



## Risk Factors of Chronic Subdural Hematoma Recurrence: A Systematic Review

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### Abstract

**Background:** Although various factors have been proposed in connection with the recurrence of chronic subdural hematoma (cSDH), the results obtained in previous studies have not been consistent. This study was conducted to describe the risk factors for cSDH recurrence, drawing upon the current literature, and to provide an integrative framework that links these factors with underlying biological mechanisms.

**Methods:** In December 2024, a systematic literature search was performed using the Scopus, Web of Science, PubMed, and Embase electronic databases. The retrieved records were screened against eligibility criteria and selected in 2 stages. The Newcastle-Ottawa Scale (NOS) was utilized for bias assessment, and the PRISMA (Preferred Reporting Items for Systematic Reviews) checklist was employed to assess the methodological rigor and reliability of the selected studies and their findings.

**Results:** After applying the inclusion and exclusion criteria, 61 studies were retained for the systematic review. The principal risk factors associated with the recurrence of cSDH were elucidated and correlated with underlying pathophysiological processes. Lower Glasgow Coma Scale (GCS) scores and elevated postoperative neutrophil counts indicate increased inflammation. The use of antiplatelet and anticoagulant agents reflects coagulation dysfunction, which raises the risk of rebleeding. Additional factors such as male sex, older age, larger hematoma size, and shorter drainage duration relate to anatomical and clinical vulnerability. Radiological signs, such as high hematoma density and midline shift, support the role of structural brain changes. Comorbidities, including diabetes and hypertension, exacerbate vascular fragility, increasing recurrence risk. Early detection, effective postoperative drainage, and higher serum HDL levels contribute to a reduced risk of recurrence.

**Conclusion:** cSDH recurrence results from the complex interplay of biological processes, including inflammation, coagulation dysfunction, and structural brain changes, with clinical risk factors. Recognizing and targeting these integrated pathways is crucial for improving prevention and management strategies.

**Keywords:** Prevalence, Risk factors, Recurrence, Subdural Hematoma

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### ↑What is “already known” in this topic:

Previous studies have identified advanced age, male sex, anticoagulant/antiplatelet use, larger hematoma volume, and specific radiological findings as risk factors for chronic subdural hematoma recurrence. However, results regarding the significance and modifiability of these factors have been inconsistent, and the role of perioperative management and newer biomarkers remains unclear.

### →What this article adds:

This systematic review of 61 studies, involving over 29,000 patients, confirms known risk factors and identifies novel predictors, including postoperative neutrophils and blood groups. It integrates clinical, hematological, and radiological variables into a pathophysiological model explaining inflammation, coagulation, and brain changes in cSDH recurrence, guiding personalized management.

## Introduction

Subdural hematoma occurs when blood collects under the dura mater, which is one of the protective layers of brain tissue under the skull (1). In the context of cSDH, this often arises specifically when there is ample space between the dura mater and the brain, as commonly seen in the aging brain (due to atrophy). This space increases the susceptibility of the bridging veins, which drain from the surface of the brain to the dura sinuses, to rupture, often following even minor trauma (1-3).

cSDH is defined as an encapsulated collection of mostly or entirely liquefied old blood located between the dura and arachnoid mater. It predominantly develops in older people after minor injuries, frequently without underlying brain parenchymal damage, and usually takes weeks to months to become clinically apparent. The peak incidence is in individuals aged 60-79 years (4). This review focuses exclusively on cSDH and its risk factors.

The development of cSDH is strongly associated with specific exposures and conditions. Head injuries, particularly those related to falls, motor vehicle accidents, or other trauma, are the most common initiating events (3). Furthermore, several significant patient factors increase the risk of developing cSDH: the use of antiplatelet agents (including aspirin and ibuprofen), anticoagulants, underlying coagulopathies, and advanced age itself (5). Critically, advanced age is not only a demographic association but also a key biological risk factor, primarily through its association with brain atrophy, creating the vulnerable subdural space (1, 5).

The incidence of cSDH rises sharply with age, reaching approximately 20.6 per 100,000 patients in the 60-79-year age group (4). A significant complication of cSDH management is recurrence, defined as the return of symptoms after initial recovery or improvement (6), is a significant concern in cSDH management, often necessitating reoperation.

The high recurrence rate in cSDH is fundamentally driven by its unique pathophysiology. Following initial bleeding from fragile bridging veins (1, 7), an inflammatory cascade is triggered, leading to the formation of outer and inner neomembranes encapsulating the hematoma (8, 9). These membranes are highly vascularized by fragile, leaky capillaries prone to recurrent hemorrhage (10, 11). Concurrently, local hyperfibrinolysis within the hematoma cavity disrupts clot stabilization and promotes ongoing ooze (12). This pathophysiological triad—(1) persistent membrane fragility and neovascularization (8, 2) ongoing local hyperfibrinolysis (13); and (3) impaired re-expansion of the atrophic brain, creating a persistent subdural space (7, 14)—forms the core theoretical framework for understanding recurrence risk. Factors such as advanced age (exacerbating brain atrophy and membrane fragility), coagulopathy/anticoagulation (impeding hemostasis), large hematoma volume (sustaining the inflammatory environment), and inadequate post-operative brain re-expansion (maintaining the dead space) are thus hypothesized to increase recurrence risk by directly interacting

with these mechanisms (5, 15).

Despite numerous studies investigating the recurrence of cSDH, the reported risk factors and recurrence rates remain inconsistent across the literature. Many previous investigations have focused on specific populations or limited clinical variables, resulting in heterogeneous findings and a lack of consensus regarding the most significant predictors of recurrence (16-18).

Although multiple clinical, hematological, and radiological risk factors have been identified, a comprehensive and integrated pathophysiological model explaining how these risk factors mechanistically contribute to recurrence remains lacking. Understanding the interplay between inflammation, coagulation dysfunction, and structural brain changes alongside patient-specific variables is essential for developing targeted therapeutic strategies and improving patient outcomes. This systematic review aims to synthesize existing evidence to construct such an integrative model, linking identified risk variables with underlying biological mechanisms of cSDH recurrence.

## Methods

### Study Design

This systematic review was conducted in adherence to the PRISMA 2020 guidelines (19). The review aimed to identify and synthesize the risk factors associated with the recurrence of cSDH. The study protocol included a comprehensive literature search, predefined eligibility criteria, and standardized data extraction and quality assessment procedures to ensure methodological rigor and transparent reporting.

### Search Strategy

A systematic literature search was conducted using 4 major electronic databases: Embase, PubMed, Scopus, and Web of Science, to locate all potentially relevant English-language records published through December 2024. A combination of relevant keywords was used to construct the search queries in different databases, a sample PubMed query is provided below: (("Hematoma, Subdural"[mesh] OR subdural hematoma[tiab] OR Subdural Hemorrhage[tiab] OR subdural bleeding[tiab]) AND ("recurrence"[mesh] OR recurrence[tiab] OR Recrudescence[tiab] OR recurrent[tiab] OR relapse[tiab]) AND ("risk factors"[mesh] OR risk factor[tiab] OR risk score[tiab] OR relative risk[tiab])).

### Inclusion and Exclusion Criteria

The inclusion criteria for study selection were defined as follows. Inclusion was restricted to (1) original research articles published in English, and (2) investigations specifically examining risk factors associated with cSDH recurrence. The exclusion criteria included (1) nonoriginal publications, including case reports, editorials, letters, review articles, meta-analyses, and conference abstracts; (2) animal or in vitro studies; (3) manuscripts for which

the full text was unavailable; and (4) articles published in languages other than English.

### Study Selection

During the preliminary search phase, 434 records were identified in Scopus, 274 in Embase, 179 in PubMed, and 2 in Web of Science, culminating in a total of 889 retrieved publications. The low number of studies retrieved from the Web of Science database is likely due to differences in journal coverage and indexing practices compared with other databases such as PubMed, Scopus, and Embase. Despite using a comprehensive and consistent search strategy across all databases, many relevant studies on cSDH recurrence and its risk factors are not indexed in Web of Science. To mitigate the risk of omitting eligible studies, all identified records underwent a comprehensive deduplication and cross-database verification process to ensure completeness. The screening procedure followed a 2-phase approach. Initially, titles and abstracts were independently assessed by two authors for relevance based on the predefined eligibility criteria. Studies deemed irrelevant at this stage were excluded. The remaining publications subsequently underwent a full-text appraisal, again conducted independently by the same authors. To ensure

data integrity, the accuracy of all extracted data was verified by an independent third author. Following this rigorous selection process, 61 studies met the inclusion criteria and were incorporated into the final systematic review (Figure 1).

### Data Synthesis and Analysis

Due to significant methodological and clinical heterogeneity across the included studies (e.g., variations in recurrence definitions, surgical techniques, and risk factor measurements), a quantitative meta-analysis was not feasible. A structured qualitative synthesis was performed as follows:

Studies were systematically grouped by risk factor category: demographic, clinical, radiological, surgical, medication-related, and comorbid disease. Key findings within each category were summarized descriptively. Risk factors were mapped to the predefined conceptual framework, which included inflammation, coagulation dysfunction, and structural brain changes.

### Quality Assessment

The methodological quality of the included studies was evaluated using the NOS (20). Based on conventional

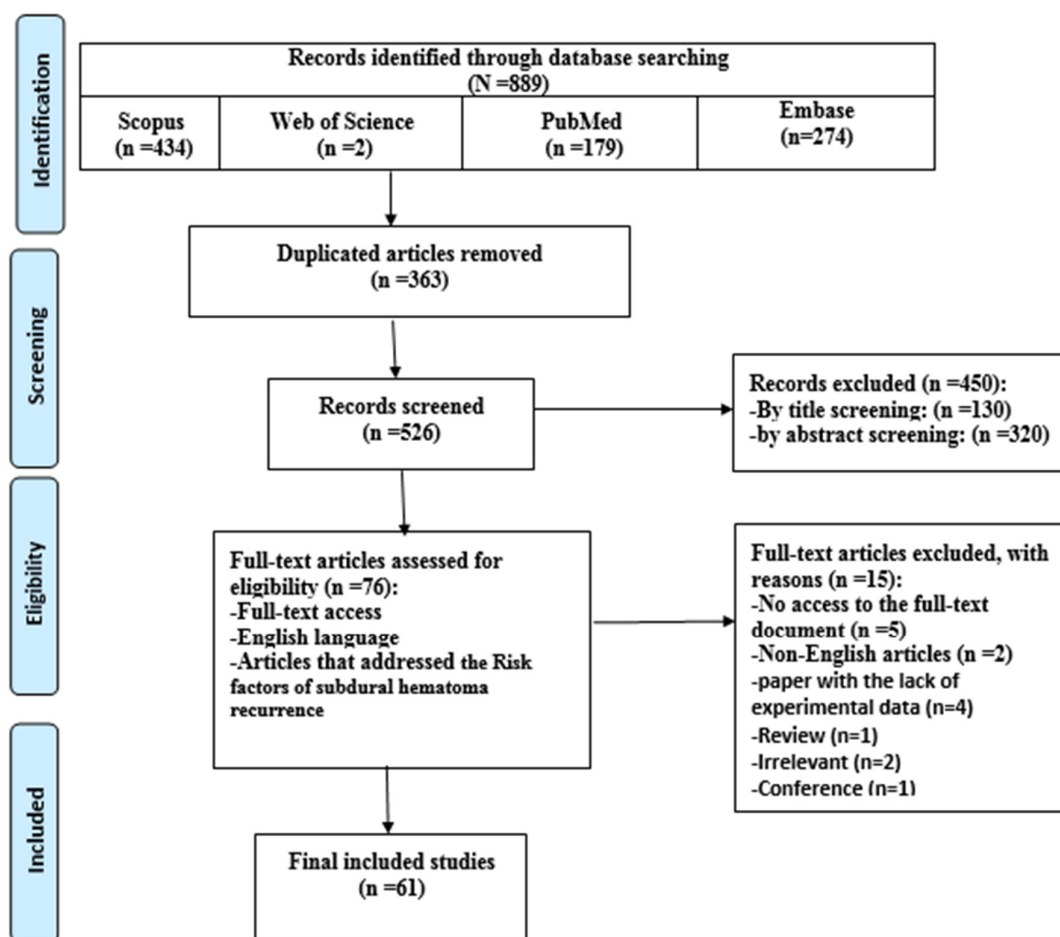


Figure 1. Flowchart of the literature screening and selection process, following PRISMA 2020 guidelines.

Table 1. Quality Assessment of Included Articles

| NO | First author (reference) | Selection (out of 4) | Comparability (out of 2) | Exposure/Outcome (out of 3) | Total (Out of 9) |
|----|--------------------------|----------------------|--------------------------|-----------------------------|------------------|
| 1  | Okano A (21)             | ****                 | **                       | ***                         | 9                |
| 2  | Pang,C.H (22)            | ****                 | **                       | ***                         | 9                |
| 3  | Jack A (23)              | ****                 | **                       | ***                         | 9                |
| 4  | Zhongrun Qian (24)       | ****                 | **                       | ***                         | 9                |
| 5  | Escosa Baé M (25)        | ****                 | **                       | ***                         | 9                |
| 6  | You, W (26)              | ***                  | **                       | ***                         | 8                |
| 7  | Zolfaghari, S(27)        | ***                  | **                       | ***                         | 8                |
| 8  | Ohba S (28)              | ****                 | **                       | ***                         | 9                |
| 9  | Hamou, H (29)            | ****                 | *                        | ***                         | 8                |
| 10 | Chen, F.M. (30)          | ****                 | *                        | ***                         | 8                |
| 11 | Wang, N (31)             | ****                 | **                       | ***                         | 9                |
| 12 | Jang, K.M (32)           | ****                 | **                       | **                          | 8                |
| 13 | Ito S (33)               | ****                 | **                       | ***                         | 9                |
| 14 | Honda M (34)             | ****                 | **                       | ***                         | 9                |
| 15 | Suero Molina E (35)      | ****                 | **                       | **                          | 8                |
| 16 | Tahsim-Oglou Y (36)      | ****                 | **                       | ***                         | 9                |
| 17 | Tugcu B (37)             | ***                  | **                       | ***                         | 8                |
| 18 | Wada M (38)              | ****                 | *                        | ***                         | 8                |
| 19 | Weigel R (39)            | ****                 | **                       | ***                         | 9                |
| 20 | Motoie R (40)            | ****                 | **                       | ***                         | 9                |
| 21 | Shen J (41)              | ****                 | **                       | **                          | 8                |
| 22 | Adachi A (42)            | ****                 | **                       | ***                         | 9                |
| 23 | de Oliveira AJM (43)     | ****                 | **                       | ***                         | 9                |
| 24 | Santos RGD (44)          | ****                 | **                       | ***                         | 9                |
| 25 | Schmidt L (45)           | ***                  | **                       | ***                         | 8                |
| 26 | Kang Min Su (46)         | ****                 | **                       | ***                         | 9                |
| 27 | Sharafat, S (47)         | ***                  | **                       | ***                         | 8                |
| 28 | Kim J (48)               | ****                 | **                       | ***                         | 9                |
| 29 | George Kolcun (49)       | ****                 | **                       | ***                         | 9                |
| 30 | Leroy HA (50)            | ****                 | **                       | ***                         | 9                |
| 31 | Liu LX (51)              | ****                 | **                       | ***                         | 9                |
| 32 | Liu WC (52)              | ****                 | **                       | **                          | 8                |
| 33 | Lutz K (53)              | ****                 | **                       | ***                         | 9                |
| 34 | Matsumoto K (54)         | ****                 | **                       | ***                         | 9                |
| 35 | Jun Shena (55)           | ****                 | **                       | ***                         | 9                |
| 36 | Sheng-Yu Cheng (56)      | ****                 | **                       | ***                         | 9                |
| 37 | Pantelis Stavrinou (57)  | ****                 | **                       | ***                         | 9                |
| 38 | Jun Shen (58)            | ****                 | **                       | ***                         | 9                |
| 39 | Tokunori Kanazawa (59)   | ***                  | **                       | ***                         | 8                |
| 40 | Yu Shimizu (60)          | **                   | *                        | ***                         | 7                |
| 41 | Makoto Oishi (61)        | ****                 | **                       | ***                         | 9                |
| 42 | Satoshi Hirai, MD (62)   | ****                 | *                        | ***                         | 8                |
| 43 | Hongbin Liu (63)         | ****                 | *                        | ***                         | 8                |
| 44 | Fabio Cofano (64)        | ****                 | **                       | ***                         | 9                |
| 45 | Shuai Han (65)           | ****                 | **                       | ***                         | 9                |
| 46 | Myung-Hoon Han (66)      | ****                 | **                       | ***                         | 9                |
| 47 | Min Xu (67)              | ****                 | **                       | ***                         | 9                |
| 48 | Byung-Soo Ko (68)        | ****                 | **                       | ***                         | 9                |
| 49 | Hyuck-Jin Oh (69)        | ****                 | *                        | ***                         | 8                |
| 50 | Jongwook Choi (70)       | ****                 | **                       | ***                         | 9                |
| 51 | Naoki Wakuta (71)        | ****                 | **                       | **                          | 8                |
| 52 | Rene Opsenak (72)        | ****                 | **                       | ***                         | 9                |
| 53 | Motaz Hamed (73)         | ****                 | **                       | **                          | 8                |
| 54 | Hiroaki Hashimoto (74)   | ****                 | **                       | **                          | 8                |
| 55 | Nadja Grübel (75)        | ****                 | **                       | ***                         | 9                |
| 56 | Kenji Yagi (76)          | ****                 | **                       | **                          | 8                |
| 57 | Samer Zawy Alsofy (77)   | ****                 | **                       | ***                         | 9                |
| 58 | Seung woo Lee (78)       | ****                 | **                       | ***                         | 9                |
| 59 | Mehmet Emin Akyuz (79)   | ****                 | **                       | ***                         | 9                |
| 60 | Maoki Matsubara (80)     | ****                 | **                       | ***                         | 9                |
| 61 | Min Chen (81)            | ****                 | **                       | **                          | 8                |

Good quality: 3 or 4 stars in the 'Selection' domain AND 1 or 2 stars in the 'Comparability' domain AND 2 or 3 stars in the 'Outcome/Exposure' domain. Fair quality: 2 stars in the 'Selection' domain AND 1 or 2 stars in the 'Comparability' domain AND 2 or 3 stars in the 'Outcome/Exposure' domain. Poor quality: 0 or 1 star in the 'Selection' domain OR 0 stars in the 'Comparability' domain OR 0 or 1 star in the 'Outcome/Exposure' domain.

NOS classifications, studies scoring 7-9, 4-6, and  $\leq 3$  were deemed to have a low, moderate, and high risk of bias, respectively (Table 1). Furthermore, to ensure methodological rigor and transparent reporting, this systematic

review was conducted in strict adherence to the PRISMA 2020 guidelines and checklist (19).

## Results

### Study Selection and Quality Assessment

A total of 889 records were identified through initial electronic database searching. A total of 363 duplicated articles were removed, and 450 studies were excluded in the first step of title and abstract screening. Then, the remaining articles were proceeded with full-text assessment, where a final selection of 61 studies was included in this review (Figure 1). The quality assessment was conducted using the NOS, and all 61 studies were rated as having "Good" quality (Table 1).

### Patient Characteristics

The final analysis comprised 61 studies, 60 of which were cohort studies (including 4 retrospective cohorts) and 1 randomized controlled trial (RCT). The total number of patients studied across these studies was 29,822. Among the 52 studies ( $n = 27,727$ ) that reported the distribution of patients' sex, 19,448 were male, and 8,279 were female. Regarding the patients included in the studies, 4083 (13.69%) experienced a recurrence of cSDH. 36 studies ( $n = 3168$ ) reported the sex of cSDH recurrence cases, in which 2,405 (75.9%) were male and 763 (24.1%) were female. Regarding the age of the participants, 49 studies reported this baseline characteristic, where it ranged from ( $61.9 \pm 17.8$ ) to ( $81.9 \pm 6.3$ ) years old. Additionally, 47 studies provided information on the mean age of cSDH recurrence, which ranged from ( $54.3 \pm 8.3$ ) to ( $81.9 \pm 6.3$ ) years old (Table 2).

### Risk Factors of Subdural Hematoma Recurrence

#### Clinical Factors

Lower Glasgow Coma Scale (GCS) scores preoperatively (81), at admission (56), and 24 hours postadmission (53) have been associated with higher recurrence rates, suggesting that impaired consciousness may reflect more severe pathophysiology or delayed intervention. Reduced consciousness may be correlated with ongoing inflammation and tissue fragility; however, one study has contested this association (75). Although data regarding the Glasgow Outcome Scale (GOS) at discharge are conflicting, both lower (53) and higher (56) scores have been associated with recurrence, possibly due to heterogeneous patient populations or differing outcome definitions. Hematological factors revealed a robust association between inflammation (elevated postoperative neutrophil counts/NLR), coagulation disorders (thrombocytopenia, liver/renal disease), and blood group A (35, 43, 62, 68, 76, 77, 80) and paradoxically O (73). With recurrence, implicating both inflammatory cascades and hemostatic imbalances in recurrence pathogenesis. Elevated neutrophil counts and a high neutrophil-to-lymphocyte ratio (NLR) drive inflammatory cascades that compromise membrane integrity and impede healing, thereby perpetuating a state of tissue vulnerability. Coagulation disorders such as thrombocytopenia and underlying liver or renal disease impair clot formation and repair, increasing the risk of hematoma recurrence. Blood groups (notably A and paradoxically O) may

influence hemostatic balance and immune responses, though their precise roles need further study.

Notably, eosinophil-rich blood ( $\geq 100/\mu\text{L}$ ) (32) emerged as a novel marker, potentially reflecting underlying immunological mechanisms. Other factors include postoperative complications, hemiplegia (74), elevated blood urea nitrogen (BUN) (31), comorbidities, alcoholism (45), structural vulnerabilities, cerebral atrophy (65), and metabolic factors (high BMI) (66), collectively underscoring the multifactorial nature of recurrence. Postoperative complications (e.g., hemiplegia), metabolic issues (high BMI), cerebral atrophy, and comorbidities (alcoholism) (45) add layers of vulnerability by weakening structural brain support and systemic health.

#### Medication Factors

Medication use represents a significant and modifiable risk factor for cSDH recurrence, with antiplatelet and anti-coagulant therapies being the most prominently studied. A majority of studies (30, 36, 38, 40, 41, 50, 58, 75, 80, 81) consistently report that these agents, particularly warfarin (40) and enoxaparin (36), elevate recurrence risk, likely due to their interference with hemostasis.

However, this association remains controversial, as 3 studies (21, 73, 77) found no significant link between antiplatelet/anticoagulant use and rebleeding. Variability may stem from differences in patient populations, timing of drug resumption after surgery, or perioperative management strategies. Beyond these, emerging evidence highlights the protective role of dexamethasone (24) and ACE inhibitors (39) in reducing recurrence, possibly through anti-inflammatory or hemodynamic mechanisms.

#### Demographic Factors

Demographic factors, particularly male sex and advanced age, have been consistently identified as significant predictors of cSDH recurrence (33, 34, 36, 40, 45, 48, 50, 57, 64, 75, 78). However, the exact biological mechanisms remain not fully elucidated, and some studies report no significant sex differences in recurrence rates.

Similarly, increasing age is strongly associated with recurrence (24, 33, 40-42, 44, 45, 52, 58, 65, 66, 69, 74, 75, 78). Older patients are at a higher risk, mainly due to brain atrophy, which increases the space between the brain and skull, leading to the stretching and fragility of bridging veins and making them more vulnerable to rebleeding. Additionally, older people often have compromised vascular integrity and impaired tissue repair capacity. Polypharmacy and comorbidities common in aged populations can also contribute to hematoma recurrence by affecting coagulation and inflammation pathways. However, one outlier study found no significant correlation between age, sex, and recurrence, possibly due to limited sample size or differing patient selection criteria (77).

#### Surgical Factors

The mechanism by which surgical factors cause relapse in cSDH revolves around issues of brain re-expansion, residual dead space, membrane characteristics, and drainage efficacy.

## Risk Factors of Chronic Subdural Hematoma Recurrence

**Table 2.** Description of Included Studies and Summary of Study Findings

| ID | First author's name      | Type of study | population | Sex                   | Age              | Recurrence (%)               | Age (Recurrence)             | Sex (recurrence) | Type of hematoma/N  | Risk factors of subdural hematoma recurrence |            |             |         |                                 |   | Other finding |  |  |  |  |
|----|--------------------------|---------------|------------|-----------------------|------------------|------------------------------|------------------------------|------------------|---|--|------------|-------------|---------|---------------------------------|---|---------------|--|--|--|--|
|    |                          |               |            |                       |                  |                              |                              |                  |   | Clinical finding                             | Medication | Demographic | Surgery | Radiological findings           | Comorbid disease                        |               | Other  |  |  |  |
| 1  | Okano A (21)             | cohort        | N=448      | Man<br>N=314 (70.1)   | 71.1<br>(19-97)  | N=40<br>(8.9%),              | N/R                          | N/R              | Bilateral<br>N=104<br>(N/R%)<br><br>Right side<br>N= 136<br>(N/R%)<br><br>Left side<br>N= 208<br>(N/R%) | N/R  | N/R        | N/R         | N/R     | Presence of bilateral hematomas | Previous history of cerebral infarction | N/R           | Did not related Antip C.H.let or anticoagulant therapy   |  |  |  |
|    | woman<br>N=134<br>(29.9) |               |            |                       |                  | Bilateral<br>N=17<br>(16.3%) |                              |                  |   |  |            |             |         |                                 |   |               |  |  |  |  |
|    |                          |               |            |                       |                  |                              | Right side<br>N= 8<br>(5.9%) |                  |   |  |            |             |         |                                 |   |               |  |  |  |  |
|    |                          |               |            |                       |                  |                              | Left side<br>N= 15<br>(7.2%) |                  |   |  |            |             |         |                                 |   |               |  |  |  |  |
| 2  | Pang, C.H (22)           | cohort        | N=303      | Man<br>N= 234 (N/R %) | 67.17            | N=37<br>(12.21%)             | 71.78 ± 7.95                 | N/R              | N/R   | N/R  | N/R        | N/R         | N/R     | N/R                             | Diabetes mellitus                       | N/R           | Recurrence did not affect the final neurological outcome |  |  |  |
|    | woman<br>N= 69<br>(N/R%) |               |            |                       |                  | Unilateral<br>N=26<br>N/R%   |                              |                  |   |  |            |             |         |                                 |   |               |  |  |  |  |
|    |                          |               |            |                       |                  | Bilateral<br>N=11<br>N/R%    |                              |                  |   |  |            |             |         |                                 |   |               |  |  |  |  |
| 3  | Jack A (23)              | cohort        | N=331      | Man<br>N=267 (80.7%)  | Man<br>69.1±14.3 | reoperation rate             | N/R                          | N/R              | N/R   | N/R  | N/R        | N/R         | N/R     | N/R                             | N/R                                     | N/R           | N/R  |  |  |  |
|    | Woman<br>N=64<br>(19.3%) |               |            | Woman<br>69.4±14.0    | N=39<br>11.8%    |                              |                              |                  |   |  |            |             |         |                                 |   |               |  |  |  |  |

Table 2. Description of Included Studies and Summary of Study Findings

| ID | First author's name | Type of study | population | Sex   | Age            | Recurrence (%)   | Age (Recurrence) | Sex (recurrence)                                   | Type of hematoma/N   | Risk factors of subdural hematoma recurrence |  |             |  |  |                  | Other finding |   |
|----|---------------------|---------------|------------|---|----------------|--|------------------|--|--|--|--|-------------|--|--|------------------|---------------|---|
|    |                     |               |            |   |                |  |                  |  |  | Clinical finding                             | Medication   | Demographic | Surgery  | Radiological findings  | Comorbid disease |               | Other   |
| 4  | Zhongrun Qian (24)  | cohort        | N= 242     | Man<br>N=148<br>N/R%<br><br>Woman<br>N=94<br>N/R%       | 66.3 ±<br>10.9 | N=39<br>(16.1%)  | 70.7 ± 10.9      | Man<br>N=25<br>16.9%<br><br>Woman<br>N=14<br>14.9% | Chronic SDH location: Right: 17 (12.2%)<br>Left: 22 (15.8%)<br>Bilateral: 0 (0%)             | N/R  | 1-DX<br>Reduced disease recurrence in patients with the separated type of hematoma<br><br>2- Treated with DX postoperatively | Age (older) | N/R  | 1-CT Hematoma density,<br>2-Preoperative midline displacement exceeding 10mm,<br>3- Degree of air collection,<br>4-hematomas presenting with Separated type  | N/R              | N/R           | Apply DX had a lower rate of second drainage procedure      |
| 5  | Escosa Baé M (25)   | cohort        | N= 312     | N/R   | N/R            | N=37 (12%)<br><br>Bilateral N= 5 (14%)<br><br>Right side<br>N= 14 (37%)<br><br>Left side<br>N= 18 (49%)        | N/R              | N/R  | N/R  | N/R  | N/R  | N/R         | N/R  | 1-Preoperative cSDH width,<br>2-Preoperative midline shift,<br>3- Postoperative Midline width,<br>4- postoperative cSDH width<br>5- Residual cSDH 1 month later<br>6- Postoperative midline Shift<br>7- Postoperative neurological deficit | N/R              | N/R           | Not related to The duration of Treatment with dexamethasone |
| 6  | You, W (26)         | cohort        | N=226      | Man<br>N=184<br>(81.4%)<br><br>Woman<br>N=42<br>(18.6%) | 65.1 ±<br>13.4 | N=34 (15%)<br><br>Bilateral N= 14 (41.2%)<br><br>Right side<br>N= 10 (29.4%)<br><br>Left side<br>N= 10 (29.4%) | 62.7 ± 14.1      | N/R  | Bilateral N= 66 (29.2%)<br><br>Right side<br>N= 67 (29.6%)<br><br>Left side<br>N= 93 (41.2%) | N/R  | N/R  | N/R         | Shorter duration of subdural drainage post-surgery | Homogenous hyper-dense hematoma  | N/R              | N/R           | N/R   |

## Risk Factors of Chronic Subdural Hematoma Recurrence

**Table 2.** Description of Included Studies and Summary of Study Findings

| ID | First author's name | Type of study | population | Sex                                     | Age         | Recurrence (%)  | Age (Recurrence)                    | Sex (recurrence)                        | Type of hematoma/N  | Risk factors of subdural hematoma recurrence |                    |             |  |  |                  | Other finding   |   |
|----|---------------------|---------------|------------|---|-------------|---|-------------------------------------|---|---|--|--------------------|-------------|--|--|------------------|---|---|
|    |                     |               |            |   |             |   |                                     |   |   | Clinical finding                             | Medication         | Demographic | Surgery  | Radiological findings  | Comorbid disease |   | Other   |
| 7  | Zolfaghari, S (27)  | cohort        | N=326      | N/R                                     | N/R         | N=N/R(26.4%)  | N/R                                 | N/R                                     | Bilateral cSDH N=326 (100%)   | N/R  | N/R                | N/R         | 1-Surgical procedure<br>2- Micraniotomy with Passive subdural drain) | N/R  | N/R              | N/R   | N/R   |
| 8  | Ohba S (28)         | cohort        | N=177      | Man N=112 (N/R %)<br>Woman N=65 (N/R%)  | 74.7        | N=20 (11.3 %)   | ≥70 N=N/R (13%)<br>< 70 N=N/R(6.5%) | Man N=N/R (13.4%)<br>Woman N=N/R (7.7%) | Bilateral N=N/R(N/R %)<br>Right side N= N/R (13%)<br>Left side N= N/R (10%) | N/R  | N/R                | N/R         | N/R  | 1-Different types of Hematoma internal architecture<br>2- Postoperative massive subdural air collection<br>3- Separated type of hematoma | N/R              | N/R   | N/R   |
| 9  | Hamou, H (29)       | cohort        | N=381      | Man N=244 (N/R%)<br>Woman N=137 (N/R %) | 75.2 ± 12.0 | N=122 (32.0%)   | 74.7 ± 11.3                         | Man N=80 (65.6%)<br>Woman N=42 (34.4%)  | N=92 (24.1%) had bilateral  | N/R  | N/R                | N/R         | N/R  | The extended hematoma classification   | N/R              | Detection and treatment at a later stage of spontaneous repair reduced risk of recurrence | Not related to postoperative depressed brain volume |
| 10 | Chen, F.M (30)      | cohort        | N=448      | Man N=354 (N/A %)<br>Woman N=94 (N/A %) | 68.1 ± 12.4 | N=60 (13.4%)<br>Bilateral N=14 (41.2%)<br>Right side N= 10 (29.4%)<br>Left side N= 10 (29.4%) | 69.6 ± 10.8                         | Man N=53 (N/R %)<br>Woman N=7 (N/R%)    | N/R   | N/R  | Anticoagulant drug | N/R         | N/R  | 1-Bilateral hematoma<br>2-Hyperdense hematoma  | N/R              | N/R   | N/R   |
| 11 | Wang, N (31)        | cohort        | N=653      | Man N=561 (85.9%)<br>Woman N=92 (14.1%) | 64,80       | N=96 (14.7%)  | 69,82                               | Man N=86 (89.6%)<br>Woman N=10 (10.4 %) | N/R   | Postoperative BUN                            | N/R                | N/R         | N/R  | N/R  | N/R              | N/R   | N/R   |
| 12 | Jang, K.M (32)      | cohort        | N=291      | Man N=208 (71.5%)<br>Woman N=83 (28.5%) | 71.8 ± 11.8 | N=29 (10.0%)  | N/R                                 | Man N=N/R (N/R%)<br>Woman N=8 (27.6%)   | Bilateral hematoma N=116 (39.9%)  | N/R  | N/R                | N/R         | N/R  | (>50 cm3) at 7 days  | N/R              | N/R   | N/R   |

Table 2. Description of Included Studies and Summary of Study Findings

| ID | First author's name | Type of study | population | Sex  | Age                               | Recurrence (%)  | Age (Recurrence)                  | Sex (recurrence)                           | Type of hematoma/N                                   | Risk factors of subdural hematoma recurrence |                                      |                               |  |   |                   | Other finding |   |
|----|---------------------|---------------|------------|--|-----------------------------------|---|-----------------------------------|--|--|--|--------------------------------------|-------------------------------|--|---|-------------------|---------------|---|
|    |                     |               |            |  |                                   |   |                                   |  |  | Clinical finding                             | Medication                           | Demographic                   | Surgery                                    | Radiological findings   | Comorbid disease  |               | Other   |
| 13 | Ito S (33)          | Retrospective | N=452      | N/R  | N/R                               | N = 59 (13.0%)  | 79 (73-86)                        | Man N=46 (77.9%)<br>Woman N=N/A(N/R%)      | N/R  | N/R  | N/R                                  | 1-Older Age<br>2- Male gender | N/R  | Subdural air at postoperative day 1   | N/R               | N/R           | N/R   |
| 14 | Honda M (34)        | cohort        | N=194      | Man N=144 (74.2%)<br>Woman N=50 (25.8%)    | 81.9 ± 6.3                        | N=22 (11.3%)  | 81.9 ± 6.3                        | Man N=21 (95%)<br>Woman N=1 (5%)           | N/R  | N/R  | N/R                                  | Male gender                   | Intraoperative hematoma volume             | 1- Hematoma volume 150 ml<br>2- Hematoma volume ≥150 ml was the strongest independent risk factor                 | Diabetes mellitus | N/R           | N/R   |
| 15 | Suero Molina E(35)  | cohort        | N=148      | Man N= 107 (72.3%)<br>Woman N= 41 (27.7%)  | ≤ 76 73 (49.3%)<br>>76 75 (50.7%) | N=35 (23.6%)  | ≤ 76 16 (21.9%)<br>>76 19 (25.3%) | Man N= 28 (26.2%)<br>Woman N= 7 (17.1%)    | N/R  | N/R  | N/R                                  | N/R                           | N/R  | 1-Preoperative hematoma thickness<br>2- thrombocytopenia<br>3- Postoperative midline shift<br>4- hematoma density | N/R               | N/R           | N/R   |
| 16 | Tahsim-Oglou Y (36) | cohort        | N=247      | N/R  | N/R                               | N=62 (25.1%)  | 77±8                              | Man N= 50 (80.65%)<br>Woman N= N/R (N/R %) | Bilateral hematoma N=17 (27.42%)                     | N/R  | Enoxaparin                           | Male gender                   | N/R  | Rinsing fluid   | N/R               | N/R           | Not related to Preoperative and postoperative Platelet counts and plasmatic coagulation |
| 17 | Tugcu B (37)        | Retrospective | N=292      | Man N= 200 (68.5%)<br>Woman N= 92 (31.5%)  | 61.9 ± 17.8                       | N=43 (14.7%)<br>Bilateral N= 19 (23.1%)<br>unilateral N= 24 (11.4%) | 65.35± 14.44                      | Man N= 34 (17%)<br>Woman N= N/R (N/R %)    | Bilateral N= 82 (28.1%)<br>Unilateral N= 210 (71.9%) | N/R  | N/R                                  | N/R                           | N/R  | Bilateral subdural Hematoma   | N/R               | N/R           | N/R   |
| 18 | Wada M (38)         | Retrospective | N=719      | Man N= 454 (N/R %)<br>Woman N= 227 (N/R %) | 72.9± 11.6                        | N=67 (N/R %)  | N/R                               | N/R  | N/R  | N/R  | Preoperative oral APA administration | N/R                           | Subdural drainage leads to less recurrence | N/R   | N/R               | N/R           | N/R   |

## Risk Factors of Chronic Subdural Hematoma Recurrence

**Table 2.** Description of Included Studies and Summary of Study Findings

| ID | First author's name  | Type of study | population                             | Sex   | Age  | Recurrence (%)  | Age (Recurrence) | Sex (recurrence)                       | Type of hematoma/N  | Risk factors of subdural hematoma recurrence |  |                           |   |   |                  | Other finding |       |
|----|----------------------|---------------|--|---|--|---|------------------|--|---|--|--|---------------------------|---|---|------------------|---------------|-------|
|    |                      |               |  |   |  |   |                  |  |   | Clinical finding                             | Medication   | Demographic               | Surgery   | Radiological findings   | Comorbid disease |               | Other |
| 19 | Weigel R (39)        | Cohort        | N=438<br>Group A N=81<br>Group B N=229 | Group A<br>Man N=63<br>Woman N=18<br>Group B<br>Man N=159<br>Woman N=70 | Group A<br>73.6 ± 11.3<br>Group B<br>70.8 ± 14.3 | N=46 (N/R%)   | N/R              | N/R                                    | N/R   | N/R  | A negative correlation between the Yearly rates of medication wACE inhibitorstors and recurrence | N/R                       | N/R   | N/R   | N/R              | N/R           | N/R   |
| 20 | Motoie R (40)        | Cohort        | N=787                                  | Man N=559 (71.0%)<br>Woman N=228 (29.0%)                                | 79 (72-85)                                       | N=96 (12.2%)  | 80 (76-87)       | Man N=77 (80.2%)<br>Woman N=19 (19.8%) | Bilateral hematomas N=116 (14.7%)   | N/R  | Warfarin   | -Age<br>-Male Sex         | N/R   | N/R   | N/R              | N/R           | N/R   |
| 21 | Shen J (41)          | cohort        | N=342                                  | Man N=280 (81.9%)<br>Woman N=62 (18.1%)                                 | 68.13 (21-88)                                    | N=52 (15.2%)  | 71.67±10.09      | Man N=41 (14.6%)<br>Woman N=11 (17.7%) | Unilateral  | N/R  | antiplatelet anticoagulant   | Age                       | N/R   | 1- The midline shift<br>2- Drainage volume<br>3- Prehv<br>4- Postpv | N/R              | N/R           | N/R   |
| 22 | Adachi A (42)        | cohort        | N=120                                  | N/R   | N/R  | N=11 (9.2%)   | 75.1±6.1         | Man N=5 (45%)<br>Woman N=6 (55%)       | Unilateral  | N/R  | N/R  | 1. Age<br>2. thrombo-cyte | 1- Irrigation solution Related To smaller recurrence rates<br>2-Type of irrigation solution | N/R   | N/R              | N/R           | N/R   |
| 23 | de Oliveira AJM (43) | cohort        | N=160                                  | Man N=95 (59.4%)<br>Woman N=65  | 69.3 ± 14.3                                      | N=36 (22.5%)<br>Bilateral N=0 (0.0%)<br>Right side N=15 (41.7%)<br>Left side N=21 (58.3%) | 73.1 ± 14.5      | Man N=25 (69.4%)<br>Woman N=N/R        | Bilateral N=4 (2.5%)<br>Right side N=72 (45.0%)<br>Left side N=84 (52.5%) | Postoperative neutrophil count and NLR       | N/R  | N/R                       | N/R   | N/R   | N/R              | N/R           | N/R   |

Table 2. Description of Included Studies and Summary of Study Findings

| ID | First author's name | Type of study | population                              | Sex  | Age   | Recurrence (%)      | Age (Recurrence)   | Sex (recurrence)   | Type of hematoma/N  | Risk factors of subdural hematoma recurrence |            |   |   |  |                                  | Other finding   |       |
|----|---------------------|---------------|---|--|---|---------------------|--|--|---|--|------------|---|---|--|----------------------------------|---|-------|
|    |                     |               |   |  |   |                     |  |  |   | Clinical finding                             | Medication | Demographic                                     | Surgery   | Radiological findings                          | Comorbid disease                 |   | Other |
| 24 | Santos RGD (44)     | cohort        | N=500                                   | Man<br>N=371<br>(74%)<br>Woman<br>N= 129               | 66<br>(52-77)   | N=27<br>(5.4%)      | Median age<br>of 59  | Man<br>N= 19<br>(70.4%)<br>Woman<br>N= N/R                   | Bilateral N= 90<br>(18%)<br><br>Hemispheres<br>N= 410<br>(82.0%)                                  | N/R  | N/R        | Age   | N/R   | N/R  | N/R                              | N/R   |       |
| 25 | Schmidt L (45)      | Cohort        | total<br>N=10158<br>recurrent<br>N=1555 | Man<br>N=6575<br>(N/R%)<br>Woman<br>N= 3583<br>(N/R %) | 20-49<br>N= 1895<br><br>50-69<br>N= 3383<br><br>70<<br>N=4880 | recurrent<br>N=1555 | 20-49<br>N= 255<br><br>50-69<br>N= 511<br><br>70<<br>N=789 | Man<br>N= 1157<br>Woman<br>N= 398                            | N/R   | Alcohol addiction                            | N/R        | 1-Male<br>gender<br>2- Older age<br>(>70 years) | 1-Surgical<br>treatment<br>2- Trauma<br>diagnoses | N/R  | Diabetes<br>mellitus             | N/R   | N/R   |
| 26 | Kang Min Su (46)    | Cohort        | N=302                                   | Man<br>N=236<br>Woman<br>N= 66                         | <30<br>N=7<br><br>30-60<br>N=86<br><br>60<<br>N=209           | N=24<br>(7.9%)      | <30<br>N=3<br><br>30-60<br>N=6<br><br>60<<br>N=15          | men<br>N= 22(9.3<br>%)<br>women<br>N= 2<br>(3%)              | N/R   | N/R  | N/R        | lower<br>recurrence                             | Layered type                                      | N/R  | N/R                              | Not related<br>to<br>1.History of<br>seizure 2.<br>diabetes 3.<br>vascular<br>disease |       |
| 27 | Sharafat, S (47)    | Cohort        | N=206                                   | Man<br>N= 164<br>(79.6%)<br>Woman<br>N= 42<br>(20.4%)  | 62.9±16.2   | N= 28<br>(13.6%)    | 62.19±17.06  | Man<br>N= 18<br>(64.3<br>%)<br>Woman<br>N= 10<br>(35.7<br>%) | Bilateral<br>N=66 (32%)<br><br>Right side<br>N=58<br>(28.2%)<br><br>Left side<br>N= 82<br>(39.8%) | N/R  | N/R        | N/R   | Subdural<br>drainage<br>duration<br>(days)        | N/R  | N/R                              | N/R   | N/R   |
| 28 | Kim J (48)          | Cohort        | N=368                                   | Man<br>N= 244<br>(72.5%)<br>Woman<br>N= 93<br>(27.5%)  | 68.6±13.12  | N=31<br>(8.4%)      | 69.00±12.43  | Man<br>N= 28<br>(90.4<br>%)<br>Woman<br>N= 3<br>(9.6<br>%)   | N/R   | N/R  | N/R        | Male gender                                     | N/R   | 1.Single layer<br>cSDH<br>2.Isodensity<br>cSDH | Malignant<br>neoplasm<br>history | N/R   | N/R   |

## Risk Factors of Chronic Subdural Hematoma Recurrence

Table 2. Description of Included Studies and Summary of Study Findings

| ID | First author's name | Type of study | population | Sex                                       | Age           | Recurrence (%)   | Age (Recurrence) | Sex (recurrence)                          | Type of hematoma/N  | Risk factors of subdural hematoma recurrence          |                                    |             |                                     |   |   | Other finding |       |
|----|---------------------|---------------|------------|---|---------------|--|------------------|---|---|---|------------------------------------|-------------|-------------------------------------|---|---|---------------|-------|
|    |                     |               |            |   |               |  |                  |   |   | Clinical finding                                      | Medication                         | Demographic | Surgery                             | Radiological findings                                   | Comorbid disease  |               | Other |
| 29 | George Kolcun (49)  | Cohort        | N=261      | men N= 188 (72%)<br>women N= 73 (28%)     | 65.6±14.8     | N=16 (6.1%)  | N/R              | N/R                                       | N/R   | N/R   | N/R                                | N/R         | N/R                                 | N/R   | Coagulopathic patients with liver disease                                   | N/R           | N/R   |
| 30 | Leroy HA (50)       | Cohort        | N=140      | Man N= 89 (63.6%)<br>Woman N= 73 (28%)    | 75.9 ± 11.0   | N=24 (17%)<br>Bilateral N= 7 (29.2%)<br>Right side N= 8 (33.3%)<br>Left side N= 9 (37.5%)        | 77.5 ± 11.0      | Man N= 19 (79.2%)<br>Woman N= N/R         | Bilateral N= 37 (26.4%)<br>Right side N= 44 (31.4%)<br>Left side N= 59 (42.4%)  | N/R   | preoperative anticoagulant therapy | Male Gender | N/R                                 | Persistence of mass effect on the postoperative CT scan | N/R   | N/R           | N/R   |
| 31 | Liu LX (51)         | Cohort        | N=328      | Man N= 281<br>Woman N= 47                 | 65.14± 13.76  | N=8 (2.44%)  | 65.75 ± 12.37    | N/R                                       | Bilateral N= 61 (19.1%)   | N/R   | N/R                                | N/R         | N/R                                 | Mixed density Hematoma                                  | N/R   | N/R           | N/R   |
| 32 | Liu WC (52)         | Cohort        | N= 274     | Man N= 223 (81.4%)<br>Woman N= 51 (18.6%) | 66.90 ± 11.79 | N= 42 (15.3%)<br>Bilateral N= 43 (18.5%)<br>Right side N= 78 (33.6%)<br>Left side N= 111 (47.8%) | 71.17 ± 11.26    | Man N= 187 (80.6%)<br>Woman N= 45 (19.4%) | Bilateral N= 53 (19.3%)<br>Right side N= 94 (34.3%)<br>Left side N= 127 (46.4%) | N/R   | N/R                                | Age         | N/R                                 | Midline shift   | 1- hypertension<br>2-diabetes mellitus<br>3-triglyceride<br>4- A higher HDL | N/R           | N/R   |
| 33 | Lutz K (53)         | RCT           | N= 220     | N/R                                       | N/R           | N= 19 (N/R%)   | 76.4 ± 12.4      | Man N= 19 (86.4%)<br>Woman N= N/R         | N/R   | 1- Lower GOS at discharge<br>2- Lower GCS at 24 hours | N/R                                | N/R         | Less intraoperative brain expansion | N/R   | N/R   | N/R           | N/R   |

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| ID | First author's name     | Type of study | population | Sex  | Age           | Recurrence (%)   | Age (Recurrence) | Sex (recurrence)                        | Type of hematoma/N                                  | Risk factors of subdural hematoma recurrence                     |                                       |                     |                                    |   |                   | Other finding |       |
|----|-------------------------|---------------|------------|--|---------------|--|------------------|---|---|--|---------------------------------------|---------------------|------------------------------------|---|-------------------|---------------|-------|
|    |                         |               |            |  |               |  |                  |   |   | Clinical finding   | Medication                            | Demographic         | Surgery                            | Radiological findings   | Comorbid disease  |               | Other |
| 34 | Matsumoto K (54)        | cohort        | N=121      | N/R  | N/R           | N= 10 (8.3%)<br>Bilateral N= 3 (30%)<br>unilateral N= 7 (70%)      | 78.6±4.3         | Man N=7 (70%)<br>Woman N= 3 (30%)       | N/R   | N/R  | N/R                                   | Drainage volume     | Hematoma Thickness                 | Diabetes mellitus   | N/R               | N/R           |       |
| 35 | Jun Shena (55)          | cohort        | N=461      | Man N=376 (82.3%)<br>Woman N=81 (17.7%)<br>died N=4 (0.8%) | 68.8 (23- 92) | N=69 (N/R%)<br>unilateral N= 48 (N/R %)<br>Bilateral N= 21 (N/R%)  | (72.8 ± 9.4)     | Man N= 56 (15%)<br>Woman N= 13 (16%)    | Unilateral N=311 (N/R %)<br>Bilateral N=146 (N/R %) | N/R  | Antiplatelet and/or anticoagulant use | Age (over 80 years) | N/R                                | 1-midline shift ≥10 mm<br>2- severe brain atrophy<br>3- severe postoperative pneumocephalus | N/R               | N/R           | N/R   |
| 36 | Sheng-Yu Cheng (56)     | cohort        | N= 342     | Man N=235 (68.7%)<br>Woman N=107 (31.3%)                   | (77.2± 11.4)  | N=N/R (11.9%)  | N/R              | Man N=N/R<br>Woman N=N/R                | Unilateral N= N/R<br>Bilateral N= N/R               | lower GCS scores on admission and higher GOS scores at discharge | N/R                                   | N/R                 | N/R                                | N/R   | Diabetes mellitus | N/R           | N/R   |
| 37 | Pantelis Stavrinou (57) | cohort        | N= 195     | Man N=134(N/R %)<br>Woman N=61 (N/R %)                     | N/R           | Total N=160(N/A%)  | (74.8± 9.8)      | Man N=105 (65.6%)<br>Woman N=55 (34.4%) | Bilateral N=48<br>Left n=76<br>Right N=n/a          | N/R  | N/R                                   | Male Gender         | The percentage of hematoma drained | The density of the postoperative subdural fluid   | N/R               | N/R           | N/R   |
| 38 | Jun Shen (58)           | cohort        | N= 102     | Man N=79 (77.45%)<br>Woman N=23 (22.55%)                   | 70.76         | N=19 (18.63%)<br>unilateral N= 14 (N/A%)<br>Bilateral N= 5 (N/R %) | (75.18 ± 9.41)   | N/R                                     | Unilateral N=0 (0%)<br>Bilateral N=102 (100%)       | N/R  | Anticoagulant use                     | N/R                 | N/R                                | 1-Severe brain atrophy<br>2-Postoperative pneumocephalus volume                             | N/R               | N/R           | N/R   |

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| ID | First author's name    | Type of study | population | Sex  | Age              | Recurrence (%)    | Age (Recurrence) | Sex (recurrence)                                    | Type of hematoma/N   | Risk factors of subdural hematoma recurrence   |                     |             |         |  |                  | Other finding                        |       |
|----|------------------------|---------------|------------|--|------------------|-------------------|------------------|---|--|--|---------------------|-------------|---------|--|------------------|--------------------------------------|-------|
|    |                        |               |            |  |                  |                   |                  |   |  | Clinical finding   | Medication          | Demographic | Surgery | Radiological findings  | Comorbid disease |                                      | Other |
| 39 | Tokunori Kanazawa (59) | cohort        | N=114      | Men<br>N=85<br>(74.6%)<br>Women<br>N=29<br>(25.4%)   | 74.9<br>(28-97)  | N=27<br>(23.68%)  | (74.89 ± 11.51)  | Men<br>N=23<br>(85.18%)<br>Women<br>N=4<br>(14.81%) | Unilateral<br>N=81<br>(71.1%)<br>Left<br>N=50<br>(61.7%)<br>Right<br>N=31<br>(38.3%)<br>Bilateral<br>N=33<br>(28.9%) | N/R  | N/R                 | N/R         | N/R     | 1-postoperative hematoma volume<br>2- percentage of hematoma drained<br>3-postoperative hematoma density<br>4- postoperative significant residual air<br>5-preoperative hematoma Entropy | N/R              | N/R                                  | N/R   |
| 40 | Yu Shimizu (60)        | cohort        | N=388      | Man<br>N=261<br>(67.2%)<br>Woman<br>N=127<br>(32.8%) | (72.4 ± 21.7)    | N= N/R<br>(13.7%) | N/R              | Men<br>N= N/R<br>Women<br>N= N/R                    | Right n=173<br>(44.6%)<br>Left n=182<br>(46.9%)<br>Bilateral<br>N=33 (8.5%)  | N/R  | N/R                 | N/R         | N/R     | 1-Midline shift > 10 mm<br>2-Gradation-density hematoma<br>3-bilateral hematoma<br>4-Volume > 150 ml   | N/R              | N/R                                  | N/R   |
| 41 | Makoto Oishi (61)      | cohort        | N=116      | Man<br>N=84<br>(72.4%)<br>Woman<br>N= 32<br>(27.6%)  | (71.1 ± 11.4)    | N=10<br>(8.6%)    | (74.2± 7.8)      | Man<br>N=8 (9.5%)<br>Woman<br>N= 2<br>(6.3%)        | Bilateral<br>N=18<br>Unilateral<br>N= 98   | 1-the incidence (history) of head injury<br><br>2-headache (as a preoperative symptom) | N/R                 | N/R         | N/R     | 1-density of hematoma on CT scan<br>2-larger amount of residual air in the postoperative hematoma cavity<br>N/R  | N/R              | Days from the appearance of symptoms | N/R   |
| 42 | Satoshi Hirai, MD (62) | cohort        | N=320      | Man<br>N=228<br>(71.3%)<br>Woman<br>N= 92<br>(28.7%) | (77.3 ± 10.9)    | N=37<br>(10.6%)   | N/R              | N/R   | N/R  | 1-blood type A<br>2- thrombocytopenia<br>3- coagulopathy                               | Anticoagulant drugs | N/R         | N/R     | N/R  | N/R              | N/R                                  | N/R   |
| 43 | Hongbin Liu (63)       | cohort        | N= 143     | Man<br>N=109<br>(76.2%)<br>Woman<br>N= 34<br>(23.8%) | 68.35<br>(43-94) | N=7/143<br>(4.9%) | 64.14±15.52      | Man<br>N= 7<br>(4.9%)<br>Woman<br>N= 0<br>(0.0%)    | Left- n= 75<br>(n/a%)<br>Right- n=52<br>(n/a%)<br>Bilateral<br>N=16<br>(11.2%)                                       | N/R  | N/R                 | N/R         | N/R     | 1- Neomembrane thickness<br>2-Hematoma cavity separation   | N/R              | N/R                                  | N/R   |

Table 2. Description of Included Studies and Summary of Study Findings

| ID | First author's name | Type of study | population | Sex   | Age             | Recurrence (%)  | Age (Recurrence)                       | Sex (recurrence)                                    | Type of hematoma/N  | Risk factors of subdural hematoma recurrence |                       |                  |  |   |                  | Other finding |       |
|----|---------------------|---------------|------------|---|-----------------|---|--|---|---|--|-----------------------|------------------|--|---|------------------|---------------|-------|
|    |                     |               |            |   |                 |   |  |   |   | Clinical finding                             | Medication            | Demographic      | Surgery  | Radiological findings   | Comorbid disease |               | Other |
| 44 | Fabio Cofano (64)   | Cohort        | N=1313     | Man<br>N=910(69.3%)<br>Woman<br>N= 403<br>(31.7%) | (76.6±9.9)      | N=132<br>(10.1%)  | N/R                                    | Man<br>N=N/A<br>(12.6%)<br>Woman<br>N=N/A<br>(7.8%) | Unilateral<br>N= 995 (75.8%)<br>Bilateral n=318<br>(24.2%)    | N/R  | Dexamethasone therapy | Male Gender      | 1- Placement of a surgical drain<br>2- (Receiving burr-hole craniotomy has the lowest recurrence rate) | N/R   | N/R              | N/R           | N/R   |
| 45 | Shuai Han (65)      | cohort        | N=295      | Man<br>N=255<br>Woman<br>N= 40                    | (65.0 ± 14.0)   | N=19<br>(6.4%)  | Total<br>N/A<br>>65<br>N=16<br>(84.2%) | Man<br>N=17<br>(89.5%)<br>Woman<br>N= 2<br>(10/5%)  | Unilateral<br>N=295 (100%)<br>Bilateral<br>N=0 (0%)           | Cerebral atrophy                             | N/R                   | Age (>65 years)  | N/R  | 1- The preoperative CT Density of the hematoma<br>2-Preoperative hematoma volume<br>3-Postoperative imaging findings: (Subdural effusion volume, Degree of cerebral re-expansion, Maximal effusion thickness (>20 mm), and Midline shift (>5 mm)) | N/R              | N/R           | N/R   |
| 46 | Myung-Hoon Han (66) | cohort        | N=756      | Man<br>N=574<br>(75.9%)<br>Woman<br>N=182(24.1%)  | (67.9 ± 8.3)    | N=104<br>(13.8%)<br>Unilateral<br>N=81<br>(77.9%)<br>Bilateral<br>N=23<br>(22.1%) | (68.6 ± 8.5)                           | Man N= 83<br>(79.8%)<br>Woman<br>N= 21<br>(20.2%)   | Unilateral<br>N=645 (85.3%)<br>Bilateral n=111<br>(14.7%)     | Body mass index                              | N/R                   | Age (> 75 years) | Bilateral operation  | N/R   | N/R              | N/R           | N/R   |
| 47 | Min Xu (67)         | cohort        | N=516      | Men<br>N=429<br>Women<br>N= 87                    | (67.09 ± 11.77) | Total<br>N=33<br>(6.40%)<br>Bilateral<br>N=24<br>(N/R %)                          | (68.48 ± 11.07)                        | Man<br>N=30<br>Woman<br>N=3                         | Bilateral<br>N=135(26.16%)<br>Unilateral<br>N=381<br>(73.84%) | N/R  | anticoagulants        | N/R              | N/R  | N/R   | N/R              | N/R           | N/R   |

## Risk Factors of Chronic Subdural Hematoma Recurrence

**Table 2. Description of Included Studies and Summary of Study Findings**

| ID | First author's name | Type of study | population | Sex  | Age         | Recurrence (%)   | Age (Recurrence) | Sex (recurrence)                                    | Type of hematoma/N  | Risk factors of subdural hematoma recurrence |  |             |         |  |                      | Other finding |   |
|----|---------------------|---------------|------------|--|-------------|--|------------------|---|---|--|--|-------------|---------|--|----------------------|---------------|---|
|    |                     |               |            |  |             |  |                  |   |   | Clinical finding                             | Medication                                   | Demographic | Surgery | Radiological findings  | Comorbid disease     |               | Other   |
| 48 | Byung-Soo Ko (68)   | cohort        | N=255      | Man<br>N=150(58.8%)<br>Woman<br>N=105<br>(41.1%)       | (64.8±10.1) | N=24<br>(9.4%)<br>right<br>N=10<br>(41.6%)<br>Left N=12<br>(50.0%)<br>Bilateral<br>N=2<br>(8.3%) | (54.3±8.3)       | Men<br>N=11<br>(45.8%)<br>Women<br>N= 13<br>(54.2%) | Right<br>N= 102<br>(40.0%)<br>Left<br>N= 131<br>(51.4%)<br>Bilateral<br>N= 22 (8.6%)                              | Bleeding tendency                            | N/R  | N/R         | N/R     | preoperative<br>Ct scan<br>density   | N/R                  | N/R           | N/R   |
| 49 | Hyuck-Jin Oh (69)   | cohort        | N=131      | N/R  | N/R         | N= 18<br>(12%)<br>Right N=4<br>(8%)<br>Left N=12<br>(16%)<br>Bilateral<br>N=2 (8%)               | N/R              | N/R   | Right<br>N= 44<br>Left<br>N= 64 Bilat-<br>eral<br>N= 23   | N/R  | N/R  | Age         | N/R     | Thick hematoma<br>(Greater than 20<br>mm)  | N/R                  | N/R           | N/R   |
| 50 | Jongwook Choi (70)  | cohort        | N=230      | Man<br>N=164<br>(71.3%)<br>Woman<br>N=66<br>(28.7%)    | (69.4±13.1) | N=49<br>(21.3%)  | (69.0±15.0)      | Man<br>N= 36<br>(73.5%)<br>Woman<br>N= N/R          | Bilateral<br>N=86 (37.4%)<br>Unilateral<br>N= (N/R )  | N/R  | Preoperative<br>antithrombotic<br>medication | N/R         | N/R     | N/R  | N/R                  | N/R           | N/R   |
| 51 | Naoki Wakuta (71)   | cohort        | N=466      | Man<br>N= 327<br>(70.2%)<br>Woman<br>N= 139<br>(29.8%) | (76.0 11.0) | N=35<br>(7.5%).  | N/R              | N/R   | Unilateral<br>N=396<br>(85.0%)<br>Right<br>N=191<br>(40.1%)<br>Left n=205<br>(44.9%)<br>Bilateral<br>N=72 (15.0%) | N/R  | N/R  | N/R         | N/R     | 1. The presence<br>of trabecular<br>structures<br>2. presence of<br>residual septa<br>3.hematoma<br>clots<br>4. stretching of<br>the cortical<br>vessels<br>5. Maximal<br>hematoma<br>thickness >20<br>mm. | Diabetes<br>mellitus | N/A           | No associa-<br>tion was<br>found with<br>the presence<br>of septa<br>within the<br>cavity |

Table 2. Description of Included Studies and Summary of Study Findings

| ID | First author's name    | Type of study | population | Sex   | Age   | Recurrence (%)   | Age (Recurrence)                           | Sex (recurrence)                                     | Type of hematoma/N   | Risk factors of subdural hematoma recurrence  |                     |                     |                             |  |                  |       | Other finding   |
|----|------------------------|---------------|------------|---|---|--|--|--|--|---|---------------------|---------------------|-----------------------------|--|------------------|-------|---|
|    |                        |               |            |   |   |  |  |  |  | Clinical finding  | Medication          | Demographic         | Surgery                     | Radiological findings  | Comorbid disease | Other |   |
| 52 | Rene Opsenak(72)       | cohort        | N=102      | Man<br>N= 76<br>(70.2%)<br>Woman<br>N= 26<br>(29.8%)  | N/R   | N=7<br>(13.7%)   | N/R  | N/R  | N/R  | N/R   | N/R                 | N/R                 | N/R                         | 1. Preoperative hematoma volume<br>(recurrence vs non-recurrence group) 122.7 ml vs 95.6 ml,<br>2. Post-evacuation hematoma cavity volume<br>(recurrence vs non-recurrence group) 72.0 ml vs 49.8 ml<br>3. postoperative pneumocephalus volume | N/R              | N/R   | N/R   |
| 53 | Motaz Hamed (73)       | cohort        | N=229      | Man<br>N= 155<br>(70.2%)<br>Woman<br>N= 74<br>(31.9%) | N/R   | N=47<br>(20.5%)  | N/R  | Man<br>N= 33<br>(70.2%)<br>Woman<br>N= 14<br>(29.8%) | Unilateral<br>Right<br>N=15<br>(31.9%)<br>Left n=20<br>(42.6%)<br>Bilateral<br>N=12<br>(25.5%) | Blood type O significantly associated   | N/R                 | N/R                 | N/R                         | N/R  | N/R              | N/R   | cSDH recurrence was not related to:<br>1. Thrombocyte aggregation inhibition<br>2. oral anticoagulants                          |
| 54 | Hiroaki Hashimoto (74) | cohort        | N=257      | Man<br>N= 164<br>(74 %)<br>Woman<br>N= 59<br>(26 %)   | Man<br>(75.8±10.4)<br>Woman<br>( 79.9± 8.3) | N= (13.5%)   | Man<br>(79.0±9.4)<br>Woman<br>( 84.6± 5.0) | Man<br>N= 23<br>Woman<br>N= 7                        | Unilateral<br>N= N/A<br>Bilateral<br>N=35(16%)   | postoperative hemiplegia  | N/R                 | Age more than 76    | ventral burr hole positions | bilateral cSDH   | N/R              | N/R   | cSDH recurrence was not related to:<br>The locations of cSDH  |
| 55 | Nadja Grübel (75)      | cohort        | N=189      | Man<br>N= 125(66.1 %)<br>Woman<br>N= 64 (33.9 %)      | Median<br>76                                | 4 weeks<br>N=35<br>(18.6)<br>8-12 weeks<br>N=4<br>(2.1%) | N/R  | N/R  | Unilateral<br>N= 120(67%)<br>Bilateral<br>N= N/R   | Binary logistic regression analysis revealed no statistically significant impact    | anticoagulation use | 1. age<br>2. gender | N/R                         | 1. the initial hemispheric type<br>2. the increasing preoperative midline shift in CT  | N/R              | N/R   | cSDH recurrence was not related to:<br>1. The presence of midline shift<br>2. operation time<br>3. CSDH width,<br>4. GCS<br>N/R |
| 56 | Kenji Yagi (76)        | cohort        | N=477      | Man<br>N= 327 (68.6%)<br>Woman<br>N= 150<br>(31.4%)   | 78.8 ± 9.3                                  | N=39<br>(8.5%)<br>of<br>N=455                            | N/R  | N/R  | N/R  | 1. decreased platelet count, 2. eosinophil-rich blood (≥100 µL in peripheral blood) | N/R                 | N/R                 | N/R                         | N/R  | N/R              | N/R   | N/R   |

## Risk Factors of Chronic Subdural Hematoma Recurrence

**Table 2.** Description of Included Studies and Summary of Study Findings

| ID | First author's name    | Type of study | population | Sex                                     | Age         | Recurrence (%) | Age (Recurrence) | Sex (recurrence)                       | Type of hematoma/N                   | Risk factors of subdural hematoma recurrence                        |  |                                  |   |  |                  | Other finding |  |
|----|------------------------|---------------|------------|---|-------------|----------------|------------------|--|--------------------------------------|---|--|----------------------------------|---|--|------------------|---------------|--|
|    |                        |               |            |   |             |                |                  |  |                                      | Clinical finding  | Medication                               | Demographic                      | Surgery   | Radiological findings  | Comorbid disease |               | Other  |
| 57 | Samer Zawy Alsofy (77) | cohort        | N=90       | N/R                                     | N/R         | N=33/3%        | 74.4 ± 2.66      | N/R                                    | N/R                                  | the existence of a coagulation disorder not treated with medication | N/R                                      | N/R                              | N/R   | 1.hematoma width<br>2.septation  | N/R              | N/R           | cSDH recurrence was not related to:<br><br>1.age,<br>2.gender<br>3. alcohol abuse<br>4. a specific location<br>5. extension over one or both hemispheres<br>6. The surgical method<br>7. anticoagulant medication<br>N/R |
| 58 | Seung woo Lee (78)     | cohort        | N=370      | Man N=256 (69.2%)<br>Woman N=114(30.8%) | 72.16       | N=25 (6.8%)    | 76.72 ± 7.00     | Man N=23 (9%)<br>Woman N=2 (1.8%)      | Unilateral N= 295<br>Bilateral N= 75 | N/R   | N/R                                      | 1.Male gender<br>2. advanced age | burr hole trephination  | 1.bilateral hematoma<br>2. moderate or severe brain atrophy<br>3. separation type<br>4. gradation type<br>5.   | N/R              | N/R           | N/R  |
| 59 | Mehmet Emin AKYUZ (79) | cohort        | N=291      | Man N=216<br>Woman N= 75                | 70.4 ± 11.3 | N=84 (28.8%)   | 70.6 ± 12.7      | Man N=69 (82.1%)<br>Woman N=15 (17.9%) | Unilateral N= 195<br>Bilateral N= 96 | N/R   | N/R                                      | N/R                              | N/R   | 1. preoperative midline shift<br>2. mixed-density hematoma<br>3.internal architecture of hematoma<br>4.membranectomy<br>5. ambient cistern compression<br>hematoma volume (10 mL per increase) | N/R              | N/R           | N/R  |
| 60 | Maoki Matsubara(80)    | cohort        | N=494      | Man N=322 (69.1%)<br>Woman N=144(30.9%) | 79.0 ± 10.1 | N=46 (9.3%)    | N/R              | N/R                                    | N/R                                  | 1.Thrombocytopenia,<br>2.eosinophil-rich peripheral blood           | use of anticoagulant drugs               | N/R                              | N/R   | 1.preoperative CT hematoma thickness,<br>2.hematoma site<br>3.hematoma density<br>4. hematoma volume<br>≤160 cm3 -0,<br>>160 cm3 -1  | N/R              | N/R           | N/R  |
| 61 | Min Chen (81)          | cohort        | N=431      | Man N=350<br>Woman N= 81                | 69.6 ± 9.82 | N=71 (16.47%)  | N/R              | N/R                                    | N/R                                  | Pre-operative GCS score,<br>coagulation function                    | whether a statin was taken after surgery | N/R                              | 1. postoperative residual gas<br>2.unilateral and bilateral surgery | 1.preoperative CT hematoma thickness,<br>2.hematoma site<br>3.hematoma density<br>4. hematoma volume<br>≤160 cm3 -0,<br>>160 cm3 -1  | N/R              | N/R           | N/R  |

Preoperative hematoma volume: larger hematoma volumes create a bigger space between the brain and skull after drainage. This "dead space" impairs brain re-expansion and increases the risk of fluid reaccumulation and hematoma recurrence (23, 34). Brain atrophy: Atrophic brains have more space for fluid collections and less capacity to fill the subdural space after hematoma evacuation. This persistent subdural space encourages rebleeding and prevents healing (23). Septation/ membrane formation: cSDHs often develop internal septations and membranes that compartmentalize the hematoma. These can block complete evacuation and contribute to ongoing inflammation and bleeding.

Drainage Strategies: Effective, prolonged drainage reduces recurrence by continuously removing subdural fluid and promoting brain re-expansion. Shorter drain durations (26), and smaller drainage volumes and smaller volumes of drained fluid correlate with higher recurrence (54). Irrigation with artificial cerebrospinal fluid (CSF) rather than saline helps preserve physiological conditions and reduces irritation and inflammation (42). Reduce risk. Techniques ensuring complete replacement of hematoma volume with CSF and maximal brain re-expansion significantly lower recurrence by eliminating dead space and reducing the stimulus for rebleeding (46).

Controversy exists regarding surgical approaches: while one study (27) found bilateral evacuation superior to unilateral, others (44, 64, 77) reported no difference. Additionally, burr hole trephination (78) and ventral burr hole placement (74) were linked to higher recurrence. Notably, comparisons across studies were complicated by technical variations, for example, irrigation solutions [saline vs artificial CSF] (42), drainage duration of 1 to 7 days (26, 47), which may confound the observed effects of specific procedures.

The most substantial evidence supports optimizing drainage protocols (e.g., longer duration, larger volumes) and using ACF irrigation (42, 46) To minimize recurrence, as these directly address residual hematoma and promote brain re-expansion. The debate over unilateral vs. bilateral evacuation may reflect patient-specific factors (e.g., hematoma laterality, atrophy severity) rather than inherent technique superiority. The increased risk with ventral burr holes underscores the importance of surgeon experience and anatomical precision (74).

### Radiological Factors

A comprehensive analysis of the literature reveals several well-established radiological predictors of cSDH recurrence. Radiological factors cause relapse of cSDH primarily through their impact on brain compression, membrane biology, and impaired healing dynamics. Preoperative imaging characteristics demonstrating a significant association include high-density hematoma, high-density hematomas, and mixed-density components, which often indicate active bleeding or recurrent bleeding episodes within the hematoma, reflecting ongoing vascular fragility and inflammation that promote relapse (24, 35, 60, 61, 65, 68, 81). A midline shift  $>5$ – $10$  mm reflects a significant mass effect and brain compression, which can impair cer-

bral perfusion and delay brain re-expansion. These factors may indirectly increase the risk of recurrence (25, 35, 41, 52, 58, 60, 65, 75, 79). However, some studies have shown conflicting results regarding the predictive value of the midline shift.

Pneumocephalus (air trapped in the cranial cavity) can postoperatively prevent brain expansion and serve as a nidus for inflammation, thereby maintaining the subdural space and encouraging recurrence (24, 28, 33, 41, 58, 59, 61, 72, 81). Preoperative hematoma thickness  $>20$  mm, and larger preoperative hematoma volume (typically  $\geq 150$  mL) and greater residual postevacuation volume (e.g., around 72 mL in recurrence groups) are significantly associated with an increased risk of cSDH (25, 35, 54, 65, 69, 71, 77, 81). Each additional 10 mL increase in volume further raises the recurrence risk due to greater subdural dead space and reduced brain re-expansion, conditions that promote inflammation and rebleeding (32, 34, 41, 59, 60, 65, 72, 80, 81).

Postoperative indicators similarly predictive of recurrence encompass a persistent high (59), iso (48), or mixed-density (51, 68, 79) collections, residual mass effect (50), abnormal subdural fluid density (57), and delayed cerebral re-expansion (65). Postoperative residual hematoma collections (high, iso, or mixed-density), residual mass effect, and abnormal subdural fluid density indicate incomplete hematoma clearance and ongoing pathological processes, such as inflammation or microbleeding. Delayed cerebral re-expansion occurs when the brain fails to fill the post-evacuation space, thereby preserving crevices for hematoma re-accumulation.

Morphological features such as bilaterality (21, 30, 37, 60), separated (28, 77, 78) or layered (46) internal architecture, and increased neo-membrane thickness (63) reflect complex hematoma structure with internal membranes that promote chronic inflammation, fluid persistence, and microvascular bleeding, all contributing to relapse. However, the literature presents some contradictions, particularly regarding the prognostic value of midline shift (75), laterality (42, 74, 77), and hemispheric extension (77).

### Comorbid Disease Factors

The association between comorbidities and the recurrence of cSDH has been investigated in multiple studies. The mechanism by which comorbid disease factors cause relapse of cSDH primarily involves impaired healing, chronic inflammation, and vascular abnormalities.

Diabetes mellitus is a key risk factor due to its association with impaired wound healing, microangiopathy (damage to small blood vessels), and chronic systemic inflammation (22, 34, 45, 52, 54, 56, 71). These effects disrupt proper neomembrane formation and hematoma resolution, leading to persistent bleeding and recurrence. Diabetes-associated capillary vasculopathy, particularly in the outer hematoma membrane's capillary network, may promote hematoma growth or recurrence.

Other significant comorbidities include a history of cerebral infarction (21): cerebral infarction history implicates prior vascular damage and possibly impaired cerebral au-

toregulation, which can contribute to fragile blood vessels and disrupted healing in the subdural space. Malignant neoplasms (48) may affect systemic inflammatory status, immunity, and coagulation pathways, all of which can alter hematoma stability and healing. Hepatic disorders with coagulopathy impair blood clotting (49) increases the risk of bleeding and reduces the body's capacity to resolve a hematoma.

Hypertension likely exacerbates vascular fragility and contributes to microvascular damage, further increasing rebleeding risk. Elevated triglyceride levels may influence inflammatory and angiogenic pathways involved in hematoma persistence (52).

Interestingly, 1 study found no association between cSDH recurrence and diabetes mellitus, vascular diseases, or seizure history (46), highlighting potential variations in study populations or follow-up protocols. Notably, a higher serum HDL level was identified as a protective factor (52), possibly by modulating lipid metabolism, inflammation, and angiogenesis favorably, thereby supporting hematoma resolution.

#### Other Findings

The temporal relationship between symptom onset and medical intervention appears to influence the recurrence risk in cSDH cases significantly. Earlier hospitalization following initial symptom presentation was associated with increased recurrence rates (61), suggesting that premature intervention during the acute inflammatory phase may disrupt natural healing processes. Conversely, delayed treatment during the later stages of spontaneous repair demonstrated protective effects against recurrence (29), potentially due to the more established formation of a neomembrane and hematoma organization. Furthermore, postoperative inflammatory markers, particularly a neutrophil-to-lymphocyte ratio (NLR)  $\geq 1$ , emerged as a significant predictor of recurrence (43), indicating that sustained systemic inflammation following surgical intervention may compromise healing and promote reaccumulation.

These findings suggest several practical considerations for clinical decision-making: For asymptomatic or minimally symptomatic cases, a carefully monitored delay in surgical intervention may be warranted to allow natural stabilization processes. Serial imaging and assessment of inflammatory markers (particularly NLR) could help identify the optimal treatment timing. Postoperative anti-inflammatory strategies merit investigation as potential adjunctive therapies. Patient stratification systems should incorporate both temporal and inflammatory parameters when estimating the risk of recurrence. The apparent contradiction between the benefits of delayed treatment and traditional surgical urgency principles highlights the need for more nuanced management algorithms that balance neurological risk with biological readiness.

#### Discussion

In the present study, we aimed to identify Risk factors of chronic subdural hematoma recurrence. The systematic review reveals critical insights into risk stratification for

chronic subdural hematoma recurrence. Foremost among these are coagulation abnormalities, demonstrated by multiple studies (62, 68, 80) Thrombocytopenia and coagulopathies are significantly associated with an increased risk of recurrence. This strong association, combined with the clinical feasibility of preoperative correction through platelet transfusion or factor replacement, positions coagulation management as the primary target for intervention. Equally compelling is the role of systemic inflammation, where elevated postoperative NLR and neutrophil counts emerge as both predictive markers and potential therapeutic targets, suggesting a possible role for anti-inflammatory strategies in high-risk patients (35, 43, 76).

The consistent association between lower GCS scores and recurrence warrants particular attention, as this may reflect either a more severe initial injury or delayed presentation (53, 56, 81). While one contradictory study exists (75), the weight of evidence supports using GCS as a crucial triage tool for intensive postoperative monitoring. The paradoxical findings regarding blood groups (A and O) present a fascinating avenue for future research, potentially revealing novel pathophysiological mechanisms involving inflammatory or coagulation pathways specific to blood group antigens (73, 76).

Of the non-modifiable factors, cerebral atrophy (65) and recurrence stands out as particularly significant, likely creating mechanical conditions favorable for reaccumulation. This suggests that surgical technique modification, such as prolonged drainage, may be warranted in these patients. The conflicting GOS data (53, 56) highlights the need for standardized outcome measures in future studies, while the less established associations recur with BMI (66) and alcohol (45) May represent secondary targets for intervention.

Antiplatelet and anticoagulant therapies (such as warfarin and enoxaparin) increase the risk of SDH recurrence by impairing blood clot formation and stabilization. These agents interfere with normal hemostatic processes, making it harder to stop bleeding and allowing the hematoma to reaccumulate. Warfarin, a vitamin K antagonist, is particularly implicated due to its strong anticoagulant effect, which can delay hematoma resolution or promote rebleeding.

Dexamethasone's anti-inflammatory action diminishes pro-inflammatory cytokines and angiogenic factors that otherwise promote rebleeding and expansion of the hematoma, thereby lowering recurrence rates, especially in patients with significant residual collections after surgery. ACE inhibitors may similarly reduce the recurrence risk through anti-inflammatory or hemodynamic effects, although the evidence is more limited.

While statins have anti-inflammatory and vascular effects that could theoretically aid in hematoma resolution, some studies suggest higher doses or particular statins may inhibit beneficial angiogenesis or endothelial repair processes, promoting recurrence (81).

The discordant findings on antiplatelet/anticoagulant effects may stem from variations in study design (e.g., dosing protocols, patient comorbidities) or follow-up duration. The protective effects of dexamethasone and ACE

inhibitors suggest that targeting inflammation or blood pressure could be therapeutic strategies, though confirmatory trials are needed. The statin-associated risk is particularly intriguing and may involve pleiotropic effects on angiogenesis or coagulation. Clinicians should weigh these risks against benefits, emphasizing individualized therapy for instance, bridging anticoagulation in high-risk patients or avoiding statins post-craniotomy when feasible (21, 24, 30, 36, 38-41, 50, 58, 73, 75, 77, 80, 81). Future research should prioritize prospective studies to clarify these associations and refine clinical guidelines.

The overwhelming consensus suggests that age is the most critical demographic risk factor for recurrence, given its strong association across multiple studies and its direct link to pathophysiological mechanisms, such as cerebral atrophy and venous vulnerability (33, 40, 75). Male sex, while less universally influential than age, remains clinically relevant, particularly in younger cohorts with traumatic etiologies (36, 48, 75). The contradictory findings in a study (77) may reflect confounding variables (e.g., anticoagulant use, surgical technique) rather than a genuine lack of association. Clinically, these factors should guide risk stratification for elderly males (especially those over 70 years old), who warrant closer monitoring and individualized management to mitigate the risk of recurrence.

The current synthesis of radiological predictors reveals several clinically significant patterns that extend beyond simple enumeration of risk factors. The differential prognostic value of hematoma density patterns (mixed vs homogeneous) likely reflects a distinct underlying pathophysiological state where heterogeneous densities may indicate active rebleeding or impaired fibrinolytic activity. In contrast, homogeneous densities suggest more stable hematoma evolution (82, 83). This biological plausibility explains why density characteristics maintain predictive value across both preoperative and postoperative assessments.

The threshold-dependent nature of midline shift significance (>5mm vs >10 mm) and its modification by brain atrophy present a crucial clinical insight. This relationship suggests that the brain's compensatory capacity, rather than the absolute magnitude of displacement alone, determines recurrence risk. Patients with preexisting atrophy may tolerate a greater shift without compromising the cortical re-expansion potential, explaining the observed discrepancies across studies (82, 84).

The consistent dose-response relationship for hematoma dimensions (width > 20 mm, volume  $\geq$  150 mL) confirms the mechanical contribution to recurrence risk, where larger collections create more substantial barriers to cortical re-expansion. However, the enhanced predictive value when combined with dynamic postoperative measures underscores the importance of evaluating not just initial lesion size, but the brain's physiological response to surgical intervention (34, 82). The identification of potentially modifiable surgical factors (membranectomy consequences, subdural fluid dynamics) shifts the recurrence paradigm from purely patient-dependent factors to treatment-modifiable elements. This has immediate clinical relevance, suggesting that surgical technique refinement could

complement patient selection in recurrence prevention (82).

The robust association between metabolic comorbidities and cSDH recurrence carries significant implications for clinical practice. For neurologists managing these cases, the findings emphasize the necessity of comprehensive metabolic evaluation before surgical intervention, particularly in diabetic patients who demonstrate consistently higher recurrence rates (85). The pathophysiological mechanisms, including microangiopathy, impaired neomembrane formation, and chronic inflammation, suggest that optimal glycemic control perioperatively may improve outcomes. The protective effect of elevated HDL levels introduces a potential modifiable factor, warranting consideration of lipid profile optimization in high-risk patients. Notably, the spectrum of significant comorbidities (cerebrovascular disease, hepatic dysfunction, and hypertension) underscores cSDH as not merely a neurosurgical condition but rather a neurological manifestation of systemic vascular pathology. This paradigm shift suggests that: (1) preoperative optimization of metabolic parameters, (2) individualized postoperative surveillance protocols based on comorbidity burden, and (3) multidisciplinary collaboration with internists and endocrinologists may significantly reduce recurrence rates (85). The occasional contradictory findings likely reflect variations in surgical techniques and population characteristics, rather than invalidating these associations, and highlight the need for standardized protocols in both surgical management and metabolic control. These insights position the neurologist as central to coordinating comprehensive care that addresses both the neurological and systemic aspects of cSDH management.

#### *Pathophysiology and Integration With Risk Factors*

The pathophysiological model of cSDH recurrence integrates key biological processes, including inflammation, coagulation dysfunction, and structural brain alterations, which collectively contribute to hematoma persistence and recurrence.

**Inflammation:** Postoperative and chronic inflammatory responses drive the formation of fragile neomembranes and aberrant angiogenesis within the subdural space. Elevated markers such as neutrophil counts and neutrophil-lymphocyte ratios consistently correlate with recurrence, reflecting heightened inflammatory activity. Clinical factors like advanced age and comorbidities (e.g., diabetes) exacerbate systemic and local inflammation, thereby increasing vascular fragility and promoting hematoma persistence. Anti-inflammatory treatments, such as dexamethasone, demonstrate protective effects, highlighting the mechanistic role of inflammation in mitigating these clinical risks.

**Coagulation Dysfunction:** The use of anticoagulants (e.g., warfarin, enoxaparin) and antiplatelet agents, alongside inherent coagulopathies and thrombocytopenia, impairs effective hemostasis at fragile neovascular sites formed during hematoma resolution. This biochemical vulnerability explains why patients under such therapies exhibit higher recurrence rates. Interestingly, specific

blood groups (A and O) also show association with recurrence, suggesting possible immunohematological involvement in coagulation or inflammation pathways.

**Structural Brain Changes:** Age-related cerebral atrophy leads to an expansion of the subdural space, thereby decreasing the brain's re-expansion potential post-evacuation. This anatomical vulnerability increases the likelihood of hematoma reaccumulation. Radiological markers such as large hematoma volume and significant midline shifts compound this risk by reflecting both mechanical stress and impaired brain compliance.

**Comorbidities and Metabolic Factors:** Chronic conditions such as diabetes mellitus and hypertension exacerbate microvascular fragility and impair wound healing, synergizing with inflammatory and coagulation abnormalities to increase the risk of recurrence. These interactions underscore the multifactorial nature of cSDH pathogenesis.

Ultimately, our model provides a comprehensive framework that illustrates how patient-specific variables mechanistically influence the recurrence of cSDH. This integrative understanding supports the development of tailored clinical interventions, combining surgical optimization with pharmacological modulation and strict management of comorbidities to reduce recurrence.

### Limitations

Despite the comprehensive inclusion of 61 studies and 29,822 patients, our systematic review has several limitations: (1) Inability to Perform Meta-Analysis: The substantial clinical, methodological, and statistical heterogeneity across studies precluded quantitative synthesis. We explicitly address in this review the variability and inconsistency in recurrence definitions (clinical versus radiological), emphasizing their implications for data synthesis and the limitations they impose on quantitative pooling.

Key sources included variability in surgical techniques (e.g., drainage duration, irrigation methods, evacuation approaches). Inconsistent definitions of recurrence (radiological vs. clinical criteria; follow-up periods ranging from 4 weeks to 12 months). Diverse study designs (retrospective cohorts vs. a single RCT). Heterogeneous patient populations (e.g., anticoagulant regimens, comorbidity profiles). Subgroup/sensitivity analyses were unfeasible due to the insufficient number of studies per stratum (e.g., only 3 studies used artificial CSF irrigation). (2) Risk of overgeneralization: Conclusions rely on narrative synthesis rather than pooled effect estimates. While we prioritized factors replicated across  $\geq 5$  studies (e.g., age  $> 70$  years, bilateral hematomas), residual confounding from unmeasured variables (e.g., surgeon experience) may affect reliability. (3) Data Reporting Gaps: Critical covariates (e.g., hematoma density thresholds, exact drainage volumes) were inconsistently reported, limiting adjustment for confounders. (4) Heterogeneity in recurrence definitions (radiological vs. clinical) precluded stratification. However, sensitivity analyses excluding ambiguously defined studies confirmed the robustness of key risk factors (e.g., bilateral hematomas, antiplatelet use). (5) Also, formal tests for publication bias (e.g., funnel plots) were

not feasible due to the narrative synthesis approach and heterogeneity in risk factor reporting. However, consistency across extensive, high-quality studies raises concerns about small-study effects. (6) Another limitation of this study is that most included studies did not adequately adjust for confounding or interaction effects between risk factors such as diabetes and hypertension. Therefore, the independent impact of each risk factor on recurrence remains unclear, and overlapping comorbidities may influence the observed associations.

### Conclusion

Building on the comprehensive integration of biological mechanisms and clinical risk factors outlined in this review, future research should prioritize investigations that develop and validate standardized perioperative protocols tailored to these intertwined pathways. This includes optimizing surgical techniques, drainage duration, and post-operative monitoring with consideration of individual biological and clinical profiles. Additionally, there is a critical need for standardized definitions, uniform follow-up protocols, and clear clinical versus radiological recurrence criteria to improve comparability and validity of future research. A key research focus should be the development of predictive models that combine clinical, radiological, laboratory, and biological markers, such as inflammatory and coagulation parameters, to enable early and precise identification of high-risk patients for targeted interventions.

Further elucidation of the mechanistic roles of non-modifiable factors, including cerebral atrophy and blood group antigens, is essential to refine tailored surgical and follow-up strategies. Additionally, understanding the long-term effects of inflammation and coagulopathy will inform pharmacological management and the development of potential novel therapies. Addressing these aims through well-designed prospective studies and multicenter clinical trials will be crucial for establishing evidence-based, biologically informed, and patient-specific management protocols that effectively reduce the recurrence of chronic subdural hematoma.

Addressing these aims through well-designed prospective studies with comprehensive data collection and large-scale, multicenter clinical trials will be crucial for establishing evidence-based, biologically informed, and patient-specific management protocols to effectively reduce cSDH recurrence.

### Authors' Contributions

S.A.S.A., S.Y., I.A.F., E.E.B., A.M., and S.N.P. designed the study, pooled data, and wrote the initial findings. S.A.S.A., E.M., F.F.R., F.F., I.A.F., H.S., E.E.B., N.M., S.N.P., S.Y., N.E., E.F., and A.T. helped with writing and edited the paper. S.Y. and A.M. performed the search and extraction of data. S.A.S.A., E.M., F.F.R., F.F., I.A.F., H.S., E.E.B., N.M., S.N.P., S.Y., N.E. were involved with editing and advice. The authors read and approved the final manuscript.

**Ethical Considerations**

Not applicable.

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Not applicable.

**Conflict of Interests**

The authors declare that they have no competing interests.

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