

Analysis of predisposing factors for chronic subdural hematoma recurrence

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SUMMARY

OBJECTIVES: To identify recurrence and its potential predisposing factors in a series of 595 patients with an initial diagnosis of Chronic Subdural Hematoma (CSDH) who underwent surgical treatment at a Reference Hospital of São Paulo.

METHODS: A retrospective descriptive study, in which the medical records of all patients with a CSDH diagnosis submitted to surgical treatment from 2000 to 2014 were analyzed.

RESULTS: The final study population consisted of 500 patients with a diagnosis of CSDH (95 patients with a diagnosis of Cystic Hygroma were excluded), of which 27 patients presented recurrence of the disease (5.4%). There were no statistically significant differences in relapses when cases were stratified by gender, laterality of the first episode or surgical procedure performed in the first episode (trepanning vs. craniotomy). It was possible to demonstrate an age-related protective factor, analyzed as a continuous variable, regarding the recurrence of the CSDH, with a lower rate of recurrence the higher the age.

CONCLUSIONS: The results indicate that, among possible factors associated with recurrence, only age presented a protective factor with statistical significance. The fact that no significant difference between the patients submitted to trepanning or craniotomy was found favors the preferential use of burr-hole surgery as a procedure of choice due to its fast and less complex execution.

KEYWORDS: Hematoma, Subdural, Chronic. Neurosurgery. Intracranial Hemorrhages. Recurrence. Surgical Procedures, Operative.

INTRODUCTION

Chronic subdural hematoma (CSDH) is a common disease characterized by the presence of encapsulated fluid resultant from blood degradation products in the subdural space, covering the surface of the brain. It has a relatively indolent progression^{1,2}. It is known that its main predisposing factors are cerebral atrophy, advanced age, alcohol abuse, and the previous mild traumatic brain injury³. It is a result, directly or indirectly, of trauma that causes lesions in

the parasagittal veins (Mittenzweig) due to the movement of the brain, after the impact, in relation to the membranes that cover it⁴. However, currently, it is clear that there are multiple causes for the expansion of CSDH after an initial traumatic event, forming a complex process of inter-related mechanisms, including inflammation, the formation of membrane, angiogenesis, and fibrinolysis¹.

In neurosurgical routine, CSDH presents itself as

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one of the most common clinical entities⁵. The overall incidence of CSDH varies from 1.72 to 20.6 per 100,000 individuals per year and has increased over the years. Such increase is attributed to population aging and the increased prevalence of use anticoagulant and antiplatelet drugs in a global context.^{2,6-8}. Its rate of recurrence after initial treatment varied between 10% and 39% in previous studies⁹.

The purpose of this study was to identify its recurrence rate and the potential risk factors associated with it in a series of 595 consecutive patients with an initial diagnosis of CSDH submitted to surgical treatment in a tertiary hospital in the state of São Paulo.

METHODS

The research was carried out after approval by the Research Ethics Committee. It is a retrospective descriptive study in which we evaluated the medical records of patients with a CSDH diagnosis submitted to surgical treatment, 2000 to 2014.

Initially, we evaluated 595 medical records of patients with a preoperative diagnosis of CSDH. We excluded from the analysis 95 patients who had a post-surgical diagnosis of subdural hygroma. Then, we identified patients who had a recurrence of the hematoma to identify potential risk factors associated with recurrence.

The data were analyzed using generalized linear models (GLM) adjusted to the binomial probability

distribution. The proportion of patients with recurrence was obtained through the ratio of the number of patients who presented the condition by the number of patients in the study. The bivariate analyzes, i.e., the comparison between the median ages and the proportion of males in the groups were achieved respectively by the Mann-Whitney and chi-square test.

The odds ratio (OR) of recurrence followed by its respective confidence interval of 95% was estimated by the exponentiation of the model coefficient (Beta) for the variable of interest. All analyses were performed using the free statistical software R 3.3.2 (R Development Core Team 2016).

RESULTS

During the period from January 2000 to December 2014, 11,164 patients received neurosurgical treatment in our service. Of these, 500 were diagnosed with CSDH and comprised the sample of this study. The patients included had a median age of 66 years (IQR: 52-77) and were predominantly male (74%, n = 371).

In 410 (82% of 500) The first lesion episode occurred in one of the hemispheres, and bilateral lesions occurred in 90 (18%) of the 500 patients. Trepanning was the first procedure carried out in 478 (95.6 % of 500), while the craniotomy was the procedure adopted in 22 (4.4%) of 500 patients.

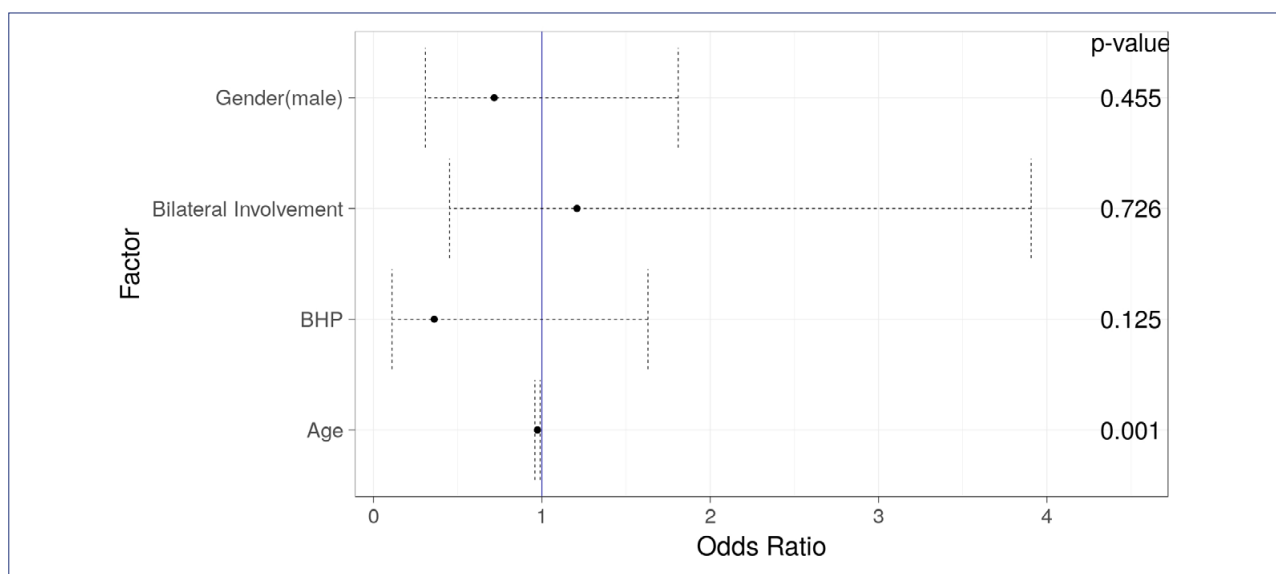


FIGURE 1 - VALUES OF ODDS RATIO OR (POINT); CONFIDENCE INTERVAL (DOTTED LINE), AND THE RESPECTIVE P-VALUES FOR EACH VARIABLE USED IN THE MULTIPLE REGRESSION MODEL. THE HORIZONTAL LINE INDICATES A OR VALUE = 1.

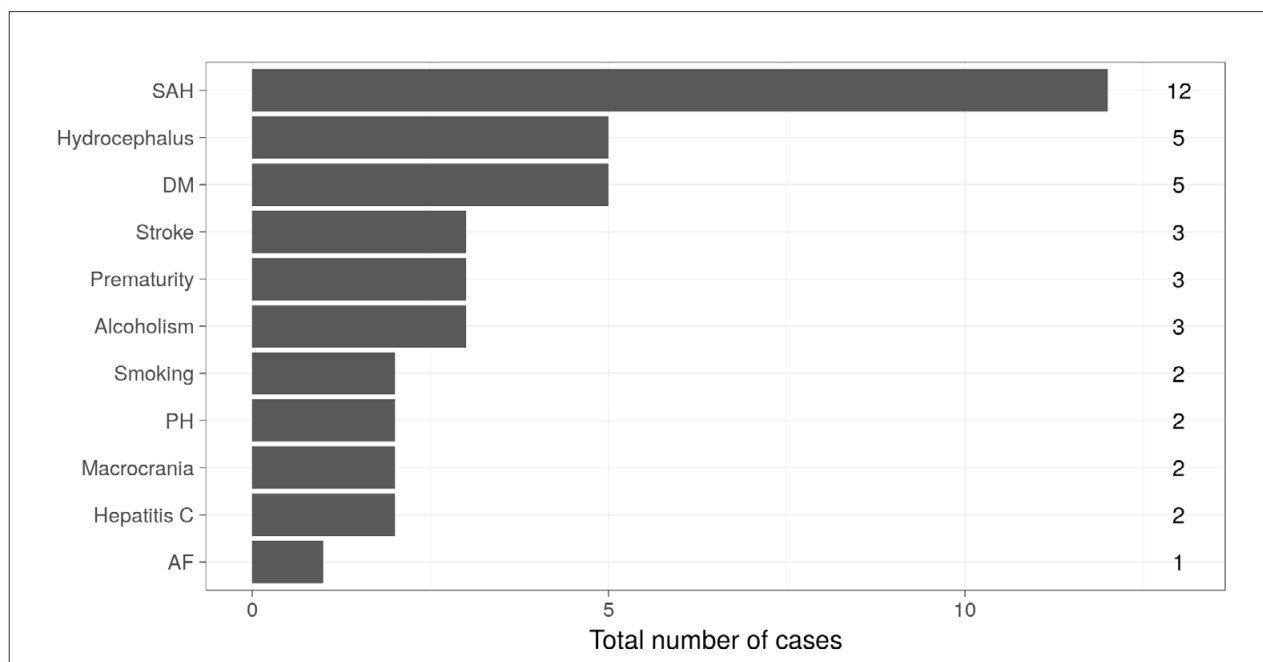


FIGURE 2 - NUMBER OF CASES OF THE MAIN DISORDERS OBSERVED IN PATIENTS WITH LESION RECURRENCE. SAH (SYSTEMIC ARTERIAL HYPERTENSION), DM (DIABETES MELLITUS TYPE II); AF (ATRIAL FIBRILLATION); CVA (CEREBROVASCULAR ACCIDENT); PH (PORTAL HYPERTENSION).

The analysis of the patients' medical records showed that 27 (5.4% of 500) presented recurrence of the hematoma. In general, patients with recurrence of the lesion had a median age of 59 years compared with 66 in the group with no recurrence; the age difference between both groups did not differ significantly from the expected at random ($W=8007$, $p=0.02$). In addition, the patients who presented recurrence were predominantly male, 19 (70.4%) of 27; in the group with no recurrence, this number was 352 (74.4% of 473). However, the difference between the groups was not significant ($\chi^2=0.05$, $df=1$, $p=0.8$).

The model analysis of multivariate logistic regression indicated that the odds ratio (OR) of a recurrence lesion was 1.20 (CI: 0.45-3.90) in patients with a bilateral lesion, although this effect is not significant ($p<0.05$). The procedure adopted did not affect the chances of recurrence, and the OR calculated for trepanning was 0.36 (CI: 0.11-1.63).0.46-1.81). The age, analyzed as a continuous variable, was found to be a protective factor for lesion recurrence, OR: 0.97 (CI: 0.95 and 0.98; $p<0.05$); therefore, the greater the age, the lower the risk of recurrence. On the other hand, we found that sex was not a risk factor (OR: 0.71, CI: 0.30-1.80)(Figure 1).

Of the patients who had a recurrence, 12 (44.4%) had no history of previously known trauma. Six pa-

tients, among the 27 with recurrence (22.2%), had previous use of antithrombotic drugs. The main previous disorders presented by patients with recurrence are shown in Figure 2.

DISCUSSION

The recurrence rate of CSDH described in the medical literature is variable. In the study by Hammer et al.¹⁰, involving 73 operated patients, they observed a recurrence rate of 26%. In contrast, a study carried out in the Bundang Hospital from the Seoul National University, which evaluated 368 cases of CSDH, showed a rate of 8.4%¹¹. In both cases, values higher than those found in the present study.

It was not possible to observe a significant difference in the recurrence rate between the sexes, which is in agreement with other studies^{12,13}.

In a retrospective analysis by Hsieh et al.¹⁴ on the differences between unilateral and bilateral CSDH in 75 patients undergoing neurosurgical treatment between 2011 and 2015, there was no statistically significant difference in the recurrence rate between both groups. Likewise, there was no statistically significant difference between the groups in the present study.

In relation to the comparison between craniot-

omy and trepanning as initial surgical procedures, a multicenter prospective study conducted in the United Kingdom with 787 patients submitted to surgical intervention showed no statistically significant difference in the rates of recurrence among patients undergoing one of these procedures¹⁵, which is compatible with the findings of this study.

The relationship between the increase in age and the incidence of recurrence is not completely clear. Qian et al.¹², in an article published in 2017, assessed 242 patients undergoing trepanning, demonstrating there is a correlation between advanced age and higher rates of recurrence, the opposite of the results presented in this study. However, the series by Mori et al.⁵ that evaluated the results of surgical treatment in 500 consecutive patients showed no correlation between these variables.

In relation to previous traumatic brain injury (TBI), although it is a classic prerogative for the emergence of CSDH, in the present study, 44.4% of patients who relapsed did not have any prior report of TBI. In a study by Souza et al.¹⁶ (2013) that evaluated 778 patients submitted to surgical treatment in Brasil, 60.4% had suffered a previous TBI. However, the study did not focus, specifically, on patients with recurrence, but those with a history of CSDH. Therefore, it was not possible to establish a parallel between previous brain trauma and the rate of recurrence.

Recent meta-analyses have demonstrated that the use of antithrombotic medication, including anticoagulants and antiplatelet drugs, is a risk factor for CSDH recurrence^{7,17}, with statistical significance for the use of antiplatelet drugs and borderline sig-

nificance for the use of anticoagulants⁷. This fact explains the data found in this sample, in which 22.2% of the patients who had recurrence used antithrombotic medication. On the other hand, a study conducted by means of a retrospective analysis of 178 patients admitted for CSDH between 2007 and 2011 showed no influence of drugs that affect hemostasis in recurrence, in addition to having demonstrated that patients in use of these drugs are less aware of a traumatic brain injury preceding the condition¹⁸.

CONCLUSION

CSDH is a condition prevalent in neurosurgical patients. Despite being frequent, there are still gaps in its physiopathology, epidemiology, and therapeutic options. Based on the data collected, we could evaluate the effect of some risk factors among the cases of recurrence.

We found a recurrence rate lower than that found in other studies, which must be evaluated with caution since this is a retrospective study and, therefore, there was no guarantee of follow-up of all patients and their possible recurrences. With regard to gender, laterality of the first episode (unilateral vs. bilateral), and initial procedure (trepanning vs. craniotomy), it was not possible to demonstrate a significant difference in the recurrence rate between the groups. Unlike other studies, the age showed to be a protective factor for recurrence. The fact that no significant difference was evidenced between patients undergoing trepanning or craniotomy favors the routine use of trepanning as the procedure of choice, due to its rapid and less complex implementation.

RESUMO

OBJETIVOS: Identificar a taxa de recidiva e seus potenciais fatores predisponentes em série de 595 pacientes consecutivos com diagnóstico inicial de hematoma subdural crônico (HSDCr) submetidos a tratamento cirúrgico em hospital terciário de São Paulo nos últimos 14 anos.

MÉTODOS: Estudo retrospectivo descritivo, no qual foram analisados os prontuários de todos os pacientes com diagnóstico de HSDCr submetidos a tratamento cirúrgico, no período de 2000 a 2014.

RESULTADOS: A amostra final consistiu em 500 pacientes com diagnóstico de HSDCr — foram excluídos 95 pacientes com diagnóstico de higroma cístico —, dos quais 27 sujeitos apresentaram recidiva do quadro (5,4%). Não foram observadas diferenças estatisticamente significativas nas recidivas quando os casos foram estratificados por gênero, lateralidade do primeiro episódio ou procedimento cirúrgico executado no primeiro episódio (trepanação vs. craniotomia). Foi possível demonstrar um fator protetor relacionado à idade, analisado como variável contínua, no que diz respeito à recidiva do HSDCr, com menor taxa de recidiva com o avançar desta

CONCLUSÕES: Os resultados indicam que, dentre os fatores possivelmente associados à recidiva, apenas a idade se apresentou como fator protetor com significância estatística. O fato de não ser demonstrada diferença significativa entre os pacientes submetidos a tratamentos cirúrgicos por trepanação ou por craniotomia favorece o uso preferencial da trepanação como procedimento de escolha, em virtude de apresentar execução rápida e menos complexa.

PALAVRAS-CHAVE: Hematoma subdural crônico. Neurocirurgia. Hemorragias intracranianas. Recidiva. Procedimentos cirúrgicos operatórios.

REFERENCES

1. Edlmann E, Giorgi-Coll S, Whitfield PC, Carpenter KLC, Hutchinson PJ. Pathophysiology of chronic subdural haematoma: inflammation, angiogenesis and implications for pharmacotherapy. *J Neuroinflammation*. 2017;14(1):108.
2. Yang W, Huang J. Chronic subdural hematoma epidemiology and natural history. *Neurosurg Clin N Am*. 2017;28(2):205-10.
3. Santos RG, Aguiar GB, Veiga JCE. Há indicação de craniotomia para tratamento do hematoma subdural crônico? *J Bras Neurocirurg*. 2015;26(4):289-94.
4. Markwalder TM. Chronic subdural hematomas: a review. *J Neurosurg*. 1981;54(5):637-45.
5. Mori K, Maeda M. Surgical treatment of chronic subdural hematoma in 500 consecutive cases: clinical characteristics, surgical outcome, complications, and recurrence rate. *Neurol Med Chir (Tokyo)*. 2001;41(8):371-81.
6. Baechli H, Nordmann A, Bucher HC, Gratzl O. Demographics and prevalent risk factors of chronic subdural haematoma: results of a large single-center cohort study. *Neurosurg Rev*. 2004;27(4):263-6.
7. Poon MTC, Al-Shahi Salman R. Association between antithrombotic drug use before chronic subdural haematoma and outcome after drainage: a systematic review and meta-analysis. *Neurosurg Rev*. 2018;41(2):439-45.
8. Balsler D, Farooq S, Mehmood T, Reyes M, Samadani U. Actual and projected incidence rates for chronic subdural hematomas in United States Veterans Administration and civilian populations. *J Neurosurg*. 2015;123(5):1209-15.
9. Weigel R, Schmiedek P, Krauss JK. Outcome of contemporary surgery for chronic subdural haematoma: evidence based review. *J Neurol Neurosurg Psychiatry*. 2003;74(7):937-43.
10. Hammer A, Tregubow A, Kerry G, Schrey M, Hammer C, Steiner HH. Predictors for recurrence of chronic subdural hematoma. *Turk Neurosurg*. 2017;27(5):756-62.
11. Kim J, Moon J, Kim T, Ahn S, Hwang G, Bang J, et al. Risk factor analysis for the recurrence of chronic subdural hematoma: a review of 368 consecutive surgical cases. *Korean J Neurotrauma*. 2015;11(2):63-9.
12. Qian Z, Yang D, Sun F, Sun Z. Risk factors for recurrence of chronic subdural hematoma after burr hole surgery: potential protective role of dexamethasone. *Br J Neurosurg*. 2017;31(1):84-8.
13. Stanic M, Pripp AH. A reliable grading system for prediction of chronic subdural hematoma recurrence requiring reoperation after initial burr-hole surgery. *Neurosurgery*. 2017;81(5):752-60.
14. Hsieh CT, Su IC, Hsu SK, Huang CT, Lian FJ, Chang CJ. Chronic subdural hematoma: differences between unilateral and bilateral occurrence. *J Clin Neurosci*. 2016;34:252-8.
15. Brennan PM, Kolias AG, Joannides AJ, Shapely J, Marcus HJ, Gregson BA, et al; British Neurosurgical Trainee Research Collaborative. The management and outcome for patients with chronic subdural hematoma: a prospective, multicenter, observational cohort study in the United Kingdom. *J Neurosurg*. 2017;127(4):732-9.
16. Sousa EB, Brandão LFS, Tavares CB, Borges IBC, Freire Neto NG, Kessler IM. Epidemiological characteristics of 778 patients who underwent surgical drainage of chronic subdural hematomas in Brasília, Brasil. *BMC Surg*. 2013;13:5.
17. Wang Y, Zhou J, Fan C, Wang D, Jiao F, Liu B, et al. Influence of antithrombotic agents on the recurrence of chronic subdural hematomas and the quest about the recommencement of antithrombotic agents: a meta-analysis. *J Clin Neurosci*. 2017;38:79-83.
18. Dziedzic TA, Kunert P, Marchel A. Clinical course and results of surgery for chronic subdural hematomas in patients on drugs affecting hemostasis. *J Korean Neurosurg Soc*. 2017;60(2):232-8.

