

## Systematic Review

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

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### 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 haemor-

rhage. Surgical drainage of CSDH is a routine operation in the modern neurosurgical practice.<sup>1,2</sup> The incidence of CSDH is 8-58 per 100,000 in individuals over 65 years of age.<sup>3</sup> 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.<sup>4</sup> 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%.<sup>1,2,5-7</sup> 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.<sup>8</sup>

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

### Search Strategy

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

Ovid *via* Medline, PubMed and google scholar search

resulted in 33 publications, which was then limited to studies in English language, Humans and the duration between 2012 and current date this limited the publications to 18 papers.

Following is a justification for the used search limitation:

English Language is an international language for healthcare, the majority of the top journals with high impact factors are in English, and is the most widely learned second language. Nevertheless, we are aware that by limiting the search to publications in a single language this could potentially affect the generalisability and possibly results in English language, selection, publication, and citation biases.<sup>11</sup> The search was also limited to humans, given the limited role for the animal derived data in this topic.

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.<sup>12</sup> 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

Table 1: Search Strategy.	
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 gather pertinent papers for consideration.
Final number	6 studies will be addressed

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.<sup>12-22</sup>

Yamamoto et al<sup>13</sup> attempted to determine independent predictors contributing to the recurrence of chronic subdural hematoma (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 re appearance 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.<sup>13</sup> By using univariate and multivariate analyses to assess the relationships among various variables and CSDH recurrence Yamamoto et al<sup>13</sup> 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.<sup>13</sup> 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 Miller<sup>10</sup> hierarchy of ranking.

Several studies support the role of seizure disorders, alcoholism, cerebrospinal fluid shunts, anticoagulation therapy and coagulopathies.<sup>13,23-25</sup> These may be variably associated with head trauma, brain atrophy and decreased 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.<sup>26</sup>

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.<sup>27</sup> This may also lead to poor brain re-expansion after the operation. Poor brain re-expansion has been correlated with recurrence in previous reports.<sup>19,28</sup>

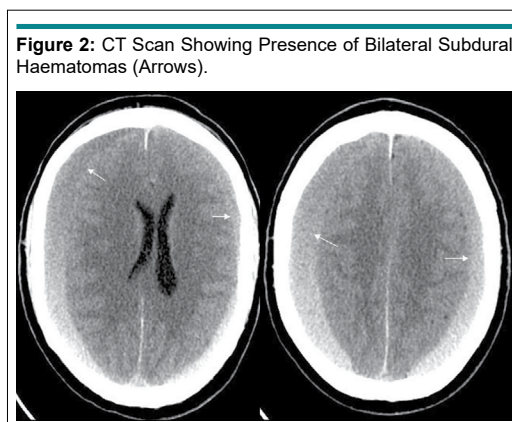
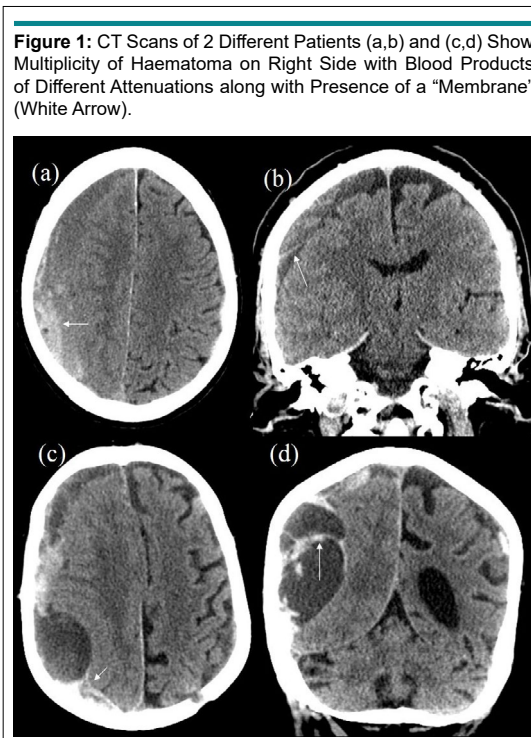
Hyperglycaemia secondary to diabetes mellitus is associated with vascular occlusive disorder secondary to the hyper-viscosity of the blood and the often encountered atherosclero-

sis.<sup>29</sup> Yamamoto et al<sup>13</sup> suggested that DM may play a role in decreasing the re-bleeding tendency of CSDH, since patients with DM has a high osmotic pressure and increased platelet aggregation.<sup>29</sup> This theory could be supported by the findings of previous study which reported that osmotherapy performed using 20% mannitol is effective in stopping repeated bleeding of a CSDH.<sup>30</sup> On the other hand capillary vasculopathy including haemorrhage (e.g., retinal haemorrhage) is one of the major complications in diabetic patients, and the exudation from the capillaries in the membrane of CSDH plays an important role in its enlargement.<sup>31,32</sup> Moreover, similar study showed increased but non-significant risk for recurrence in patients with DM, it was also found that patients with bilateral CSDH tend to have DM.<sup>17</sup>

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,<sup>2,33</sup> other concluded it is associated with lower rates of recurrence.<sup>13</sup> 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,<sup>2,33</sup> 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).<sup>5,13</sup>

Torihashi et al<sup>17</sup> 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).<sup>17</sup> 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.<sup>10</sup> Further studies also supported bilateral CSDH as a risk factor for recurrence (Figure 2).<sup>18,19</sup> It is though that patients with bilateral CSDH tend to have previous brain atrophy increasing the risks of recurrence as discussed earlier.

Abouzari et al<sup>20</sup> conducted a study looking at the role of posture in post-operative patients in the recurrence of surgically managed traumatic CSDH.<sup>20</sup> 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.<sup>34</sup> The limitations of Abouzari et al<sup>20</sup> 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,<sup>35</sup> this very homogenous study group



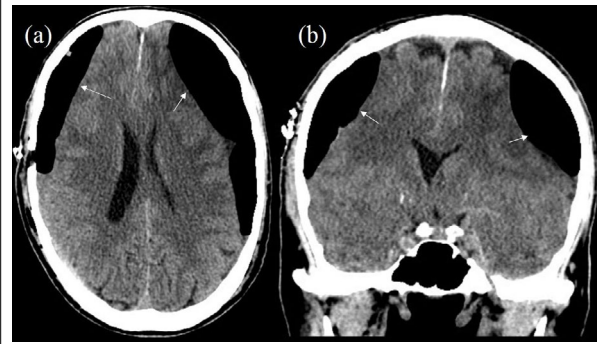
in the Abouzari et al<sup>20</sup> trial brings the generalizability of the trial into question. In the same study recurrence was defined by radiological criteria, and despite the radiological recurrence rate was significantly higher in the patients who assumed a head-elevated position immediately after surgery, these recurrences did not seem to affect the patients' clinical recovery and only one patient required surgery to drain the recurrent haematoma,<sup>20</sup> the study was inadequately powered and no details for statistical analysis was included, therefore scored 1 in the Harbour and Miller hierarchy of ranking.<sup>10</sup>

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

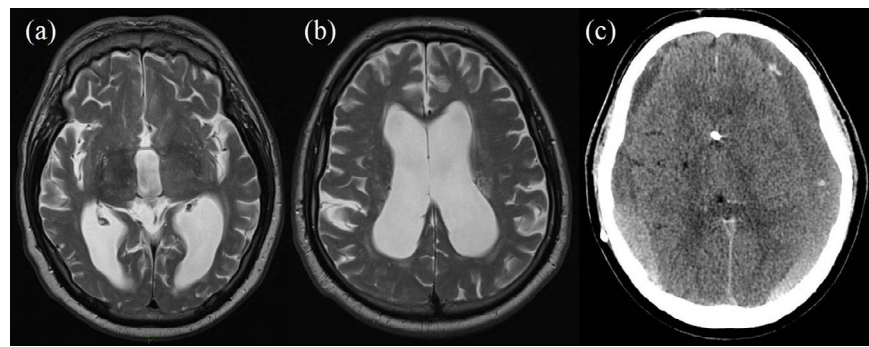
no subdural air on the CT scan (Figure 3).<sup>12</sup> Similar observation was drawn by Nagata et al<sup>36</sup> showing that the amount of subdural air found postoperatively correlated negatively with the resolution rate of CSDH.

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-

**Figure 3:** CT Scans Showing Significant Amount of Air in the Subdural Cavities on both Sides Post Drainage (White Arrows).



**Figure 4:** MRI Scan (a, b) Shows Dilated Ventricular System in a Patient Clinically Presenting with Normal Pressure Hydrocephalus. Post Drainage, CT (c) Shows Bilateral Subdural Haematomas with a Decompressed Ventricular System.



vere brain atrophy.<sup>35,37</sup> Moreover, Nakaguchi et al<sup>12</sup> 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.<sup>12</sup> 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.<sup>38</sup> Nakaguchi et al scored 2+ in the 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.<sup>10,38</sup>

Another theory is the inflammatory theory, first proposed In 1857 by Virchow who described CSDH as a dural inflammatory disease and called it “pachymeningitis hemorrhagica interna.” He was the first to stress the importance of inflammation for the onset and development of CSDH.<sup>39</sup> Later on several studies demonstrated that CSDH is the result of a local inflam-

matory reaction of the dura to an injurious stimulus.<sup>35,40</sup> Frati et al<sup>21</sup> conducted a prospective study over 2 years period to determine role of local inflammation in the pathogenesis and post-operative recurrence of chronic subdural hematoma (CSDH).<sup>21</sup> The study - although significantly under powered - has included only patients who can clearly recall history of head trauma, and showed evidence of an inflammatory process within the dural border cell layer, this has a clear impact on the generalisability of the trial, scoring 2+ in the Harbour and Miller hierarchy of ranking.<sup>10</sup> 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.<sup>22</sup> 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.<sup>41</sup>

Most recently the British Neurosurgical Trainee Research Collaborative (BNTRC) published the largest multi-center, prospective, observational cohort study looking at the management and outcome for patients with chronic subdural

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.<sup>10</sup>

Article	Aim of study	Factors associated with increased risk for CSDH recurrence	Strengths	Weaknesses	Score
Yamamoto et al <sup>2</sup>	To determine independent predictors contributing to the recurrence of CSDH	- Width of the hematoma. - Multiplicity of hematoma cavities. - Seizures - Negative history of DM	- Clear definition for recurrence - Robust statistical analysis	- Retrospective - Small sample size	2+
Torihashi et al <sup>21</sup>	To determine independent predictors contributing to the recurrence of CSDH	- Bilateral CSDH	- Larger sample size - Robust statistical analysis.	- Retrospective	2++
Abouzari et al <sup>27</sup>	To evaluate the relationship between recurrence rate of CSDH and patient posture postoperatively	- Assuming an upright posture soon after burr-hole surgery	- Randomized double blinded controlled trial	- Generalizability - Underpowered - Radiologically defined recurrence with very limited clinical sequel	1-
Nakaguchi et al <sup>8</sup>	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+
Fрати et al <sup>34</sup>	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 al <sup>42</sup>	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.

haematomas.<sup>42</sup> 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.<sup>42</sup> 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 ( $p=0.019$ ).<sup>20,35</sup> 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.<sup>13</sup>

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.<sup>42</sup> 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 surgical drainage technique (burr hole drainage) which was the 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

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.

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## Appendix I

### Harbour and Miller hierarchy of evidence<sup>10</sup>

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.