Chronic Subdural Haematoma: Systematic Review Highlighting Risk Factors for Recurrent Bleeds

Mohamed Abdelsadg, MBBS, PgDip; Avinash Kumar Kanodia, MD, DM, FRCR; Athar Abbas, MBBS; Asim Sheikh, FRCS

1Department of Neurosurgery, Ninewells Hospital, Dundee, UK
2Department of Radiology, Ninewells Hospital, Dundee, UK
3Department of Neurosurgery, Leeds General Infirmary, Leeds, UK

ABSTRACT

Introduction: Chronic subdural haematoma (CSDH) is one of the commonest forms of intracranial haemorrhage. Surgical drainage of CSDH is a routine operation in the modern neurosurgical practice which has shown to be the most effective way in treating this entity; however, the incidence of recurrence of the haematoma post operatively remains as high as 26.5%. The risk factors for CSDH recurrence remains an area of ongoing research.

Objective: We have conducted a systematic review to evaluate the available literature addressing the risk factors for CSDH recurrence, aiming to minimise or at least identify patients at higher risk of recurrence in order to decrease associated morbidity.

Methods: Ovid via Medline, PubMed, and Google scholar databases were searched for eligible studies, search results were then limited to studies in English language, Humans and studies published within the last 5 years. The included studies were critically appraised using the Critical Appraisal Skills Programme (CASP) tool, and each study has then been ranked using the Harbour and Miller hierarchy of ranking.

Results: Based on available evidence, we classified the risk factors associated with recurrence to patients’, radiological, and surgical factors. Patient factors include history of seizures, trauma, alcoholism, brain atrophy, and presence of CSF shunts, while the role of diabetes in relation to the recurrence is controversial. Radiologically the presence of air in the subdural space post-operatively, the width of the haematoma, and the presence of bilateral CSDHs are associated with increased risk of recurrence. While the predictive value of multiple membranes in the CSDH remains controversial. Surgically, the risk of recurrence was noted to be higher in patients with parietal or occipital compared to those who had frontal burr hole drainage, also placing a subdural drain decreases the chance of recurrence and some evidence showed better outcomes for frontally placed drains. The role of anti-inflammatory agents (including steroids) remains an area of ongoing debate.

Conclusions: Risk factors for CSDH can be divided into patients’, radiological, and surgical factors. We encourage health care providers to minimize if not prevent potentially avoidable factors. Patients with increased risks for recurrence should be identified early by the treating team and when possible should be informed about their higher than usual risk of recurrence. Moreover this review highlights the general lack of a sufficiently powered class I evidence addressing this topic and that further research is required in this topic.

KEY WORDS: Chronic subdural haematoma; Recurrence; Bur hole drainage; Outcome.

ABBREVIATIONS: CSDH: Chronic subdural haematoma; CASP: Critical Appraisal Skills Programme; CT: Computed Tomography; DM: Diabetes Mellitus.

INTRODUCTION

Chronic subdural haematoma (CSDH) is one of the commonest forms of intracranial haemorrhage...
rhage. Surgical drainage of CSDH is a routine operation in the modern neurosurgical practice.\(^1\)\(^2\) The incidence of CSDH is 8-58 per 100,000 in individuals over 65 years of age.\(^3\) However, with continuous rise of life expectancy together with a widening usage of anti-coagulants and anti-platelets medications worldwide, the incidence of this is likely to continue rising.\(^4\) Clinically, as the name suggests, CSDH does not present acutely and it may remain silent for variable periods of times and may present insidiously or with non-specific features. Surgical intervention has been shown to be the most effective way in treating this entity; however, the incidence of recurrence ranges from 9.2-26.5%.\(^1\)\(^2\)\(^5\)-\(^7\) The recurrence can also remain silent with delay in diagnosis and associated morbidity and mortality.

We have conducted this Systematic review to evaluate the available literature addressing the risk factors for CSDH recurrence, aiming to minimise or at least identify patients at higher risk of recurrence in order to decrease associated morbidity. Moreover, this Systematic review will address areas where further research is required to provide robust evidence in the topic, as the implementation of evidence based medicine provides high quality standard medical care at the lowest cost.\(^8\)

A brief analysis of the literature will be conducted using the Critical Appraisal Skills Programme (CASP) tool\(^9\) and then each study will be ranked using the Harbour and Miller\(^10\) hierarchy of ranking. See appendix I.

**Search Strategy**

Table 1 below summarises the search strategy used for the literature search.

| Keywords | The following key words were set to be recognised within article title, abstract, and/or keywords: Subdural Hematoma, chronic subdural haematoma, recurrence, risk factors |
|---------|----------------------------------------------------------------------------------------------------------------------------------|
| Search terms | -Chronic subdural haematoma (OR) subdural haematoma -Recurrence (AND) risk factors -Chronic subdural haematoma (OR) subdural haematoma, (AND) recurrence (AND) risk factors |
| Limitations | The search was limited to the following: English Language. Humans. Between 2012 and current date. |
| Inclusion criteria | The search included patients with chronic subdural haematoma (unilateral or bilateral, surgically or non-surgically managed) The search also included systematic reviews, RCTs, cohort studies, and literature reviews. |
| Exclusion criteria | The search excluded: Solely pregnant and post-partum patients. Neonates and paediatrics. Case reports. Descriptive reports. |
| Databases used | Ovid SP (MedLine/Embase), PubMed, Google Scholar |
| Screening evidenced | Following the search, studies titles and abstracts were screened for relevance, inclusion and exclusion criteria, and non-qualifying articles were then excluded. Reference lists of included papers were reviewed with ‘backward chaining’ employed to include seminal papers. Following limiting the search to the above, 18 studies were screened, and limited by the type of this review only 6 papers will be discussed. |
| Final number | 6 studies will be addressed |

With regards to publication period this was limited to the last 5 years to ensure contemporaneous evidence. Nevertheless, following the search, studies titles and abstracts were screened for relevance, and reference lists of included papers were reviewed with ‘backward chaining’ employed to include seminal papers. Following limiting the search to the above, 18 studies were screened, and limited by the type of this review only 6 papers will be discussed.

**Review of Literature**

CSDH is one of the most commonly encountered conditions in neurosurgery; however, there is no consensus regarding clinical features, correlating factors, or causes of recurrence.\(^12\) Clinically, recurrent bleed can also be challenging and both clinical and imaging factors can be used to make a positive diagnosis. Moreover, presence of a rebleed does not always result in repeat surgery and similarly, significant rebleed may remain clinically
silent and undiagnosed for variable periods of time, potentially with adverse outcomes. It is therefore important that the risk factors associated with rebleeding are identified and such patients are observed and followed-up more closely. Multiple studies have been conducted to identify potential risk factors contributing to the pathogenesis of CSDH and its recurrence with numerous factors reported.12-22

Yamamoto et al13 attempted to determine independent predictors contributing to the recurrence of chronic subdural haematoma (CSDH) in 105 patients who underwent CSDH surgery over 9 years period, with follow-up computed tomography (CT) scanning performed 1 day, 1 week, 1 month, 3 months, and 6 months post-operatively. The criteria used to define recurrence were radiological; however, clinical recurrence (prompted by reappearance of symptoms) warranted earlier scanning. The radiological recurrence was an increase in the hematoma thickness and a change in hematoma density on follow-up CT scans within 3 months post-operatively.19 By using univariate and multivariate analyses to assess the relationships among various variables and CSDH recurrence Yamamoto et al13 reported four independent variables affect the recurrence of CSDH: a positive history of seizures and the width (maximum diameter) of the hematoma were positively associated with increased risk of recurrence, while a positive history of diabetes mellitus (DM) and the multiplicity of hematoma cavities (multiple membrane) on CT scans were both associated with less risk for recurrence. Brief discussion regarding these factors will follow.13 However, the aforementioned study was a retrospective cohort study, and thus is potentially subject to sources of bias and variation. The sample size of the study was limited, and when considering the incidence of the disease the study will be under-powered; hence, further investigation is required to assess the independent predictors revealed in the study. The study was therefore scored 2+ in the Harbour and Miller10 hierarchy of ranking.

Several studies support the role of seizure disorders, alcoholism, cerebrospinal fluid shunts, anticoagulation therapy and coagulopathies.13,23-25 These may be variably associated with head trauma, brain atrophy and increased blood homeostasis. Seizures can be associated to the recurrence of CSDH due to the occasional head injury associated with certain types of seizures, or as a result of coagulopathy due to some anticonvulsants or to their effect on the liver causing disruption of the coagulation cascade.26

While the width of the hematoma is often determined at the level of the maximum thickness of the clot, it has been reported to be associated with the patient age, with the underlying atrophy of the aging brain providing the space for the hematoma to grow and/or recur.27 This may also lead to poor brain re-expansion after the operation. Poor brain re-expansion has been correlated with recurrence in previous reports.10,28

Hyperglycaemia secondary to diabetes mellitus is associated with vascular occlusive disorder secondary to the hyper-viscosity of the blood and the often encountered atheroscler-

With regards to multiplicity of the hematoma cavity conflicting reports were published. While previous studies reported multiplicity to be positively correlated with recurrence of CSDH,2,33 other concluded it is associated with lower rates of recurrence.15 This conflicting evidence could be attributed at least partially to the discrepancy in defining “multiplicity of the haematoma”. In some studies with a positive correlation, the authors identified “multiplicity” as multiple CSDHs,2,33 whereas Yamamoto et al defined multiplicity of hematoma cavities as the involvement of multiple cavities, similar to what has been previously described as trabecular haematoma (Figure 1).5,13

Torihashi et al17 conducted a study to determine independent predictors associated with CSDH recurrence. The results demonstrated that bilateral CSDH was an independent risk factor for the recurrence of CSDH. Although, anti-platelet and anticoagulant therapy had no statistically significant effect on CSDH recurrence, the time interval between the injury and the first operation for patients with anti-platelet and/or anti-coagulant therapy was shorter (29.9 vs. 44.2 days).17 The relative strengths of the above study were the bigger sample size and the fact they used a logistic regression model in performing a multivariate statistical analysis of the recurrence factors. Nonetheless being a retrospective study it scores 2+ in the Harbour and Miller hierarchy of ranking.10 Further studies also supported bilateral CSDH as a risk factor for recurrence (Figure 2).1,8,18 It is though that patients with bilateral CSDH tend to have previous brain atrophy increasing the risks of recurrence as discussed earlier.

Abouzari et al20 conducted a study looking at the role of posture in post-operative patients in the recurrence of surgically managed traumatic CSDH.20 The study concluded that assuming an upright posture soon after burr-hole surgery is associated with an increased incidence of CSDH recurrence. Another study showed similar but statistically non-significant higher recurrence rate of CSDH with early sitting up posture in comparison to 3 days of bed rest.14 The limitations of Abouzari et al study was that they only studied patients with a history of head trauma and excluded those with shunts, seizures, alcohol abuse or use of anticoagulants. While up to 40% of patients with CSDH cannot recall a history of trauma, this very homogenous study group...
in the Abouzari et al\textsuperscript{20} trial brings the generalizability of the trial into question. In the same study recurrence was defined by radiological criteria, and despite the radiological recurrence rate was significantly higher in the patients who assumed a head-elevated position immediately after surgery, these recurrences did not seem to affect the patients’ clinical recovery and only one patient required surgery to drain the recurrent haematoma,\textsuperscript{20} the study was inadequately powered and no details for statistical analysis was included, therefore scored 1 in the Harbour and Miller hierarchy of ranking.\textsuperscript{10}

Another study looking at the “radiological factors” associated with risks of CSDH recurrence, showed increased risk of rebleed in patients with parietal or occipital drainage compared to those who had frontal burr hole drainage. It also showed that patient with residual subdural air on CT scans obtained 7 days post-surgery had a higher recurrence rate than those with no subdural air on the CT scan (Figure 3).\textsuperscript{12} Similar observation was drawn by Nagata et al\textsuperscript{36} showing that the amount of subdural air found postoperatively correlated negatively with the resolution rate of CSDH.

To further explain the effect of different risk factors, different theories have been proposed to explain post-operative recurrence of CSDH. One is the pressure difference theory which emphasises pressure imbalance between the outside and inside of the inner haematoma membrane (subdural space and the subarachnoid/subpial space); that is high pressure in the hematoma cavity and/or low pressure in the subarachnoid space (Figure 4). The earlier situation is indicated by massive subdural air collection, residual SDH and persistent widening of the hematoma cavity (ongoing bleeding in the subdural space). The latter situation is indicated by excessive fluid loss such as dehydration, anemia, excessive cerebrospinal fluid drainage or impact of se-
Moreover, Nakaguchi et al. also reported that patients with a subdural space more than 10 mm wide on CT scans obtained 7 days post-surgery had a higher recurrence rate than those with a space measuring 10 mm or less. The study concluded that post-operative re-accumulation of CSDH can be reduced by placing the tip of the drainage catheter in the frontal convexity and by removing subdural air during or after surgery. This is explainable by the fact that air accumulates in the frontal convexity while the patient is supine immediately after surgery. With the same principle in mind for draining extra fluid and air from the subdural space, Cambridge conducted a randomised trial of using a subdural drain versus no drain following evacuation of CSDH concluded that the use of a drain after burr-hole drainage of chronic subdural haematoma is safe and associated with reduced recurrence and mortality at 6 months. Nakaguchi et al scored 2+ in the Harbour and Miller hierarchy of ranking, while the Cambridge trial scores 1+ as a well conducted randomised controlled trial with low risk of bias. The study concluded that higher levels of inflammatory cytokines were positively correlated with recurrence and re-accumulation of the CSDH. Frati et al advocated for a prolonged post-operative course of anti-inflammatory medicine given as prophylaxis to minimise the risks of CSDH recurrence. Similar rationale and conclusion were reached by another recently published study advocating the use of steroids following the surgical evacuation of CSDH to prevent recurrence. The role of steroids in CSDH remains a controversial topic; nonetheless, an ongoing trial in the UK is currently addressing this and hopefully will put an end to this debate.

Most recently the British Neurosurgical Trainee Research Collaborative (BNTRC) published the largest multicenter, prospective, observational cohort study looking at the management and outcome for patients with chronic subdural...
This has included centres throughout the United Kingdom (UK) and Ireland, and showed the rates of CSDH mortality (2%), symptomatic recurrence (9%), and unfavorable functional outcome (22%) were all acceptable when audited against predefined criteria from the literature.42 However, multivariate analysis demonstrated that failure to insert a drain intraoperatively independently predicted recurrence ($p=0.011$) as well as unfavorable functional outcome ($p=0.048$). Reinforcing previous studies conclusions, the BNTRC group detected statistically significant unfavorable functional outcomes following prescribed post-operative bed rest ($p=0.019$).30,35 It also concluded that Increasing patient age ($p<0.00001$) is associated with unfavorable functional outcome; however, there was no significant difference in relation to recurrence, consolidating previous reports recommendations.13

Unlike previous studies; the BNTRC had clear definition to the recurrence of CSDH, which was clinical recurrence of CSDH symptoms, confirmed radiologically, and requiring surgery within 60 days.42 On the other hand one of the study’s limitations was the lack of long term follow as patients were observed only during their admission course at the neurosurgical unit (NSU). Moreover, the study cohort was skewed to single modality used in 89% of operated cases; hence, making predicting outcome in patients treated with other surgical techniques (e.g., mini craniotomy) an area of ongoing debate.

The study nevertheless was well conducted and scores 2++ in the in the Harbour and Miller hierarchy of ranking (Table 2).

**CONCLUSION**

The review highlights the lack of unified definition for CSDH recurrence as different studies use different methods in labelling recurrence; nonetheless the majority combine clinical features as well as imaging modalities to identify recurrence of CSDH. The available evidence is generally underpowered and more research is required in this topic.

There are different factors contributing to the recurrence of CSDH, which can be divided into patient factors, radiological factors, surgical/technical factors, and post-operative factors.

Patient factors include history of seizures, trauma, alcoholism, brain atrophy, and presence of CSF shunts, while there is conflicting evidence regarding the role of DM in relation to recurrence risk of CSDH.

Radiological factors include presence of air in the subdural space in the post-operative scan, width of the haematoma, width of the subdural space and presence of bilateral CSDH. The predictive value of presence of multiple membranes in the

---

**Table 2: Summary of the Studies Discussed in this Paper, the Aim of Each, Concluded Factors for CSDH Recurrence, Strengths, Weaknesses, and Score in the Harbour and Miller hierarchy of ranking.**

| Article | Aim of study                                                                 | Factors associated with increased risk for CSDH recurrence | Strengths                                                                 | Weaknesses                                                                 | Score |
|---------|------------------------------------------------------------------------------|----------------------------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|-------|
| Yamamoto et al20 | To determine independent predictors contributing to the recurrence of CSDH | Width of the hematoma, Multilocularity of hematoma cavities, Seizures, Negative history of DM | Clear definition for recurrence, Robust statistical analysis | Retrospective, Small sample size | 2+    |
| Torihashi et al35 | To determine independent predictors contributing to the recurrence of CSDH | Bilateral CSDH, Larger sample size | Randomized double blind controlled trial | Retrospective | 2++   |
| Abouzari et al27 | To evaluate the relationship between recurrence rate of CSDH and patient posture postoperatively | Assuming an upright posture soon after burr-hole surgery | Prospective study, Over 9 years, Long term follow-up | Single center, Small sample size, Recurrence defined radiologically with no clinical correlation | 1- |
| Nakaguchi et al21 | To determine features of CSDHs recurrence rate on the basis of the natural history of these lesions and their intracranial extension | Subdural space more than 10 mm wide on CT 7 days post-surgery, Subdural drain not placed on the frontal convexity, Presence of subdural air, Intra or post operatively, Cranial base type of CSDHs was high | Prospective study, Over 9 years, Long term follow-up | Single center, Small sample size, Recurrence defined radiologically with no clinical correlation | 2+    |
| Frati et al22 | To determine role of local inflammation in the pathogenesis and recurrence of CSDH | Higher levels of inflammatory cytokines | Prospective study | Under powered, Generalizability | 2+    |
| Brennan et al42 | To examine the management and outcome for patients with CSDH across the UK | Failure to insert a drain intraoperatively | Multicenter, Prospective, Clear definition for recurrence | Lack of long term follow-up, Skewed to single surgical drainage technique | 2++   |

CSDH: Chronic subdural haematoma, CT: Computed Tomography.
CSDH remains controversial.

With regards to the surgical factors, there are different techniques adopted, nonetheless it was found that burr hole craniotomy is the most adopted method, and there is lack of evidence testing outcomes of other surgical techniques. The risk of CSDH recurrence is higher in patients with parietal or occipital drainage compared to those who had frontal burr hole drainage. Placing a subdural drain was noted to decrease the chance of recurrence and some evidence showed better outcomes for frontally placed drains.

Post-operative patient positioning seems to affect the recurrence risk, with the current evidence promoting avoidance of early sitting up of patients with CSDH. It is clearly noted that more studies are necessary to address this topic.

The role of anti-inflammatory agents (including steroids) remains an area of hot debate. There is a need of well conducted adequately powered multicentre randomised trial(s) to increase our understanding and deliver more robust recommendation regarding the topic.

Finally, we have briefly described the factors thought to be associated with increased risk of recurrent CSDH and highlighted areas of ongoing debate.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

REFERENCES

1. Asano Y, Hasuo M, Takahashi I, Shimosawa S. Recurrent cases of chronic subdural hematoma--its clinical review and serial CT findings. No to Shinkei. 1992; 44(9): 827-831.

2. El-Kadi H, Miele VJ, Kaufman HH. Prognosis of chronic subdural hematomas. Neurosurg Clin N Am. 2000; 11: 553-556.

3. Ducruet AF, Grobelny BT, Zacharia BE, et al. The surgical management of chronic subdural hematoma. Neurosurg Rev. 2012; 35: 155-169. doi: 10.1007/s10143-011-0349-y

4. Aspegren OP, Astrand R, Lundgren MI, Romner B. Anticoagulation therapy a risk factor for the development of chronic subdural hematoma. Clin Neurol Neurosurg. 2013; 115: 981-984. doi: 10.1016/j.clineuro.2012.10.008

5. Nakaguchi H, Tanishima T, Yoshimasu N. Factors in the natural history of chronic subdural hematomas that influence their postoperative recurrence. J Neurosurg. 2001; 95: 256-262.

6. Wakai S, Hashimoto K, Watanabe N, Inoh S, Ochiai C, Nagai M. Efficacy of closed-system drainage in treating chronic subdural hematoma: A prospective comparative study. Neurosurgery. 1990; 26: 771-773.

7. Zumkeller M, Höllerhage HG, Dietz H. Treatment outcome in patients with chronic subdural hematoma with reference to age and concurrent internal diseases [In German]. Wien Med Wochenschr. 1997; 147: 55-62.

8. Lewis S, Orland B. The importance and impact of evidence-based medicine. J Manag Care Pharm. 2004: 10(5 Suppl A): 3-5. doi: 10.18553/jmcp.2004.10.S5-A.S3

9. Critical Appraisal Skills Programme (CASP). 2010 Tools. [Online]. Web site. http://www.casp-uk.net/#checklists/cb36. Accessed April 19, 2017.

10. Harbour R, Miller J. Education and debate: A new system for grading recommendation in evidence based guidelines. BMJ. 2001; 323: 334-336.

11. Egger M, Smith GD. Bias in location and selection of studies. BMJ. 1998; 316(7124): 61-66.

12. Nakaguchi H, Tanishima T, Yoshimasu N. Relationship between drainage catheter location and postoperative recurrence of chronic subdural hematoma after burr-hole irrigation and closed-system drainage. J Neurosurg. 2000; 93(5): 791-795. doi: 10.3171/jns.2000.93.5.0791

13. Yamamoto H, Hirashima Y, Hamada H, Hayashi N, Origasa H, Endo S. Independent predictors of recurrence of chronic subdural hematoma: Results of multivariate analysis performed using a logistic regression model. J Neurosurg. 2003; 98(6): 1217-1221. doi: 10.3171/jns.2003.98.6.1217

14. Foelholm R, Waltimo O. Epidemiology of chronic subdural haematoma. Acta Neurochir. 1975; 32: 247-250. doi: 10.1007/BF01405457

15. Fogelholm R, Heiskanen O, Waltimo O. Chronic subdural hematoma in adults. Influence of patient’s age on symptoms, signs, and thickness of hematoma. J Neurosurg. 1975; 42: 43-46. doi: 10.3171/jns.1975.42.1.0043

16. Fukuhara T, Gotoh M, Asari S, et al. The relationship between brain surface elastance and brain reexpansion after evacuation of chronic subdural hematoma. Surg Neurol. 1996; 45: 570-574. doi: 10.1016/0090-3019(95)00471-8

17. Torihashi K, Sadamasu N, Yoshida K, Narumi O, Chin M, Yamagata S. Independent predictors for recurrence of chronic subdural hematoma: A review of 343 consecutive surgical cases. Neurosurgery. 2008; 63(6): 1125-1129. doi: 10.1227/01. NEU.0000335782.60059.17

18. Probst C. Peritoneal drainage of chronic subdural hematomas in older patients. J Neurosurg. 1988; 68: 908-911. doi:
19. Robinson RG. Chronic subdural hematoma: Surgical management in 133 patients. J Neurosurg. 1984; 61: 263-268. doi: 10.3171/jns.1984.61.2.0263

20. Abouzari M, Rashidi A, Rezaei J, et al. The role of postoperative patient posture in the recurrence of traumatic chronic subdural hematoma after burr hole surgery. Neurosurgery 2007; 61(4): 794-797. doi: 10.1227/01.NEU.0000298908.94129.67

21. Frati A, Salvati M, Mainiero F, et al. Inflammation markers and risk factors for recurrence in 35 patients with a posttraumatic chronic subdural hematoma: A prospective study. J Neurosurg. 2004. 100(1) 24-32. doi: 10.3171/jns.2004.100.1.0024

22. 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): 84-88. doi: 10.1080/02688697.2016.1260686

23. Nomura S, Kashiwagi S, Fujisawa H, et al. Characterization of local hyperfibrinolysis in chronic subdural haematomas by SD-SPAGE and immunoblot. J Neurosurg. 1994; 81: 910-913. doi: 10.1017/s00903019.94.00910

24. Oishi M, Toyama M, Tamatani S, et al. Clinical factors of recurrent chronic subdural hematoma. Neurol Med Chir. 2001; 41: 382-386. doi: 10.2176/nmc.41.382

25. Park CK, Choi KH, Kim MC, et al. Spontaneous evolution of posttraumatic subdural hygroma into chronic subdural haematoma. Acta Neurochir. 1994; 127: 41-47. doi: 10.1007/BF01808545

26. So CC, Wong KF. Valproate-associated dysmyelopoiesis in elderly patients. Am J Clin Pathol. 2002; 118: 225-228. doi: 10.1309/4TEF-LVGX-WEQ9-R8W8

27. Foelholm R, Waltimo O. Epidemiology of chronic subdural haematoma. Acta Neurochir. 1975; 32: 247-250. doi: 10.1007/BF01405457

28. Morii 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: 371-381. doi: 10.2176/nmc.41.371

29. Kernan WN, Inzucchi SE, Viscoli CM, et al. Insulin resistance and risk for stroke. Neurology. 2002; 59: 809-815. doi: 10.1212/WNL.59.6.809

30. Suzuki J, Takaku A. Nonsurgical treatment of chronic subdural hematoma. J Neurosurg. 1970; 33(5): 548-553. doi: 10.3171/jns.1970.33.5.0548

31. Ito H, Komai T, Yamamoto S. Fibrinolytic enzyme in the lining walls of chronic subdural hematoma. J Neurosurg. 1978; 48: 197-200. doi: 10.3171/jns.1978.48.2.0197

32. Tokmak M, Iplikcioglu AC, Bek S, Gökdemar CA, Erdal M. The role of exudation in chronic subdural hematomas. J Neurosurg. 2007; 107: 290-295. doi: 10.1037/JNS-07.08.0290

33. Tanikawa M, Mase M, Yamada K, et al. Surgical treatment of chronic subdural hematoma based on intrahematomatal membrane structure on MRI. Acta Neurochir. 2001; 143: 613-619. doi: 10.1007/s007010170067

34. Nakajima H, Yasui T, Nishikawa M, Kishi H, Kan M. The role of postoperative patient posture in the recurrence of chronic subdural hematoma: A prospective randomized trial. Surg Neurol. 2002; 58: 385-387. doi: 10.1016/S0080-9039(02)00921-7

35. Markwalder TM. Chronic subdural hematoma: A review. J Neurosurg. 1981; 54: 637-645. doi: 10.3171/jns.1981.54.5.0637

36. Nagata K, Asano T, Basugi N, et al. Studies on the operative factors affecting the reduction of chronic subdural hematoma, with special reference to the residual air in the hematoma cavity. No Shinkei Geka. 1989;17: 15-20.

37. Smyth H, Livingston K. Ventricular infusion in the operative management of subdural hematoma. In: Morley T, ed. Current Controversies in Neurosurgery. Philadelphia, USA: WB Saunders; 1976: 566-571.

38. Santarius T, Kirkpatrick PJ, Ganesan D et al. Use of drains versus no drains after burr-hole evacuation of chronic subdural haematoma: A randomised controlled trial. The Lancet. 2009; 374(9695): 1067-1073. doi: 10.1016/S0140-6736(09)61115-6

39. Virchow R. Das Hamaton der dura mater [In German]. Verch Phys Med Ges Wurzburg. 1857; 7: 134-142

40. Markwalder TM, Steinsiepe KF, Rohner M, et al. The course of chronic subdural haematoma with special reference to the residual air in the hematoma cavity. Acta Neurochir. 1978; 48: 197-200. doi: 10.3171/jns.1978.48.2.0197

41. DEXamethasone in Chronic SubDural Haematomat (DexCSDH trial). A randomised, double blind, placebo-controlled trial of a two-week course of dexamethasone for adult patients with a symptomatic chronic subdural haematoma. Web site. http://www.dexcsdh.org/. Accessed Appril 02, 2017.

42. Brennan PM, Kolias AG, Joannides AJ, et al. The management and outcome for patients with chronic subdural hematoma: A prospective, multicenter, observational cohort study in the United Kingdom. J Neurosurg. 2017: 1-8. Ahead of print. doi: 10.3171/2016.8.JNS16134
Appendix I

Harbour and Miller hierarchy of evidence

1++ High quality meta analyses, systematic reviews of RCTs or RCTs with a very low risk of bias.
1+ Well conducted meta analyses, systematic reviews of RCTs, or RCTs with a low risk of bias.
1- Meta analyses, systematic reviews of RCTs, or RCTs with a high risk of bias.
2++ High quality systematic reviews of case-control or cohort studies. High quality case-control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is casual.
2+ Well conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is casual.
2- Case-control or cohort studies with a high risk of confounding, bias, chance and a significant risk that the relationship is not casual.
3 Non-analytic studies, e.g., case reports, case series.
4 Expert opinion.