure of the distal end of the ventriculoperitoneal shunt catheter through the patient's anus.

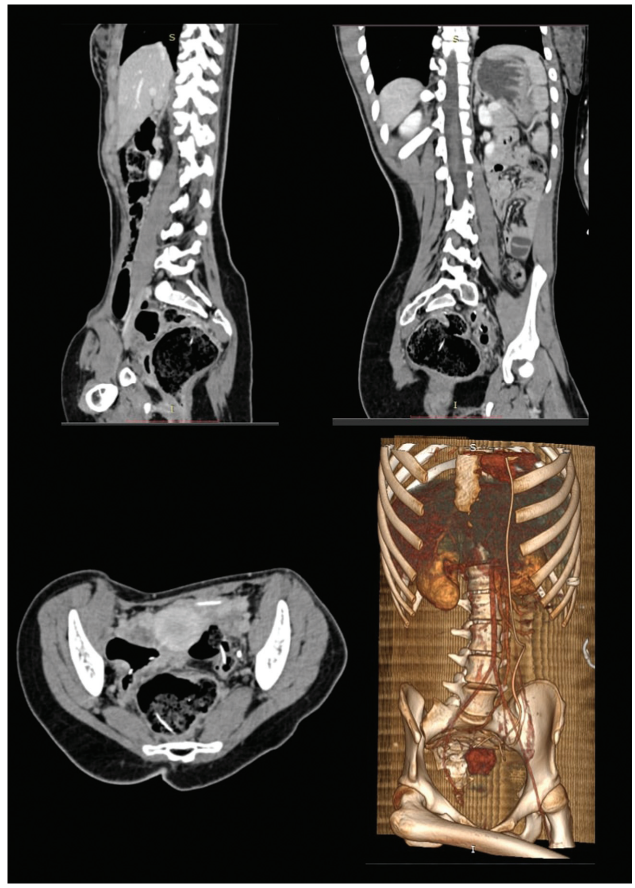


Fig. 2 Abdominal computed tomography scan showing the peritoneal catheter perforating the descending colon.

catheter perforating the descending colon and being extruded through the anus. The patient underwent surgery to remove the proximal portion of the VPS and to implant an external ventricular drain (EVD), without complications (►**Fig. 2** and **3**).

During hospitalization, antimicrobial prophylaxis with ceftriaxone and vancomycin was prescribed, the former being replaced on the seventh day by meropenem. While evaluating the possibility of laparoscopic exploration with the general surgery team, the patient spontaneously expelled the distal portion of the catheter on the ninth day of hospitalization (►**Fig. 4**). A new abdominal CT scan was requested, and no abscesses or signs of infection were noted. The CSF culture did not show bacterial growth, but showed normal glucose levels. With antimicrobial prophylaxis and the contralateral VPS performed, the patient evolved without further complications until discharge.

Discussion

Spontaneous intestinal perforation is an extremely uncommon complication, which was first reported by Wilson and Bertran[5] in 2 pediatric patients in 1966. From the initial report to the present day, approximately 112 cases of intestinal perforation associated with a VPS have been reported in the literature, half of them in patients aged up to 10 years. The combination of thin intestinal musculature in the

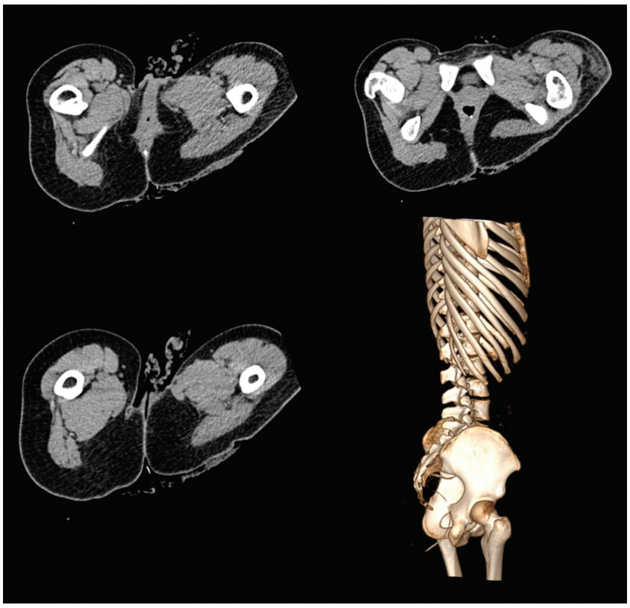


Fig. 3 Abdomen computed tomography scan, after the surgery to remove the proximal portion of the ventriculoperitoneal shunt and to implant an external ventricular drain (seven days later), showing the peritoneal catheter being extruded through the patient's anus.

Fig. 4 The patient spontaneously expelled the distal portion of the catheter on the ninth day of hospitalization.

myelomeningocele, placement of rigid peritoneal catheters, and local infectious adhesions can predispose intestinal perforation.[3]

In cases submitted to surgical intervention or autopsy, the authors[4] have described a fibrotic scar that anchors the tube in an region of the intestine and causes ulceration and, theoretically, eventual perforation.

Although not found in the case herein reported, significant abdominal symptoms or peritonitis affect up to 25% of the cases.[6] Surgeons must be aware of this complication to prevent the development of infections such as meningitis, ventriculitis and sepsis, which are associated with mortality in up to 15% of the cases.[4]

In the presence of pneumoperitoneum, radiographs can confirm the diagnosis of intestinal perforation. The exam also shows the trajectory of the peritoneal catheter to the perineal region. Meanwhile, abdominal CT scans enables physicians to rule out the presence of abscesses, in addition to suggesting a more precise location for the point of perforation.[7] In view of the evidence, these were the tests chosen for the assessment of the case herein reported. Although there was no pneumoperitoneum, the radiographs enabled the observation of the catheter path, while the abdominal CT scan showed perforation in the descending colon.

The management of intestinal perforation is individualized and depends on the signs and symptoms of the patient. In a patient with intestinal perforation, but without other complications, a formal exploratory laparotomy is not necessary. Our patient fits into the subset of patients who can, therefore, be treated without laparotomy, by means of externalization of the ventricular shunt and antimicrobial prophylaxis until the CSF bacteriological cultures become negative. It is important to emphasize that, when making a new derivation, it is recommended to choose a different terminal of the abdominal cavity, as there is a concern that the factors that triggered the perforation may still be present.[8]

If there is concern about abdominal abscess or peritonitis, laparotomy is the preferred treatment to control bacterial infection.[9] In some cases, the knot of the long shunt catheter itself or tangling of the tube in the intestinal loops makes laparotomy mandatory, even in the absence of peritonitis. As an alternative, laparoscopic visualization and disconnection of the derivation tube can be performed.[10]

Although intestinal perforation is a complication already reported in the literature, we have not identified any reports of spontaneous anal extrusion from the distal portion of the catheter after surgical removal of the proximal portion and antimicrobial prophylaxis. Assessing the infection-free evolution of the patient, this strategy can avoid unnecessary laparotomies, reducing the cost, the risk of infections, and excessive invasive interventions in patients who are often debilitated.

Conclusion

Intestinal perforation with anal catheter extrusion is an uncommon complication, usually asymptomatic, more common in children, and which has a good prognosis in most cases. In the case herein reported, its treatment consisted of removing the proximal portion of the catheter and administering antibiotics. Laparotomy with repair of the perforation should be performed mainly in cases of peritonitis, intra-abdominal abscess, or catheter tangling. Knowledge of this atypical complication and of the natural evolution will enable early recognition and more accurate surgical indications.

Funding

The authors declare that they have received no financial support for the research, authorship, and/or publication of the present article.

Conflict of Interests

The authors have no conflict of interests to declare.

References

1 Agha FP, Amendola MA, Shirazi KK, Amendola BE, Chandler WF. Unusual abdominal complications of ventriculo-peritoneal shunts. Radiology 1983;146(02):323–326. Doi: 10.1148/radiology.146.2.684907

2 Hasan A, Sharma S, Chopra S, Purohit DK. Anal Extrusion of Ventriculoperitoneal Shunt: A Report of Two Cases and Review of Literature. J Pediatr Neurosci 2018;13(01):8–12. Doi: 10.4103/JPN.JPN_97_17

3 Bakshi S. Spontaneous trans-anal extrusion of caudally migrated ventriculo-peritoneal shunt tip in a child: a case report. Surg Case Rep 2020;6(01):50

4 Panagea S, Cartmill TD, Panigrahi H. Intracerebral sepsis due to intestinal perforation by ventriculo-peritoneal shunts: two cases. J Infect 1997;35(01):86–88. Doi: 10.1016/s0163-4453(97)91217-2

5 Wilson CB, Bertan V. Perforation of the bowel complicating peritoneal shunt for hydrocephalus. Report of two cases. Am Surg 1966;32(09):601–603

6 Handa R, Kale R, Harjai MM. Unusual complication of ventriculoperitoneal shunt: anal extrusion. Med J Armed Forces India 2007;63(01):82–84. Doi: 10.1016/S0377-1237(07)80122-5

7 Zhou F, Chen G, Zhang J. Bowel perforation secondary to ventriculoperitoneal shunt: case report and clinical analysis. J Int Med Res 2007;35(06):926–929. Doi: 10.1177/147323000703500624

8 Bales J, Morton RP, Airhart N, Flum D, Avellino AM. Transanal presentation of a distal ventriculoperitoneal shunt catheter: Management of bowel perforation without laparotomy. Surg Neurol Int 2016;7(Suppl 44):S1150–S1153

9 Hai A, Rab AZ, Ghani I, Huda MF, Quadir AQ. Perforation into gut by ventriculoperitoneal shunts: A report of two cases and review of the literature. J Indian Assoc Pediatr Surg 2011;16(01):31–33. Doi: 10.4103/0971-9261.74521

10 Sharma A, Pandey AK, Radhakrishnan M, Kumbhani D, Das HS, Desai N. Endoscopic management of anal protrusion of ventriculo-peritoneal shunt. Indian J Gastroenterol 2003;22(01):29–30

Thermocoagulation for the Treatment of Anorexia Nervosa Associated with Obsessive-Compulsive Disorder: Case Report

Termocoagulação para tratamento de anorexia nervosa associada a transtorno obsessivo compulsivo: Relato de caso

Cristiano Mendonça Sarkis[1] Jordana Gonçalves de Miranda Amaral[1] Ledismar José da Silva[1]

[1] School of Medicine, Pontifícia Universidade Católica de Goiás, Goiânia, GO, Brazil

Arq Bras Neurocir 2022;41(4):e386–e390.

Address for correspondence Ledismar José da Silva, MSc, School of Medicine, Pontifícia Universidade Católica de Goiás (PUC-Goiás), Avenida Universitária, 1440, Setor Universitário, 74605-010, Goiânia, GO, Brazil (e-mail: ledismarsilva@gmail.com).

Abstract

Anorexia nervosa (AN) and obsessive-compulsive disorder (OCD) are two psychiatric disorders that often overlap or are diagnosed as distinct disorders in the same individual. Although neurosurgical treatment is currently reserved for patients with refractory chronic OCD, it has been evidenced that it is also effective for the treatment of AN, since these two disorders share some pathophysiological neurocircuits. The present study aimed to report the case of a patient with AN, OCD, schizophrenia, and comorbid depression who underwent thermocoagulation of the nucleus accumbens associated with anterior cingulotomy and anterior capsulotomy, all of them bilaterally. Follow-up, performed 16 months after the procedure, showed substantial improvement in AN, OCD, and schizophrenia symptoms, demonstrating the effectiveness of this type of intervention in patients refractory to conservative treatment.

Keywords

- ► stereotaxic technique
- ► radiofrequency
- ► anorexia nervosa
- ► obsessive-compulsive disorder
- ► schizophrenia

Resumo

A anorexia nervosa (AN) e o transtorno obsessivo-compulsivo (TOC) são dois transtornos psiquiátricos que, muitas vezes, se sobrepõem ou são diagnosticados como transtornos distintos no mesmo indivíduo. Embora o tratamento neurocirúrgico seja atualmente reservado para pacientes com TOC crônico refratário, foi evidenciado que também é eficaz para o tratamento de AN, uma vez que estes dois distúrbios compartilham alguns neurocircuitos fisiopatológicos. O presente estudo teve como objetivo relatar o caso de uma paciente com AN, TOC, esquizofrenia e depressão comórbida submetida a termocoagulação de nucleus accumbens em associação com cingulotomia anterior e capsulotomia anterior, todos bilateralmente. O seguimento, realizado 16 meses após o procedimento, mostrou melhora substancial de AN, TOC e sintomas de esquizofrenia, demonstrando a eficácia deste tipo de intervenção em pacientes refratários ao tratamento conservador.

Palavras-chave

- ► técnica estereotáxica
- ► radiofrequência
- ► anorexia nervosa
- ► transtorno obsessivo-compulsivo
- ► esquizofrenia

received
May 24, 2021
accepted
April 6, 2022

DOI https://doi.org/10.1055/s-0042-1748846.
ISSN 0103-5355.

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

Introduction

Anorexia nervosa (AN) is a psychiatric and eating disorder characterized by distorted perception of body size, weight, and shape, which leads to a radical eating restriction and/or excessive and purgative behaviors to achieve an idealized body.[1,2] It is usually accompanied by other psychiatric disorders such as major depression, generalized anxiety, obsessive compulsive disorder (OCD), and personality disorders, in addition to the risk of predisposition to alcohol use disorders as well as to drug abuse and addiction.[3]

The average age at onset of AN ranges between 15 and 19 years old, and AN affects $\sim$ 0.7% of individuals worldwide, in a female-to-male ratio of 10:1.[2] The mortality rate is the highest among all psychiatric disorders, ranging from 6 to 11%, and the most frequent causes of mortality are suicide and medical complications.[4] An estimated 21% of patients diagnosed with AN present with severe chronic cases, and those affected for $>$ 10 years are unlikely to recover.[5]

Obsessive compulsive disorder (OCD), in turn, is an anxiety disorder that consists of the overlapping of obsession, defined as uncontrollable, repetitive, persistent, and stereotyped ideas or thoughts, which generates great anxiety, fear, anguish, and compulsion, characterized by repetitive behaviors or mental acts induced by obsessive thoughts.[6,7] Obsession is a cause of great suffering and, in most cases, compulsion is a subterfuge.

Neurosurgery is a treatment predominantly indicated to patients presenting with chronic OCD refractory to conservative treatment. However, a strong correlation between AN and OCD has been evidenced, since the prevalence of OCD in patients with AN ranges from 35 to 44%, whereas AN is observed in up to 10% of women with OCD.[8,9] In addition, recent studies in children and adults diagnosed with OCD or AN show converging lines of evidence, suggesting that the two disorders involve the same regions of the cortico-striatal-thalamic-cortical circuit.[10–13] Moreover, the association of the etiopathogenesis of OCD with AN is possibly the explanation for the recurrence of restrictive eating behaviors after the pharmacological neuromodulation of the limbic circuitry and the use of ablative surgical techniques for the treatment of OCD.[5,14–16] The targets frequently used in these surgical procedures are the nucleus accumbens, the anterior cingulate, and the anterior capsule.[5,12–14]

Taking into consideration the current surgical approaches, the surgical treatment of AN associated with OCD is a viable option, since it can relieve suffering and improve the quality of life of patients with these disabling disorders, and is more cost-effective than conventional treatments.[5,17–19] For patients with chronic and refractory AN associated with OCD, several studies suggest that the adoption of two or more surgical procedures should be considered.[5,20] Therefore, the present study aimed to report the case of a patient with AN, OCD, schizophrenia, and comorbid depression who underwent thermocoagulation of the nucleus accumbens associated with anterior cingulotomy and anterior capsulotomy, all of them bilaterally.

Case Report

The present study was approved by the Ethics Committee of the Pontifícia Universidade Católica de Goiás (CAAE: 33641220.5.0000.0037). It was conducted following the principles of the Helsinki Declaration[21] and of the Resolution 2.165/2017, which regulates neuropsychosurgeries in Brazil.[22] The patient signed a written consent.

A 39-year-old female patient diagnosed with AN, OCD, schizophrenia, and comorbid depression, weighing 48 kg (body mass index [BMI] = 17.02), was referred by 2 independent psychiatrists to a tertiary referral neurosurgical unit in Goiânia, state of Goiás, Brazil, in July 2019. The symptoms of AN were distorted body image, cachexia, and uncontrollable thoughts about food, weight, and shape. She had an extremely restricted dietary pattern, consuming little to no food for many consecutive days, due to an unavoidable desire to lose weight, and had constant and intense abdominal cramps. Although she was never satisfied with the weight she reached, she believed she was on the right path, which motivated her to continue losing weight. Nonetheless, whenever she ate, she exaggerated the amount of food and vomited immediately afterwards. She reported that, after a few years, vomiting became spontaneous, with no need for self-inducing it. In addition, she used laxatives and exercised excessively aiming to lose weight.

She was diagnosed with AN at the age of 17 years old. The lowest weight achieved was 35 kg, which generated important anatomical-functional repercussions, such as reduced muscle strength, gait impairments, and syncope. Since the beginning of the disease, the patient had several mandatory hospitalizations and treatments.

The onset of OCD symptoms occurred at the age of 18 years old. The patient had recurrent obsessive thoughts, which forced her to perform compulsive rituals that impaired her quality of life and social life. The most obvious compulsions were for buying and cleaning, mainly washing the same clothes several times a day. According to the patient, neither the avoidance behavior nor the performance of compulsive acts was able to ward off obsessive thoughts, having a significant impact on her life.

The patient also had schizophrenia, characterized by the presence of disabling visual and auditory hallucinations, usually involving seeing deceased people or hearing their commands for suicide and escape, and a history of several depressive episodes. The delusions of persecution were constant, and together with the depression due to her comorbidities, led her to attempt suicide in 2015.

Before the initial appointment, she had been undergoing treatment with a combination of benzodiazepines, selective serotonin reuptake inhibitors, and antipsychotics, with a small beneficial effect on OCD, but with no significant improvements in AN, schizophrenia, or depression. Due to the long-term stigmatizing psychiatric conditions, she has always lived with her parents and had significant impairments in social life and unstable relationships with friends and family members, especially her father.

Preoperative Assessment

A qualiquantitative assessment was performed preoperatively based on the subjective history reported by the patient and her mother, as well as on the scores of the questionnaires applied. At first, an outpatient clinical examination was performed, and the following variables were analyzed: anthropometric measurements (weight and BMI), AN, OCD, relationship between AN and OCD, psychiatric comorbidities (depression and schizophrenia), and the interference of the underlying diseases in her quality of life. During anamnesis, the diagnostic criteria according to the DSM-5 for all the disorders previously diagnosed were identified and confirmed.[6] Subsequently, the clinical data were quantified through the application of four questionnaires.

To assess the presence and type of eating disorders, the Eating Disorder Inventory-3 (EDI-3) was used.[23] Additionally, the Eating Disorder Examination Questionnaire (EDE-Q) was applied to assess the severity of behaviors and attitudes secondary to eating disorders.[24]

Regarding the assessment of OCD, the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) was used.[25] This instrument was developed and validated with the objective of measuring the severity of OCD symptoms. Its essential feature is the capacity to assess the severity of OCD symptoms regardless of the types of compulsion presented by the patient.

The Hamilton Depression Rating Scale (HDRS) was used to assess the severity of depressive symptoms, acting as an indirect measure of the biopsychosocial impact of underlying disorders on the mood and social life of the patient.[26] This is the most widely used clinician-administered depression assessment scale.

Surgical Procedure

The complete previous medical history, neuropsychological assessment, psychiatric diagnoses, and results of the questionnaires were examined by a multiprofessional team. Confirmation of the diagnosis of OCD refractory to treatment and of the chronicity of this condition ($>$ 10 years) were in accordance with the inclusion criteria for OCD stereotactic neurosurgery.[16]

The surgery was performed in July 2019, with the patient under general anesthesia, and the stereotaxic procedure was guided by computed tomography (CT) and magnetic resonance imaging (MRI). Based on the experience of the neurosurgery team and on evidence that the use of multiple targets in the same surgical procedure increases its effectiveness, with low postoperative morbidity,[27] the surgeons decided to carry out the ablation of the nucleus accumbens associated with anterior cingulotomy and anterior capsulotomy, all of them bilaterally. Thermocoagulation was performed percutaneously, using a 244-mm long probe, with a 4-mm long and 1.5-mm diameter exposed tip at 70°C for 70 seconds. The radiofrequency coagulation probe was guided using the fluoroscopic technique.

Postoperative Assessment

During the hospitalization period, the postoperative assessment of the patient was performed subjectively, based on her daily evolution. Subsequently, she was monitored twice, 1 week and 1 month after hospital discharge, by telephone conversations and exchange of messages.

In November 2020, the definitive assessment of the clinical evolution of the patient was performed in a video interview, due to the pandemic, applying the same questionnaires of the preoperative phase. The interview was structured to allow the comparison between the preoperative and postoperative clinical data. It aimed to verify the efficacy of the neurosurgical procedure in the treatment of her most evident psychiatric disorders, AN and OCD, and to analyze qualitatively, through the own perceptions of the patient, the changes provided by this therapeutic strategy in her daily life.

The surgical procedure had a positive effect on AN, since it favored a body weight gain of 14.5 kg in 16 months (►**Table 1**). During the interview, the patient reported a drastic improvement in her interpersonal relationships, quality of life, mood, and mainly body self-perception, because she currently perceives herself as a healthier person. She reached complete remission of vomiting and considers it one of the most important results of the surgery in her life. Nowadays, she eats in a balanced and healthy way, without feeling guilty or sad. The patient affirmed that she had absolute improvement in the organic and functional complaints reported before the surgery, such as abdominal cramps and nausea. However, she still uses laxatives due to frequent constipation, a problem not completely solved after surgery.

The patient experienced a substantial improvement in OCD symptoms after the procedure, completely breaking the cycle of compulsive buying and achieving a drastic decrease in cleaning rituals. In addition, the patient had an important improvement in schizophrenia and depression symptoms, perhaps the factors that most contributed to her psychological distress and social isolation preoperatively. She reported

Table 1 Patient assessment preoperatively (baseline) and 16 months after stereotaxic neurosurgery

Type of assessment	Result	
	Preoperatively	Postoperatively
Body weight (kg)	48	62.5
Body mass index	17.02	22.14
Eating Disorder Inventory-3 (EDI-3)	Binging-purging anorexia nervosa with bulimia	Improbable eating disorder
Eating Disorder Examination Questionnaire (EDE-Q)	5.1	0.05
Yale-Brown Obsessive Compulsive Scale (Y-BOCS)	33	8
Hamilton Depression Rating Scale (HDRS)	43	4

that, after surgery, both visual and auditory hallucinations completely disappeared.

Classification scores at baseline and at the 16-month follow-up improved for both the primary psychiatric disorders (AN and OCD) and the secondary one (depression) (Table 1). The results of EDI-3 showed that she met the classification criteria for the subtype "binging-purging" of AN and extremely severe bulimia at the beginning of the study; however, at the follow-up, the patient no longer met the criteria for any eating disorders. Moreover, the EDE-Q score significantly improved 16 months after the procedure.

Compared with the preoperative baseline, the severity of OCD symptoms, measured using Y-BOCS, decreased by 25 points 16 months after surgery. The assessment of depression using the HDRS revealed substantial improvement of symptoms in the postoperative period as well.

Discussion

The simultaneous and substantial drop in the scores of the applied questionnaires after 16 months of the procedure corroborates the hypothesis that the targets classically implicated in the reverberation of an anomalous neuronal circuitry of OCD also extend to AN.[19] The AN of this patient was classified as of the "binging-purging" subtype, because after long periods of fasting, she ingested large amounts of food and then caused vomiting due to the feeling of guilt that dominated her.[7] A Chinese experimental study that investigated the effects of the ablation of the nucleus accumbens, using stereotactic surgery, in patients with AN not responsive to clinical treatment, showed a substantial increase in the physiological drive of the patients to eat,[20] corroborating the findings of our study, given that the patient in the present report had a considerable weight gain postoperatively.

The surgical treatment also provided substantial suppression of OCD symptoms, improving the quality of life of the patient, since this disorder is a source of great psychological distress.[6] Thus, the thermocoagulation approach proved to be an excellent alternative to conservative treatment in refractory and chronic OCD cases, which is in line with the results of other studies.[28]

Although the primary objective of the present study did not involve assessing the benefits of the proposed treatment to control the symptoms of schizophrenia, given that this disorder was not the major complaint that motivated the patient to seek help, based on the patient report, confirmed by her family, the auditory and visual hallucinations prior to the surgical procedure completely disappeared postoperatively. This finding substantiates the hypothesis of some authors that patients with refractory schizophrenia may also benefit from neurosurgical approaches, such as deep brain stimulation and stereotactic surgery.[29]

Conclusion

Thermocoagulation of brain areas whose circuits are classically implicated in the pathogenesis of OCD, AN, and schizophrenia proved to be effective in the long term for our patient. The results of the applied questionnaires showed a complete resolution of AN and symptoms of schizophrenia, an important remission of OCD symptoms, and a substantial improvement in the quality of life and general condition of the patient. The substantial decrease in the HDRS score suggests a relationship with the alterations in limbic circuits caused by surgery. Nevertheless, this hypothesis needs validation in future analytical studies. Although the surgery performed was indicated because of refractory OCD, the results of the present study also corroborated its effectiveness in the simultaneous treatment of AN and visual and auditory hallucinations due to schizophrenia.

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

Acknowledgments
The authors would like to thank Suzana Oellers for her invaluable dedication in reviewing and formatting the present manuscript and Dr. João Batista Arruda for the essential contribution to the surgical procedure.

References

1 Schmidt E, Mata GF. Anorexia nervosa: uma revisão. Fractal Rev Psicol 2008;20(02):387–400
2 Lipsman N, Lam E, Volpini M, et al. Deep brain stimulation of the subcallosal cingulate for treatment-refractory anorexia nervosa: 1 year follow-up of an open-label trial. Lancet Psychiatry 2017;4 (04):285–294
3 Norrington A, Stanley R, Tremlett M, Birrell G. Medical management of acute severe anorexia nervosa. Arch Dis Child Educ Pract Ed 2012;97(02):48–54
4 Galmiche M, Déchelotte P, Lambert G, Tavolacci MP. Prevalence of eating disorders over the 2000-2018 period: a systematic literature review. Am J Clin Nutr 2019;109(05):1402–1413
5 Sun B, Li D, Liu W, Zhan S, Pan Y, Zhang X. Surgical treatments for anorexia nervosa. In: Sun B, Salles A, editors. Neurosurgical treatments for psychiatric disorders. Dordrecht: Springer;. 2015:175–187
6 American Psychiatric Association. Diagnostic and statistical manual of mental disorders: DSM-5™. 5th ed. Washington, DC:: American Psychiatric Publishing;; 2013
7 Brock H, Hany M. Obsessive-compulsive disorder (OCD). In: StatPearls [Internet]. Treasure Island: StatPearls Publishing 2021 Accessed on: 17 May 2021 at: https://www.ncbi.nlm.nih.gov/books/NBK553162/
8 LaSalle VH, Cromer KR, Nelson KN, Kazuba D, Justement L, Murphy DL. Diagnostic interview assessed neuropsychiatric disorder comorbidity in 334 individuals with obsessive-compulsive disorder. Depress Anxiety 2004;19(03):163–173
9 Pinto A, Mancebo MC, Eisen JL, Pagano ME, Rasmussen SA. The Brown Longitudinal Obsessive Compulsive Study: clinical features and symptoms of the sample at intake. J Clin Psychiatry 2006;67(05):703–711
10 Haynos AF, Hall LMJ, Lavender JM, et al. Resting state functional connectivity of networks associated with reward and habit in anorexia nervosa. Hum Brain Mapp 2019;40(02):652–662
11 Uniacke B, Wang Y, Biezonski D, et al. Resting-state connectivity within and across neural circuits in anorexia nervosa. Brain Behav 2019;9(01):e01205
12 Cha J, Ide JS, Bowman FD, Simpson HB, Posner J, Steinglass JE. Abnormal reward circuitry in anorexia nervosa: A longitudinal,

multimodal MRI study. Hum Brain Mapp 2016;37(11): 3835–3846
13 Ehrlich S, Lord AR, Geisler D, et al. Reduced functional connectivity in the thalamo-insular subnetwork in patients with acute anorexia nervosa. Hum Brain Mapp 2015;36(05):1772–1781
14 Silva LJ, Naciff TH, Oliveira MFV. Deep brain stimulation as a treatment approach for anorexia nervosa: a systematic literature review. Arq Bras Neurosurg 2019;38(03):175–182
15 Brockmeyer T, Friederich HC, Schmidt U. Advances in the treatment of anorexia nervosa: a review of established and emerging interventions. Psychol Med 2018;48(08):1228–1256
16 Doshi PK. Surgical treatment of obsessive compulsive disorders: Current status. Indian J Psychiatry 2009;51(03):216–221
17 Mueller J, Skogseid IM, Benecke R, et al; Deep-Brain Stimulation for Dystonia Study Group. Pallidal deep brain stimulation improves quality of life in segmental and generalized dystonia: results from a prospective, randomized sham-controlled trial. Mov Disord 2008;23(01):131–134
18 O'Sullivan D, Pell M. Long-term follow-up of DBS of thalamus for tremor and STN for Parkinson's disease. Brain Res Bull 2009;78(2-3):119–121
19 Goodman WK, Alterman RL. Deep brain stimulation for intractable psychiatric disorders. Annu Rev Med 2012;63:511–524
20 Wang J, Chang C, Geng N, Wang X, Gao G. Treatment of intractable anorexia nervosa with inactivation of the nucleus accumbens using stereotactic surgery. Stereotact Funct Neurosurg 2013;91(06):364–372
21 World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA 2013;310(20):2191–2194
22 Conselho Federal de Medicina. Resolução CFM n° 2.165, de 23.06. 2017 Altera a alínea "b" do parágrafo 4° do artigo 20 da Resolução CFM n° 2.057/2013, publicada no D.O.U. de 12 de novembro de 2013, Seção I, p. 165–171, em seu capítulo VIII, da Neuropsicocirurgia. Diário Oficial União 2017;Seção 1:64, Aug. 15
23 Clausen L, Rosenvinge JH, Friborg O, Rokkedal K. Validating the Eating Disorder Inventory-3 (EDI-3): a comparison between 561 female eating disorders patients and 878 females from the general population. J Psychopathol Behav Assess 2011;33(01): 101–110
24 Aardoom JJ, Dingemans AE, Slof Op't Landt MC, Van Furth EF. Norms and discriminative validity of the Eating Disorder Examination Questionnaire (EDE-Q). Eat Behav 2012;13(04): 305–309
25 Goodman WK, Price LH, Rasmussen SA, et al. The Yale-Brown Obsessive Compulsive Scale. I. Development, use, and reliability. Arch Gen Psychiatry 1989;46(11):1006–1011
26 Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry 1960;23(01):56–62
27 Borges TJB, D'Assunção APA, Silva LJ. Oliveira LAG, Araújo PH. A importância de múltiplos alvos no tratamento cirúrgico da agressividade refratária. Rev Med Saúde Brasília 2017;6(02): 193–202
28 Stein DJ, Costa DLC, Lochner C, et al. Obsessive-compulsive disorder. Nat Rev Dis Primers 2019;5(01):52
29 Agarwal P, Sarris CE, Herschman Y, Agarwal N, Mammis A. Schizophrenia and neurosurgery: A dark past with hope of a brighter future. J Clin Neurosci 2016;34:53–58

Ultrasound-Guided In-Plane Interlaminar Lumbar Endoscopic Approach with Smartphone and Portable Light Source: Description of a New Surgical Technique

Acesso Endoscópico Interlaminar lombar em plano guiado por ultrassom com smartphone e luz portátil: descrição de uma nova técnica cirúrgica

João Paulo Souza de Castro[1] Roger Schmidt Brock[1] Manoel Jacobsen Teixeira[1] Eberval Gadelha Figueiredo[1]

[1] Departament of Neurology, Hospital das Clínicas da Universidade de São Paulo, São Paulo – SP, Brazil.

Arq Bras Neurocir 2022;41(4):e391–e396.

Address for correspondence João Paulo Souza de Castro, MD, Neurosurgeon and Spine Surgeon, Departamento de Neurologia, Hospital das Clínicas da Universidade de São Paulo, João Paulo Souza de Castro, Rua Maria Figueiredo, Número 249, Apartamento 43, Paraíso, CEP 04002001, São Paulo – SP, Brazil (e-mail: souzacastro.jp@gmail.com).

Abstract

Introduction Endoscopic spine surgery enables the minimally invasive treatment of pathologies affecting the spinal cord and roots. Herein we describe an unprecedented technique of Ultrasound-Guided in-plane interlaminar lumbar endoscopic approach with a smartphone and portable light source.

Methods The interlaminar approach was performed in a cadaveric specimen at L4 to 5 and L5 to S1 bilaterally. A curvilinear 2 to 5 MHz ultrasound probe was employed, the puncture was performed with the needle, a guide wire was inserted until the flavum ligament, followed by the dilator and working cannula. A 30° spinal endoscope, with an optical adapter of the endoscope camera for smartphone and portable endoscope lighting was inserted, the flavum ligament was visualized, and an opening in this site was performed with the scissors. Open dissection of the specimen was subsequently performed by identifying the puncture site in the interlaminar window.

Results The four interlaminar punctures were successfully guided by ultrasound; the opening of the ligamentum flavum was performed in the most lateral part of the interlaminar space, near the junction of the superior and inferior articular processes of the corresponding vertebrae in all the punctures.

Discussion The ultrasound makes possible to identify facets, foramina, transverse processes, and the interlaminar space. It is possible to minimize the use of radioscopy and its associated risks, both for patients and health professionals.

Keywords
- spine
- endoscopy
- ultrasonography
- interventional

received
May 30, 2022
accepted
June 22, 2022

DOI https://doi.org/10.1055/s-0042-1756459.
ISSN 0103-5355.

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

Conclusions The ultrasound-guided, in-plane, interlaminar, lumbar endoscopic approach with smartphone-adapted endoscope and portable light source is feasible and practical, minimizing radiation risks and making it possible to perform endoscopic spinal surgery.

Resumo

Introdução A cirurgia endoscópica da coluna possibilita o tratamento minimamente invasivo de patologias que acometem a medula espinhal e raízes. Aqui descrevemos uma técnica inédita de acesso endoscópica, interlaminar, lombar, em plano guiado por ultrassom com um smartphone e fonte de luz portátil.

Métodos A abordagem interlaminar foi realizada em espécime cadavérico em L4 a 5 e L5 a S1 bilateralmente. Foi utilizado um transdutor de ultrassom curvilíneo de 2 a 5MHz, realizada a punção com a agulha, inserido um fio guia até o ligamento amarelo, seguido do dilatador e da cânula de trabalho. O endoscópio de coluna de 30° com adaptador óptico para smartphone e iluminação portátil foi inserido, visualizando o ligamento amarelo, que foi aberto com tesoura. A dissecção aberta do espécime foi realizada posteriormente, identificando o local da punção na janela interlaminar.

Resultados As quatro punções interlaminares foram guiadas com sucesso por ultrassom; a abertura do ligamento amarelo realizada foi na parte mais lateral do espaço interlaminar, próximo à junção dos processos articulares superior e inferior das vértebras correspondentes em todas as punções.

Discussão A ultrassonografia permite identificar facetas, forames, processos transversos e o espaço interlaminar. É possível minimizar o uso da radioscopia e seus riscos associados, tanto para pacientes quanto para profissionais de saúde.

Conclusões A abordagem endoscópica, interlaminar, lombar, em plano guiada por ultrassom, com endoscópio adaptado à smartphone e fonte de luz portátil, é viável e prática, minimizando os riscos de radiação e possibilitando a realização de cirurgia endoscópica da coluna vertebral.

Palavras-chave
- coluna
- endoscopia
- ultrassonografia intervencionista

Introduction

Degenerative diseases of the lumbar spine have a high prevalence, reaching 27.3% of the population and increasing with age and risk factors such as obesity.[1] Degenerative disc disease occurs in 12.2% of the patients, and is frequently associated with low back pain and lumbosciatalgia.[2]

Minimally invasive spine surgery includes procedures that have the common aim of avoiding biomechanical complications, preventing damage to crucial posterior stabilizers, and preserving the stability and structural integrity of the spine.[3] So it is possible to perform surgeries with less tissue aggression, faster postoperative recovery, and shorter hospital stays with viability and efficiency, increasing its accessibility in the last two decades.[2]

The percutaneous endoscopic, or full-endoscopic, discectomy technique has been scientifically proven to be a good alternative to open discectomy, especially for lumbar disc herniation, and the main surgical field has been shifted from the intradiscal space to the epidural space.[4] Percutaneous endoscopic lumbar discectomy becomes particularly attractive for sequestrectomies, with the advent of angled scopes allowing 360° visualization and enabling the removal of extruded lumbar disc fragments while preserving the disc.[5]

The two major approaches of endoscopic spine surgery are transforaminal and interlaminar, with different techniques and indications.[6] The interlaminar endoscopic technique is used for discectomies involving mostly central-lateral disc herniations, specially at the L4 to 5 and L5 to S1 levels, which correspond to the majority of lumbar disc hernias.[7] Classically, the approach is performed with the aid of fluoroscopy during the surgical procedure, which assists in the puncture of the interlaminar window and the positioning of the working cannula for the endoscope insertion.

Ultrasonography can visualize spine anatomy, including the ligaments, erector spinae muscles, facet joints, transverse processes, foramina, and interlaminar spaces; it can also guide injections and interventional procedures.[8]

The use of radioscopy can pose risks to patients and healthcare professionals related to radiation. To minimize the use of intraoperative radioscopy and its risks, we describe in this paper an unprecedented technique, consisting of the ultrasound-guided, in-plane, interlaminar, lumbar endoscopic approach, with a smartphone-adapted endoscope and portable light source.

Materials and Methods

The technique was demonstrated in a cadaveric specimen using the Sonosite M-Turbo Ultrassound (FujiFilm SonoSite, Bothell, WA, USA) to perform the interlaminar in plane lumbar L4–5 and L5-S1 approach bilaterally with the

Fig. 1 Optical smartphone camera adapter attached to the endoscope in addition to a portable LED lamp.

Fig. 2 Sacrum is identified by seeing an hyperechogenic ramp on ultrasound.

Fig. 3 Spinous processes of L5 and L4, which appear as more superficial hyperechoic structures with a deeply acoustic shadow.

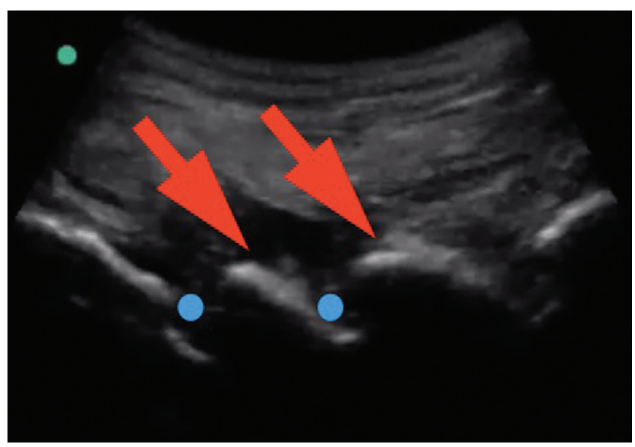


Fig. 4 Laminas are visualized as non-continuous hyperechoic structures that resemble the image of a "horses race" (arrow); between then it becomes possible to identify the flavum ligament as part of the posterior complex (circle).

puncture of the interlaminar window guided by ultrasound using a 2–5MHz curvilinear probe. An optical smartphone camera adapter MedEasy (MedEasy, São Paulo, SP, Brazil) was attached to the endoscope in addition to a portable LED lamp PhlatLight (Luminus Devices Inc., Woburn, MA, USA) (►**Fig. 1**).

The punctures were then performed in the L4 to 5 and L5 to S1 interlaminar windows bilaterally, guided by ultrasound and directed to the V point, which corresponds to the intersection of the inferior articular process of the superior vertebra with the superior articular process of the inferior vertebra and ligamentum flavum.

The step-by-step technique was didactically elaborated in 10 steps, which are presented in the results.

Subsequently, an open dissection of the specimen was performed with identification of the opening sites of the flavum ligament.

Results

Technical Note

1. With the specimen in the prone position and using a low frequency (2–5 MHz) curvilinear ultrasound probe oriented longitudinally in the midline, the sacrum is identified by seeing an hyperechogenic ramp on ultrasound (►**Fig. 2**).
2. In the midline, the transducer is directed cranially, allowing the identification of the spinous processes of L5 and L4, which appear as more superficial hyperechoic structures with a deeply acoustic shadow (►**Fig. 3**).
3. From the midline, the transducer is moved laterally by 1 cm, making it possible to visualize the non-continuous, hyperechoic structures that resemble the image of a "horses' race", constituting the sonographic image of the laminas. Between the laminas, it becomes possible

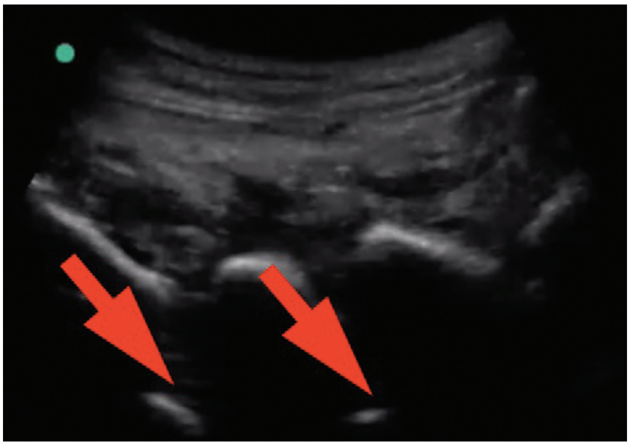


Fig. 5 Anterior complex formed by the posterior longitudinal ligament, disc and ventral dura mater.

Fig. 7 Needle tip going through the flavum ligament. A resistance is felt at this moment.

to identify the flavum ligament as part of the posterior complex (►**Fig. 4**).

4. Going laterally, it is also possible to see the anterior complex, formed by the posterior longitudinal ligament, disc, and ventral dura mater (►**Fig. 5**).
5. Proceeding with the transducer for approximately 1 cm more laterally, it is possible to identify more rounded hyperechoic structures resembling "mountains and valleys", which corresponds to the facet joints (►**Fig. 6**).
6. With the ultrasound positioned longitudinally in a paramedian position for approximately 1 to 1.5 cm, having identified the most lateral portion of the laminas and visualizing it on the ultrasound screen, the puncture needle is introduced in a caudal to cranial direction in-plane with the ultrasound probe. The puncture needle is inserted with its direct visualization by the ultrasound screen, progressing from a caudal to cranial direction, parallel to the laminas, until it touches the flavum ligament of the correspond level. At this point, resistance is felt due to the presence of the flavum ligament. The puncture needle is inserted with its blade positioned posteriorly, and the bevel opening is in a cranial direction in order not to enter the lamina of the superior vertebra (►**Fig. 7**).
7. After contact with the flavum ligament, a guide wire is inserted through the needle up to the flavum ligament. The needle is removed, and an incision of approximately 1 cm is made in the skin and muscle fascia (►**Fig. 8**).
8. The dilator is inserted up to the flavum ligament (►**Fig. 8**).

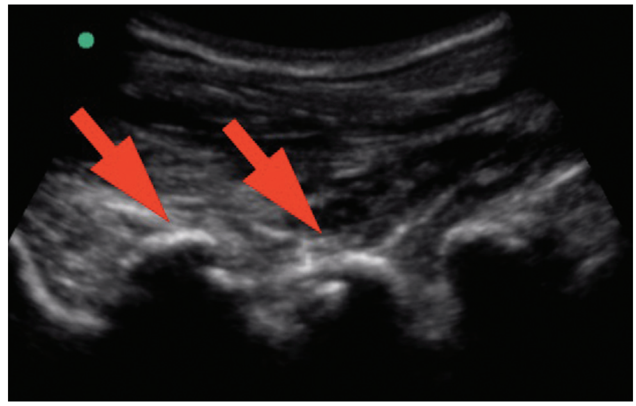


Fig. 6 Facet joints resembling to "mountains and valleys".

Fig. 8 Needle, guide wire, dilator, working cannula and endoscope insertion.

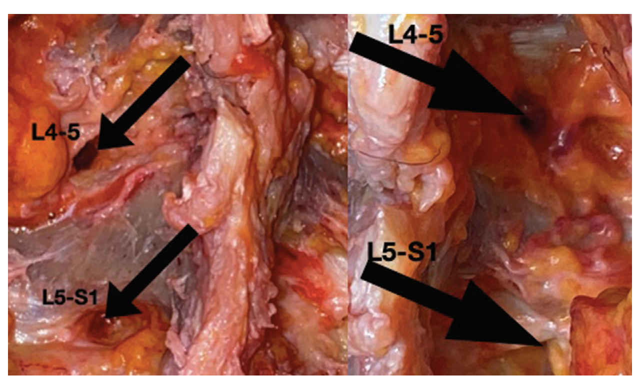


Fig. 9 Punctions sites.

9. The working cannula is inserted over the dilator, with its blade directed laterally and the bevel opening medially until it reaches the flavum ligament (►**Fig. 8**).
10. A 30° endoscope is introduced with an optical adapter from the endoscope camera to a smartphone and portable endoscopic lighting, visualizing the flavum ligament. The ligament is opened at this site with endoscopic scissors. These steps are performed in L4 to 5 and L5 to S1, bilaterally (►**Fig. 8**).

The ultrasound enabled the identification of the interlaminar space in all the punctures performed.

In all punctures, the opening of the ligamentum flavum was performed in the most lateral part of the interlaminar window, near the junction of the superior and inferior articular processes of the corresponding vertebrae (►**Fig. 9**).

Discussion

Endoscopic spine surgery has been increasingly used to treat spinal cord and nerve roots pathologies, promoting a paradigm shift in minimally invasive spine surgery.[9] The beginnings of this technique date back to 1983, when Forst and Hausmann[10] used an arthroscope to access the intervertebral disc, followed by the first description of an endoscopic discectomy by Kambin et al., in 1988.[11]

The intraforaminal, or transforaminal, approach Is the oldest technique allowing intradiscal and extradiscal access.[12] The transforaminal endoscopic approach was initially the most used procedure for performing endoscopic discectomies.[13] However, in 2006, Choi et al.[14] reported for the first time the successful endoscopic removal of a herniated L5 to S1 disc using the interlaminar approach, which is currently one of the most used techniques for percutaneous decompression procedures.

The interlaminar approach is an interesting option for the most caudal levels of the spine, especially L5 to S1, making it possible to avoid the iliac crest and to access more medially based pathologies.[15] The chance of herniated lumbar disc to occur either at L4 to 5 or L5 to S1, in patients between 25 and 55 years old, is approximately 95%.[16] Besides, medial disc herniations (central and subarticular) are more common than lateral ones (foraminal and extra foraminal), corresponding to 79 and 21%, respectively.[7] These are some of the reasons associated with the growing indication of the interlaminar approach.

In a recent meta-analysis, Kim et al.[17] showed the endoscopic lumbar discectomy having better results than the open lumbar discectomy concerning improvement to the visual analogue scale for pain and the Oswestry disability index, resulting in lower hospital stay and operative times.

The radiation dose to which patients and medical professionals who work with the use of fluoroscopy in the intraoperative period are exposed is of great concern, and it is good practice to develop strategies that can minimize the use of such methods. Ahn et al.[18] published a prospective study aiming to determine the radiation dose to which surgeons are exposed during percutaneous endoscopic lumbar discectomy; their results demonstrated that, without proper radiation protection, a surgeon performing 291 endoscopic discectomies annually would be exposed to the maximum allowable radiation dose.

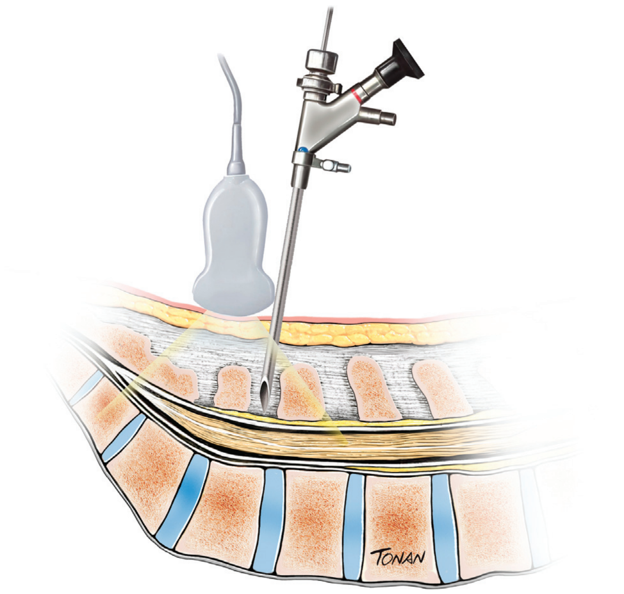


Fig. 10 Ultrasound Guided lumbar interlaminar in plane endoscopic approach.

Ultrasonography has been used either as a complement or a replacement to the use of radioscopy for surgical procedures in several areas. To visualize the lumbosacral spine sonoanatomy, a low frequency (2–5MHz) curvilinear ultrasound probe is used, as the adult lumbar spine's neuraxial structures are situated in a depth of 5 to 7 cm.[19] In the spine, ultrasound allows medical professionals to perform percutaneous procedures such as facet and foraminal infiltrations, enabling the visualization of spinal structures to reduce the use of intraoperative radioscopy with favorable results.[20] While radioscopy-guided procedures are based in the extrapolation of the position of soft tissues, such as muscles, blood vessels, and nerves, based on their anatomical relationship to the bone structures visualized, the ultrasonography makes it possible to visualize bones, muscle layers, nerves, and blood vessels directly, while also eliminating, or at the very least reducing, radiation exposure for both patients and healthcare professionals. Moreover, this method enables the visualization in real time of the needle's insertion, facilitating the use of instruments during the procedures.[21]

This is the first publication in the literature describing the step by step use of ultrasound to guide the in-plane, interlaminar, lumbar endoscopic approach (►**Fig. 10**). The technique is feasible and viable, minimizing the risks of exposure to radiation for the patient and surgical team, as well as making it possible to visualize bone and ligament structures.

Conclusions

The in-plane, interlaminar, endoscopic approach can be successfully performed under ultrasound guidance. Herein, we describe the step by step process to an unprecedented technique of the ultrasound-guided, in-plane, interlaminar, lumbar approach for endoscopic spine surgeries, with a smartphone-adapted endoscope and portable light source. This technique has the potential to minimize the exposure of patients and health care professionals to radiation while using fluoroscopy.

Declaration of Authors' Contribution

Each author contributed individually and significantly to the development of this article entitled "Ultrasound Guided Lumbar Interlaminar In-Plane Endoscopic Approach with Smartphone-Adapted Endoscope and Portable Light Source: Description of a New Surgical Technique." Castro JPS: writing and performing the dissection; Brock RS: data analysis and performing the dissection; Teixeira MJ: review of the article; Figueiredo EG: review of the article and intellectual concept of the article.

Conflict of Interests

The authors have no conflict of interests to declare.

Acknowledgment

We thank Rodrigo Tonan for the talent and dedication to the medical illustration represented in ►**Fig. 10**.

References

1 Parenteau CS, Lau EC, Campbell IC, Courtney A. Prevalence of spine degeneration diagnosis by type, age, gender, and obesity using Medicare data. Sci Rep 2021;11(01):5389. Doi: 10.1038/s41598-021-84724-6

2 Vaishnav AS, Othman YA, Virk SS, Gang CH, Qureshi SA. Current state of minimally invasive spine surgery. J Spine Surg 2019;5 (Suppl 1):S2–S10. Doi: 10.21037/jss.2019.05.02

3 Banczerowski P, Czigléczki G, Papp Z, Veres R, Rappaport HZ, Vajda J. Minimally invasive spine surgery: systematic review. Neurosurg Rev 2015;38(01):11–26, discussion 26. Doi: 10.1007/s10143-014-0565-3

4 Ahn Y. A Historical Review of Endoscopic Spinal Discectomy. World Neurosurg 2021;145:591–596. Doi: 10.1016/j.wneu.2020.08.008

5 Priola SM, Ganau M, Raffa G, Scibilia A, Farrash F, Germanò A A Pilot Study of Percutaneous Interlaminar Endoscopic Lumbar Sequestrectomy: A Modern Strategy to Tackle Medically-Refractory Radiculopathies and Restore Spinal Function. Neurospine 2019;16(01):120–129. Doi: 10.14245/ns.1836210.105

6 Yin J, Jiang Y, Nong L. Transforaminal approach versus interlaminar approach: A meta-analysis of operative complication of percutaneous endoscopic lumbar discectomy. Medicine (Baltimore) 2020;99 (25):e20709. Doi: 10.1097/MD.0000000000020709

7 Lee JH, Lee SH. Clinical and Radiological Characteristics of Lumbosacral Lateral Disc Herniation in Comparison With Those of Medial Disc Herniation. Medicine (Baltimore) 2016;95(07): e2733. Doi: 10.1097/MD.0000000000002733

8 Darrieutort-Laffite C, Hamel O, Glémarec J, Maugars Y, Le Goff B. Ultrasonography of the lumbar spine: sonoanatomy and practical applications. Joint Bone Spine 2014;81(02):130–136. Doi: 10.1016/j.jbspin.2013.10.009

9 Moon ASM, Rajaram Manoharan SR. Endoscopic Spine Surgery: Current State of Art and the Future Perspective. Asian Spine J 2018;12(01):1–2. Doi: 10.4184/asj.2018.12.1.1

10 Forst R, Hausmann B. Nucleoscopy–a new examination technique. Arch Orthop Trauma Surg 1983;101(03):219–221. Doi: 10.1007/BF00436774

11 Kambin P, Nixon JE, Chait A, Schaffer JL. Annular protrusion: pathophysiology and roentgenographic appearance. Spine 1988;13(06):671–675

12 Butler AJ, Alam M, Wiley K, Ghasem A, Rush Iii AJ, Wang JC. Endoscopic Lumbar Surgery: The State of the Art in 2019. Neurospine 2019;16(01):15–23. Doi: 10.14245/ns.1938040.020

13 Ruetten S, Komp M, Godolias G. An extreme lateral access for the surgery of lumbar disc herniations inside the spinal canal using the full-endoscopic uniportal transforaminal approach-technique and prospective results of 463 patients. Spine 2005;30 (22):2570–2578. Doi: 10.1097/01.brs.0000186327.21435.cc

14 Choi G, Lee SH, Raiturker PP, Lee S, Chae YS. Percutaneous endoscopic interlaminar discectomy for intracanalicular disc herniations at L5-S1 using a rigid working channel endoscope. Neurosurgery 2006;58(1, Suppl)ONS59–ONS68, discussion ONS59–ONS68. Doi: 10.1227/01.neu.0000192713.95921.4a

15 Ruetten S, Komp M, Godolias G. A New full-endoscopic technique for the interlaminar operation of lumbar disc herniations using 6-mm endoscopes: prospective 2-year results of 331 patients. Minim Invasive Neurosurg 2006;49(02):80–87. Doi: 10.1055/s-2006-932172

16 Jordan J, Konstantinou K, O'Dowd J. Herniated lumbar disc. Clin Evid 2009;2009:1118

17 Kim M, Lee S, Kim HS, Park S, Shim SY, Lim DJ. A Comparison of Percutaneous Endoscopic Lumbar Discectomy and Open Lumbar Microdiscectomy for Lumbar Disc Herniation in the Korean: A Meta-Analysis. BioMed Res Int 2018;2018:9073460. Doi: 10.1155/2018/9073460

18 Ahn Y, Kim CH, Lee JH, Lee SH, Kim JS. Radiation exposure to the surgeon during percutaneous endoscopic lumbar discectomy: a prospective study. Spine 2013;38(07):617–625. Doi: 10.1097/BRS.0b013e318275ca58

19 Karmakar MK, Li X, Kwok WH, Ho AM, Ngan Kee WD. Sonoanatomy relevant for ultrasound-guided central neuraxial blocks via the paramedian approach in the lumbar region. Br J Radiol 2012; 85(1015):e262–e269. Doi: 10.1259/bjr/93508121

20 Chi M, Chen AS. Ultrasound for Lumbar Spinal Procedures. Phys Med Rehabil Clin N Am 2018;29(01):49–60. Doi: 10.1016/j.pmr.2017.08.005

21 Provenzano DA, Narouze S. Sonographically guided lumbar spine procedures. J Ultrasound Med 2013;32(07):1109–1116. Doi: 10.7863/ultra.32.7.1109

ISSN 0103-5355

Instruções aos Autores

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

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

Os artigos submetidos serão classificados em uma das categorias abaixo:

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

Normas gerais para publicação

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

Normas para submeter os artigos à publicação

Os autores devem enviar os seguintes arquivos:

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

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

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

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

Normas para a estrutura dos artigos

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

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

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

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

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

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

Artigo de revista

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

Capítulo de livro

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

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

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

Tese e dissertação

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

Anais e outras publicações de congressos

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

Artigo disponível em formato eletrônico

International Committee of Medial Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. Writing and editing for biomedical publication. Updated October 2007. Disponível em: http://www.icmje.org. Acessado em: 2008 (Jun 12).

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

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

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

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

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

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

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

Thieme Publishers
Acquisitions Editor
Ana Bluhm, MSc., PhD

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

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

ISSN 0103-5355

Instructions to Authors

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

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

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

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

General standards for publishing

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

Standards for submission

Authors must send the following files:

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

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

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

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

Standards for articles structure

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

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

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

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

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

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

Journal Article

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

Book Chapter

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

Book

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

Theses and dissertations

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

Annals and other congresso publications

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

Available Article in ahead of print

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

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

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

9. Legends and captions: numbered by Arabic numerals according to its citation in the text; edited in double space, using separate files; identify eventual labels present in the figure (arrows, characters, lines etc.); image previously published must have publisher authorization and credits.

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

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

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

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

Editorial Contacts:
Thieme Publishers
Acquisitions Editor
Ana Bluhm, MSc., PhD

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

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