Factors correlated with the postoperative recurrence of chronic subdural hematoma: An umbrella study of systematic reviews and meta-analyses

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Summary

Background Chronic subdural hematoma (CSDH) is a common neurological disease, and the surgical evacuation of subdural collection remains the primary treatment approach for symptomatic patients. Postoperative recurrence is a serious complication, and several factors are correlated with postoperative recurrence.

Methods We searched Embase, Web of Science, PubMed, and Cochrane Library from their establishment to September 2020. Reports on randomized, prospective, retrospective, and overall observational studies on the management of surgical patients with CSDH were searched, and an independent reviewer performed research quality assessment. Factors that affect the postoperative recurrence of CSDH were extracted: social demographics, drugs (as the main or auxiliary treatment), surgical management, imaging, and other risk factors. We evaluated the recurrence rate of each risk factor. A random effect model was used to perform a meta-analysis, and each risk factor affecting the postoperative recurrence of CSDH was then evaluated and graded.

Findings In total, 402 studies were included in this analysis and 32 potential risk factors were evaluated. Among these, 21 were significantly associated with the postoperative recurrence of CSDH. Three risk factors (male, bilateral hematoma, and no drainage) had convincing evidence. The classification of evidence can help clinicians identify significant risk factors for the postoperative recurrence of CSDH.

Interpretation Only few associations were supported by high-quality evidence. Factors with high-quality evidence may be important for treating and preventing CSDH recurrence. Our results can be used as a basis for improving clinical treatment strategies and designing preventive methods.

Funding No funding was received.

Keywords: Chronic subdural hematoma; Recurrence; Risk factors; Meta-analyses; Umbrella review

EClinicalMedicine 2022;43: 101234
Published online xxx
https://doi.org/10.1016/j.eclinm.2021.101234

Introduction

Chronic subdural hematoma (CSDH) is a collection of fluid, blood, and blood degradation products between the arachnoid membrane and the dura that cover the brain surface. The annual incidence of CSDH is approximately 1.7 per 100,000 people worldwide, and the incidence significantly increases with age (8–58 per 100,000 patients aged >65 years).[1] The average age at CSDH onset is 76.8 years.[2] CSDH evacuation has been projected to become the most common cranial neurosurgical procedure among adults by the year 2030 in the United States.[3] The occurrence and progression of CSDH are correlated with a high permeability of new pathological blood vessels, inflammatory mediator release, and local coagulation mechanisms.[4] The surgical evacuation of subdural collection remains the primary treatment approach for symptomatic patients.[5]

The recurrence rate of hematoma after surgery is 10.9%–26.3%.[6,7] Recurrence is a serious complication that leads to a significant economic burden to the society and family.[8] The postoperative recurrence of subdural hematoma is a tertiary outcome defined as a symptomatic recurrence that leads to the reoperation of a previously evacuated ipsilateral CSDH.[5]

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Research in context

Evidence before this study

Chronic subdural hematoma (CSDH) is one of the most common neurosurgical disorders, and while most cases are resolved by cranial drilling, its recurrence is still a problem for clinicians. The risk factors for postoperative CSDH recurrence include general clinical characteristics, surgical skills, perioperative management methods, and imaging characteristics. The factors that play a major role in postoperative recurrence are unclear.

Added value of this study

We performed an umbrella study of systematic reviews and meta-analyses of CSDH recurrence risk factors. In total, thirty-two risk factors were investigated. Among them, twenty-one were significantly associated with the postoperative recurrence of CSDH. According to predefined credibility criteria, three risk factors had convincing evidence, one risk factor had highly suggestive evidence, six risk factors had suggestive evidence, and eleven risk factors had weak evidence.

Implications of all the available evidence

Among the risk factors affecting postoperative recurrence, three risk factors (male sex, bilateral hematoma, and no drainage) had convincing evidence. Further high-quality randomized controlled trials will help to confirm the results of our study and provide support for clinical treatment in the future.

Different strategies have been used to assess the risk factors of CSDH. The most common factors have been evaluated via a comparative study between the nonrecurrent and recurrent groups. Moreover, factors correlated with recurrence have been analyzed via a single-center study. The recurrence rate of CSDH is relatively low; hence, in studies with a limited sample size, the number of patients in the recurrence group is relatively small. Based on a multivariate analysis, evident biases can affect imaging results. In this study, the recurrence-related risk factors differed and the impact of these factors on recurrence was not fully elucidated. A previous literature review revealed that several clinical studies and meta-analyses have investigated the existing risk factors of CSDH recurrence.[6,9,10] These factors include the general clinical characteristics of patients, surgical skills, perioperative management methods, and imaging characteristics. However, the results of these studies are not the same (e.g., sex[11,12], and density of hematoma[13,14]). Moreover, which factors play a primary and secondary role in postoperative CSDH recurrence has not been studied. Therefore, this study aimed to perform a systemic review and meta-analysis to collect, update, and assess evidence across existing clinical research and meta-analyses and to provide an overview of the risk factors associated with postoperative CSDH recurrence. Moreover, the amount and strength of evidence, presence of biases, and robustness of the associations between the potential risk factors and recurrence were evaluated.

Methods

Protocol

We performed a systematic review and meta-analysis; the research protocol was established based on the Meta-analysis Of Observational Studies in Epidemiology and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses.[15,16]

Literature search

We performed a systematic search in Embase, Web of Science, PubMed, and Cochrane Library from their establishment to September 2020. Key words and medical subject heading terms associated with the condition (i.e., CSDH, chronic subdural, hematoma, haematoma, hemorrhage, hemorrhage, and recurrence) were cross-referenced with terms pertinent to postoperative recurrence (i.e., burr hole, twist drill, percutaneous, craniotomy, endoscopy, embolization of middle meningeal artery (MMA), steroid, atorvastatin, Goreisan, ACEI, management, treatment, surgery, evacuation, irrigation, drainage, computed tomography (CT) or magnetic resonance imaging, systematic reviews, and meta-analyses) in relevant combinations. All studies considered relevant by the evaluator were included, and qualified research references were manually retrieved. All identified publications underwent a parallel review of titles, abstracts, and full texts.

Eligibility criteria

Duplicate references and articles with a sample size of <15 consecutive patients were not included. Moreover, we excluded references regarding the treatment outcomes of mixed acute and subacute subdural hematomas as well as references with mixed conservative and surgical treatment outcomes. Studies without clear treatment options and those with nonsurgical treatment outcomes and reports that only examined infants with CSDH and nonhuman species were not considered. Incomplete reports, case reports, abstracts provided in meetings, and letters to the editor were also excluded. Studies that evaluated the treatment of patients with clinical symptoms on radiology and those with one or more follow-up management outcomes were included. Most studies recorded only the first recurrence. Compared with the first postoperative recurrence, the second recurrence after surgery has many interfering factors. Therefore, we recorded only the first recurrence in our analysis. Finally, when there were two or more meta-

analyses examining the correlation between the same risk factors and outcomes, the most recent meta-analysis with the largest number of events was prioritized and included for further analysis. Finally, we assessed whether the results reported in overlapping meta-analysis were consistent in terms of direction, statistical significance, and relevance.

Data extraction

Data were extracted by five investigators and assessed by a sixth investigator. Disagreements were resolved via a consensus discussion. We collected information from eligible articles. Data about the following items were then extracted: study information (title, first author, publication year, study design, total number of treated patients, follow-up time, and CSDH recurrence), patient data (age, sex, Markwalder grading, and GCS and GOS scores), total number of CSDHs (including bilateral cases), disease history (hypertension, diabetes, cardiovascular disease, brain atrophy, cerebral infarction, and epilepsy), number of patients who previously used antiplatelet or anticoagulant drugs, imaging findings (internal structure of the hematoma, density on CT, hematoma width, midline shift distance, and hematoma volume), main drug therapy (atorvastatin, Goreisan, steroids, and ACEI), and surgical management (percutaneous twist-drilling drainage, burr hole, craniotomy, single or multiple holes, use of drainage, duration of drainage, flushing of the drainage cavity, type of fluid used for drainage cavity flushing, location of the drainage tube, drainage volume, position of the head of the bed after surgery, and time spent in bed).

Evidence extraction and quality assessment

Research quality was evaluated by five reviewers. The modified Jadad Scale was used to evaluate the quality of RCT, with a score of 1–3 and 4–7 indicating low and high quality, respectively. The Newcastle–Ottawa Quality Assessment Scale was used to assess the quality of observational research, and a score of >4 indicated high-quality research. Based on the evaluation results, we performed a meta-analysis of high-quality studies. Any differences between the two examiners were resolved via a consensus discussion with the third examiner (Supplementary material 1).

Statistical analyses

We individually analyzed each risk factor that affects postoperative CSDH recurrence (Supplementary material 2). First, we use a random effects model to calculate the weighted mixing ratio. If $I^2 > 50\%$ after the random effects model calculation, a subgroup analysis was performed according to study type or score quality.[17] All results generated a forest map. A p value of < 0.05 was considered statistically significant. We then calculated relative risks and 95% confidence intervals. Publication bias was visually evaluated using the funnel plot and quantified using the Egger's and Begg's tests ($p < 0.05$ indicated publication bias). We performed a sensitivity analysis of each independent study. Based on these indicators, we used a grading system for the strength of evidence.[18,19] The credibility of the evidence for each risk factor was assessed, and the evidence was classified into convincing (class I), highly suggestive (class II), suggestive (class III), and weak (class IV) (Supplementary material 4: Table S33). Stata 12.0 (StataCorp. Stata statistical software: Release 12.StataCorp, 2011) was used for all statistical analyses.

Role of the funding source

No funding was received. Fulei Zhu, Haifeng Wang and Wenchen Li, who contributed equally as the corresponding authors, took the responsibility of data deposit, collection of all information from the other authors, and submitting the current manuscript.

Results

Literature review

In total, 7530 studies were retrieved from the systematic search of databases. Via duplicate checking, the title and abstract of all articles were screened and irrelevant studies were excluded. After reviewing the full-text versions of the remaining publications, 131 articles were excluded (Figure 1). Finally, 402 studies met the inclusion criteria (Supplementary material 3) and 32 risk factors associated with the postoperative recurrence of CSDH were analyzed (Supplementary material 4).

Meta-analysis of risk factors for the postoperative recurrence of CSDH

We identified 32 meta-analyses on the risk factors for the postoperative recurrence of CSDH (Table 1). Overall, 21 of the 32 unique meta-analyses reported an effect size of $p < 0.05$. According to the predefined credibility criteria, three risk factors had convincing evidence, one risk factor had highly suggestive evidence, six risk factors had suggestive evidence, and eleven risk factors had weak evidence (Figure 2). More than 1000 patients presented with 25 risk factors, and 1 risk factors had significant heterogeneity ($I^2 > 50\%$). In addition, four risk factors showed publication bias.

Epidemiological risk factors

Three risk factors (male (RR, 1.32; 95%CI, 1.50 - 1.51; $I^2 = 0$; $p < 0.001$) and bilateral hematomas (RR, 1.41; 95%CI, 1.20 - 1.67; $I^2 = 28.2$; $p < 0.001$)) had convincing (class I) evidence, one risk factor (diabetes mellitus (RR, 1.40; 95%CI, 1.18 - 1.68; $I^2 = 28.7$; $p < 0.001$) and brain atrophy (RR, 1.94; 95%CI, 1.26 - 3.01; $I^2 = 26.6$; $p = 0.003$)) had suggestive (class III) evidence, and one

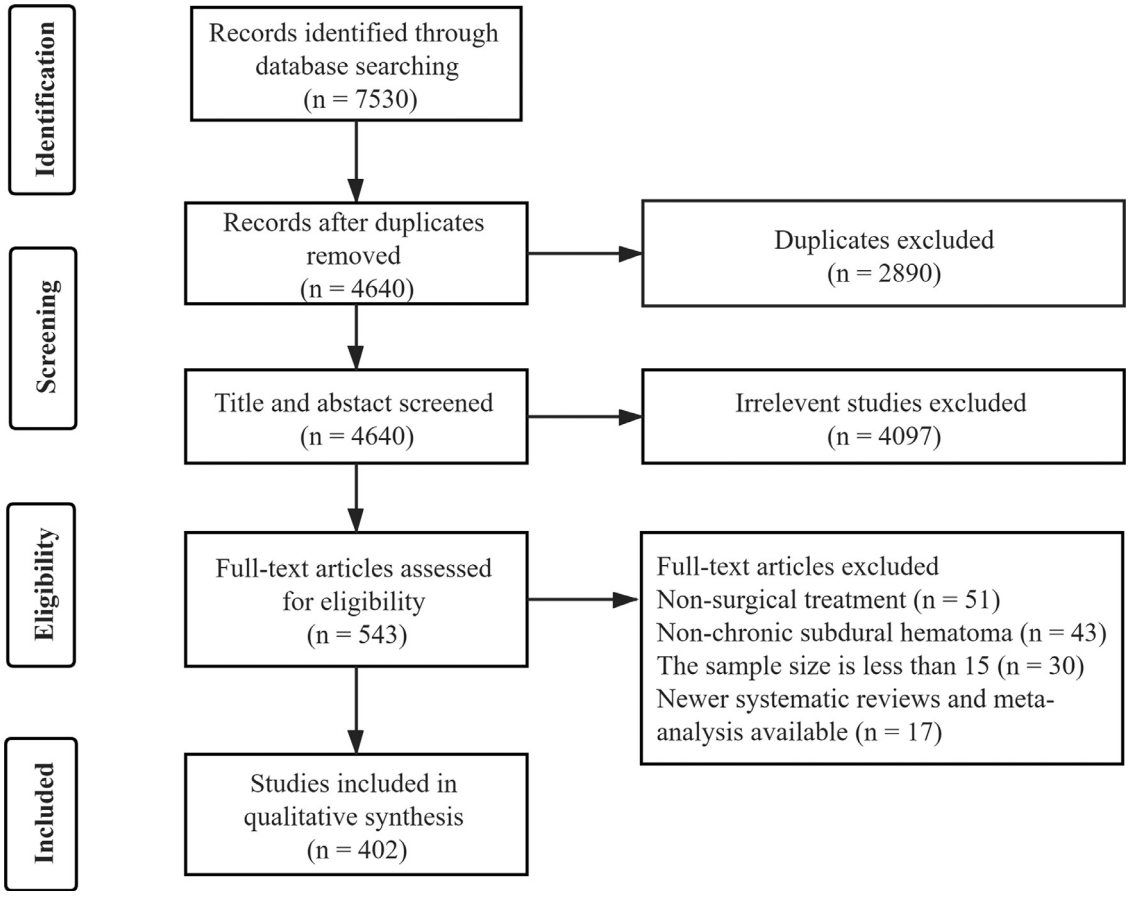


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

risk factor (liver injury (RR, 1.15; 95%CI, 1.02 - 1.31; $I^2 = 0$; $p = 0.026$)) had weak (class IV) evidence. However, hypertension, heart disease, alcohol abuse, epilepsy, and cerebral infarction were not significant.

Drug use

Two risk factors (non-goreisan (RR, 0.79; 95%CI, 0.67 - 0.93; $I^2 = 0$; $p = 0.005$) and antithrombotic drugs (RR, 1.29; 95%CI, 1.14 - 1.45; $I^2 = 18.8$; $p < 0.001$)) had suggestive (class III) evidence and two risk factors (non-corticosteroid (RR, 0.41; 95%CI, 0.24 - 0.70; $I^2 = 0$; $p = 0.001$) and non-atorvastain (RR, 0.31; 95%CI, 0.14 - 0.69; $I^2 = 0$; $p = 0.005$)) had weak (class IV) evidence.

Surgical management

One risk factor (no drainage of hematoma cavity (RR, 0.45; 95%CI, 0.33 - 0.60; $I^2 = 0$; $p < 0.001$)) had convincing (class I) evidence, five risk factors (craniostomy (RR, 0.71; 95%CI, 0.52 - 0.99; $I^2 = 40.8$; $p = 0.042$), nonfrontal drainage position (RR, 0.61; 95%CI, 0.37 - 1.00; $I^2 = 25.9$; $p = 0.048$), no MMA embolization (RR, 0.24; 95%CI, 0.08 - 0.75; $I^2 = 39.5$; $p = 0.014$), endoscopic hematoma diaphragm resection (RR, 0.39; 95%CI, 0.17 - 0.92; $I^2 = 41.4$; $p = 0.031$), and non-artificial cerebrospinal fluid lavage (RR, 0.35; 95%CI, 0.19 - 0.63; $I^2 = 0$; $p < 0.001$)) had weak (class IV) evidence.

Imaging risk factors

One risk factor (larger hematoma volume (RR, 0.73; 95%CI, 0.51 - 0.94; $I^2 = 38.6$; $p < 0.001$)) had highly suggestive (class II) evidence; two risk factors (hematoma width ≥ 20 mm (RR, 2.37; 95%CI, 1.56 - 3.60; $I^2 = 24.1$; $p < 0.001$) and midline shift ≥ 10 mm (RR, 1.61; 95%CI, 1.17 - 2.22; $I^2 = 41.7$; $p = 0.004$)) had suggestive (class III) evidence and two risk factors (high + mixed density hematoma (RR, 1.78; 95%CI, 1.13 - 2.78; $I^2 = 73.6$; $p = 0.011$) and heterogeneous hematoma (RR, 0.76; 95%CI, 0.60 - 0.98; $I^2 = 43.4$; $p = 0.030$)) had weak (class IV) evidence.

Discussion

We initially extracted and evaluated the evidence regarding risk factors for postoperative CSDH recurrence. In 402 clinical studies, 32 risk factors for the postoperative recurrence of CSDH were identified and evaluated.

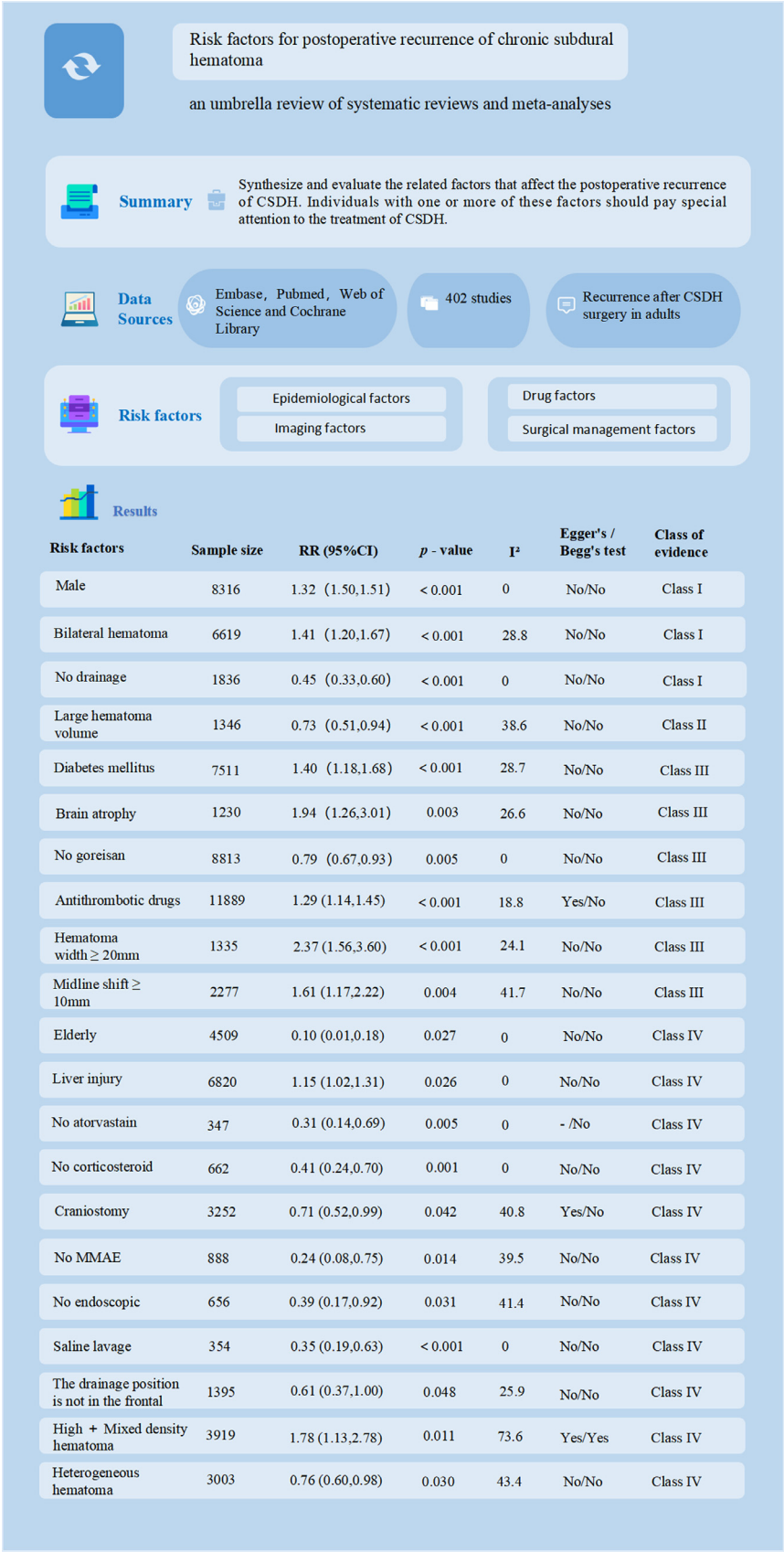
	Rick factors	Study	Comparison	Sample size	Number of studies	RR/SMD (95%CI)	p-value	95%PI	I^2(%)	Egger's / Begg's test	Largest study RR/SMD (95%CI)	Class of evidence
Epidemiological factors	Age	Table S1	(Recurrence group) vs (No recurrence group)	4509	21	0.10 (0.01,0.18)	0.027	(0.01,0.19)	0	0.55 / 0.70	−0.04 (−0.31,0.23)	IV
	Sex	Table S2	Male vs Female	8316	36	1.32 (1.50,1.51)	<0.001	(1.13,1.73)	0	0.14 / 0.19	1.65 (1.03,2.67)	I
	Hematoma site	Table S3	Bilateral vs Unilateral	6619	28	1.41 (1.20,1.67)	<0.001	(0.80,2.76)	28.2	0.70 / 0.49	1.65 (1.09,2.50)	I
	Hypertension	Table S4	Yes vs No	6956	25	1.00 (0.88,1.13)	0.983	(0.78,1.25)	1.1	0.76 / 0.66	1.34 (0.92,1.94)	ns
	Diabetes mellitus	Table S5	Yes vs No	7511	26	1.40 (1.18,1.68)	<0.001	(0.77,2.79)	28.7	0.42 / 0.31	0.98 (0.61,1.57)	III
	Cardiovascular disease	Table S6	Yes vs No	4036	14	1.13 (0.94,1.36)	0.206	(0.87,1.44)	0	0.80 / 0.74	1.13 (0.72,1.77)	ns
	Liver injury	Table S7	Yes vs No	6820	13	1.15 (1.02,1.31)	0.026	(1.00,1.41)	0	0.29 / 0.43	1.11 (0.96,1.28)	IV
	Alcohol abuse	Table S8	Yes vs No	2494	9	1.28 (0.97,1.68)	0.84	(0.89,1.94)	0	0.55 / 0.60	1.40 (0.86,2.31)	ns
	Brain atrophy	Table S9	(Definite and severe) vs (No and mild)	1230	6	1.94 (1.26,3.01)	0.003	(0.61,7.86)	26.6	0.72 / 0.71	5.59 (2.09,15.00)	III
	Epilepsy	Table S10	Yes vs No	1842	8	1.22 (0.68,2.20)	0.511	(0.41,2.66)	0	0.96 / 0.71	3.78 (0.93,15.42)	ns
	Cerebral infarction	Table S11	Yes vs No	979	4	1.41 (0.87,2.30)	0.167	(0.27,7.62)	0	0.22 / 0.73	1.36 (0.59,3.13)	ns
Drug factors	Atorvastain	Table S12	Yes vs No	347	2	0.31 (0.14,0.69)	0.005	—	0	— / 1.0	0.35 (0.14,0.86)	IV
	Goreisan	Table S13	Yes vs No	8813	6	0.79 (0.67,0.93)	0.005	(0.60,1.00)	0	0.52 / 0.71	0.78 (0.64,0.93)	III
	Corticosteroid	Table S14	Yes vs No	662	5	0.41 (0.24,0.70)	0.001	(0.13,0.93)	0	0.187 / 0.806	0.41 (0.18,0.93)	IV
	Antithrombotic drugs	Table S15	Yes vs No	11,889	39	1.29 (1.14,1.45)	<0.001	(0.87,2.02)	18.8	0.004 / 0.14	1.02 (0.66,1.57)	III
		Table S15	Anticoagulation vs No	6866	27	1.31 (1.09,1.56)	0.003	(0.80,2.17)	23.9	0.32 / 0.32	1.09 (0.64,1.89)	III
		Table S15	Antiplatelet vs No	8120	28	1.27 (1.07,1.50)	0.006	(0.68,2.48)	28.6	0.283 / 0.678	0.76 (0.40,1.43)	III
		Table S15	Anticoagulation vs Antiplatelet	2408	22	1.09 (0.87,1.37)	0.464	(0.57,2.09)	25.5	0.79 / 0.82	1.86 (0.88,3.94)	ns
Surgical management factors	Type of anesthesia	Table S16	General vs Local	2244	6	1.02 (0.82,1.27)	0.878	(0.71,1.47)	0	0.13 / 0.13	0.98 (0.65,1.46)	ns
	Surgical techniques	Table S17	BHC vs TDC	1889	10	1.11 (0.73,1.68)	0.634	(0.31,3.90)	45.7	0.40 / 0.28	1.22 (0.85,1.75)	ns
		Table S18	SBHC vs DBHC	1458	8	1.05 (0.74,1.49)	0.793	(0.48,2.35)	17.5	0.45 / 0.54	1.91 (0.88,4.16)	ns
		Table S19	BHC vs Craniostomy	3252	14	0.71 (0.52,0.99)	0.042	(0.23,2.09)	40.8	0.01 / 0.10	0.69 (0.40,1.19)	IV
		Table S20	MMAE vs No	888	4	0.24 (0.08,0.75)	0.014	(0.00,63.32)	39.5	0.81 / 0.73	0.05 (0.01,0.36)	IV
		Table S21	Endoscopic vs No	656	5	0.39 (0.17,0.92)	0.031	(0.02,5.52)	41.4	0.20 / 0.09	0.04 (0.002,0.67)	IV
	Irrigation	Table S22	Yes vs No	1109	9	0.86 (0.49,1.51)	0.591	(0.13,5.23)	42.3	0.51 / 0.75	1.17 (0.69,1.99)	ns
	Irrigation solution	Table S23	(ACF group) vs (Normal saline group)	354	2	0.35 (0.19,0.63)	<0.001	—	0	— / 1.00	0.38 (0.20,0.72)	IV
	Drainage	Table S24	Yes vs No	1836	9	0.45 (0.33,0.60)	<0.001	(0.25,0.59)	0	0.31 / 0.35	0.51 (0.29,0.88)	I
	Drainage methods	Table S25	SPGD vs SDD	4215	13	0.86 (0.72,1.03)	0.094	(0.67,1.06)	0	0.08 / 0.73	0.66 (0.50,0.87)	ns

Table 1 (Continued)

	Rick factors	Study	Comparison	Sample size	Number of studies	RR/SMD (95%CI)	p-value	95%PI	I^2(%)	Egger's / Begg's test	Largest study RR/SMD (95%CI)	Class of evidence
	Position of drainage	Table S26	Frontal vs Others	1395	7	0.61 (0.37,1.00)	0.048	(0.14,2.13)	25.9	0.56 / 1.00	0.78 (0.40,1.46)	IV
	Postoperative bed header position	Table S27	Supine vs Sitting	234	4	0.88 (0.41,1.87)	0.737	(0.03,23.43)	28.3	0.51 / 1.00	0.13 (0.02,0.96)	ns
Imaging factors	Hematoma density	Table S28	(High+Mixed density) vs (Iso+Low density)	3919	20	1.78 (1.13,2.78)	0.011	(0.25,15.81)	73.6	0.01 / 0.001	1.53 (0.81,2.91)	IV
	Hematoma structure	Table S29	Heterogeneous vs Homogeneous	3003	16	0.76 (0.60,0.98)	0.030	(0.29,1.78)	43.4	0.78 / 0.89	0.84 (0.54,1.30)	IV
		Table S29	Type 1 vs Type 2	1997	10	0.79 (0.59,1.05)	0.1	(0.32,1.72)	35.6	0.70 / 0.37	0.78 (0.50,1.23)	ns
		Table S29	Type A vs Type B	1997	10	1.38 (1.08,1.76)	0.011	(0.77,2.85)	19.9	0.005 / 0.07	1.09 (0.70,1.70)	IV
	Hematoma width	Table S30	≥20 mm vs <20mm	1335	7	2.37 (1.56,3.60)	<0.001	(1.07,6.74)	24.1	0.28 / 0.23	1.61 (0.82,3.15)	III
	Hematoma volume	Table S31	(Recurrence group) vs (No recurrence group)	1346	8	0.73 (0.51,0.94)	<0.001	(0.20,1.26)	38.6	0.08 / 0.04	0.55 (0.06,1.04)	II
	Midline shift	Table S32	≥10 mm vs <10mm	2277	11	1.61 (1.17,2.22)	0.004	(0.65,4.74)	41.7	0.29 / 0.21	1.01 (0.62,1.65)	III

***Table 1*: Risk factors showing convincing (class I), highly suggestive (class II), suggestive(class III), or weak (class IV) evidence of association with postoperative recurrence of chronic subdural hematoma.**

Abbreviations: CI, confidence interval; I^2, heterogeneity; RR, Relative risk; PI, prediction interval; SMD, Standardized mean difference; ns, Not significant; SBHC, single burr hole Craniostomy; DBHC, double burr hole Craniostomy; TDC, twist burr Craniostomy; MMAE, Embolization of middle meningeal artery; SDD, subdural drainage; SPGD, subperiosteal or subgaleal drainage; ACF, Artificial cerebrospinal fluid; Type 1 (Isodense and hypodense types); Type 2 (hyperdense, laminar, separated, gradation and trabecular types); Type A (hyperdense, laminar and separated, gradation types); Type B (Isodense, hypodense and trabecular types); Table S1 to Table S32 are presented in the supplementary material 4.



Risk factors	Sample size	RR (95%CI)	*p* - value	I^2	Egger's / Begg's test	Class of evidence
Male	8316	1.32 (1.50,1.51)	< 0.001	0	No/No	Class I
Bilateral hematoma	6619	1.41 (1.20,1.67)	< 0.001	28.8	No/No	Class I
No drainage	1836	0.45 (0.33,0.60)	< 0.001	0	No/No	Class I
Large hematoma volume	1346	0.73 (0.51,0.94)	< 0.001	38.6	No/No	Class II
Diabetes mellitus	7511	1.40 (1.18,1.68)	< 0.001	28.7	No/No	Class III
Brain atrophy	1230	1.94 (1.26,3.01)	0.003	26.6	No/No	Class III
No goreisan	8813	0.79 (0.67,0.93)	0.005	0	No/No	Class III
Antithrombotic drugs	11889	1.29 (1.14,1.45)	< 0.001	18.8	Yes/No	Class III
Hematoma width ≥ 20mm	1335	2.37 (1.56,3.60)	< 0.001	24.1	No/No	Class III
Midline shift ≥ 10mm	2277	1.61 (1.17,2.22)	0.004	41.7	No/No	Class III
Elderly	4509	0.10 (0.01,0.18)	0.027	0	No/No	Class IV
Liver injury	6820	1.15 (1.02,1.31)	0.026	0	No/No	Class IV
No atorvastain	347	0.31 (0.14,0.69)	0.005	0	- /No	Class IV
No corticosteroid	662	0.41 (0.24,0.70)	0.001	0	No/No	Class IV
Craniostomy	3252	0.71 (0.52,0.99)	0.042	40.8	Yes/No	Class IV
No MMAE	888	0.24 (0.08,0.75)	0.014	39.5	No/No	Class IV
No endoscopic	656	0.39 (0.17,0.92)	0.031	41.4	No/No	Class IV
Saline lavage	354	0.35 (0.19,0.63)	< 0.001	0	No/No	Class IV
The drainage position is not in the frontal	1395	0.61 (0.37,1.00)	0.048	25.9	No/No	Class IV
High + Mixed density hematoma	3919	1.78 (1.13,2.78)	0.011	73.6	Yes/Yes	Class IV
Heterogeneous hematoma	3003	0.76 (0.60,0.98)	0.030	43.4	No/No	Class IV

Figure 2. Summary of factors correlated with the postoperative recurrence of chronic subdural hematoma.

CSDH primarily occurs in elderly individuals, with an average age of 76.8 years at onset.[2] Results showed that the recurrence group was significantly older than the nonrecurrence group. Recurrence among elderly individuals may be attributed to the more frequent use of antiplatelet and anticoagulant drugs, brain atrophy, poor postoperative re-expansion of brain tissues, and increased incidence of minor trauma (including falls). Therefore, relapse is more likely to occur in this patient group.[20–22]

The incidence of CSDH was significantly higher in men than in women. In addition, men had a significantly higher recurrence rate than women.[6,23] Sex is a class II risk factor correlated with postoperative recurrence. Men have a higher incidence of chronic diseases, including diabetes[24] and liver damage,[25] and are more frequently treated with dual antibodies,[26] which is a high-risk factor of recurrence. Thus, men have a high recurrence rate.

The incidence of single CSDH is significantly higher than that of bilateral CSDH.[27] Nevertheless, bilateral recurrence is more likely to occur.[28] It is a class I risk factor associated with postoperative recurrence. The age at the onset of bilateral CSDH is advanced, and brain atrophy is more evident at that age. Hence, postoperative cerebral expansion is poor, hematoma cavity is large, and hematoma is more likely to accumulate again and lead to recurrence.[27]

The CSDH population primarily comprises elderly individuals with chronic diseases. Diabetes, brain atrophy, liver disease, and use of antithrombotic drugs are the risk factors of postoperative recurrence. Diabetes can cause microvascular disease as well as exudation and bleeding around the microvessels and increase the fragility of the microvessel walls.[29,30] Meanwhile, liver disease and the use of dual antibody treatment can cause coagulation disorders.[31] Brain atrophy plays a critical role in the occurrence and progression of CSDH. Brain atrophy in patients with CSDH will progress further, leading to dementia.[32] Moreover, it reduces the compliance of brain tissues. The compressed brain tissue after surgery is not easy to expand, leading to hematoma recurrence.[33]

Hypertension, cardiovascular disease, alcohol abuse, and cerebral infarction were not correlated with recurrence. Previous studies have reported that the perioperative period of CSDH may be secondary to epilepsy.[34] However, whether it is correlated with recurrence was not validated.

The pathophysiological mechanism of CSDH is a complex cascade of reactions that is correlated with the high permeability of new pathological blood vessels, inflammatory mediator release, and local coagulation mechanisms.[4] The type of drug selected can affect the abovementioned pathophysiological factors, and some drugs can significantly reduce postoperative recurrence. Among the drugs, steroids have been proposed by European and American scholars,[35] atorvastatin by Chinese scholars,[36] and Goreisan by Japanese scholars.[37] The mechanisms of action of the three drugs differ. Steroids can effectively inhibit inflammation.[35] Atorvastatin primarily reduces pathological vascular proliferation and has anti-inflammatory effects.[36] Goreisan, a Japanese herbal Kampo medicine, regulates the expression and function of AQP4, which is expressed on the outer membranes of CSDH and correlated with the degree of inflammatory cell invasion.[37] A number of clinical studies are being currently conducted to evaluate the effect of perioperative drug treatment against CSDH recurrence.[36,38,39] However, more clinical trials are needed.

Surgical CSDH treatment is based on the surgeons' preference and the pathological characteristics of the hematoma. Previous studies have compared the relationship between different surgical methods and recurrence.[11,40] We updated and summarized clinical studies and analyzed the relationship between different surgical procedures and recurrence. Results showed that single- and double-hole as well as twist-drill surgeries did not affect the development of recurrence. Compared with twist-drill surgery, open valve surgery is associated with a higher recurrence rate. Single-hole surgery causes less damage and is easier to perform. Twist-drill surgery can be performed under local anesthesia at bedside; hence, it can be considered. Craniotomy causes more damage and is associated with a high recurrence rate. Thus, it is not the primary choice of treatment for routine cases. Burr-hole irrigation and drainage performed via endoscopy may be a suitable option, as recommended by previous research.[41] The use of a neuroendoscope can facilitate the safe removal of clots, residual septa, and trabecula structures as well as the coagulation of bleeding source in the hematoma cavity via direct visualization to promote brain expansion.[42] Moreover, the device could be used to identify the color of the outer membrane of the hematoma capsule, which is classification of may connection with the histopathological classification of CSDH. The white outer membrane is likely a site of recurrence. Hence, patients may require a cautious follow-up.[43]

Some problems, including prolonged surgical time and inadequate endoscopic surgical skill, cannot be overcome. Thus, clinicians should cautiously select patients based on clinical information associated with the risk factors of recurrence.[44]

The dura mater supplies blood and nutrients to the cerebral membranes. MMA is the main blood vessel supplying the hematoma at the outer membrane.[45] Endovascular embolization devascularizes the dural supply in these neomembranes, and the procedure has recently gained popularity as a putative standalone treatment and possible adjunct to surgical evacuation.[46] In particular, for refractory relapsed CSDH, the use of interventional therapy to control capsular bleeding is

effective in treating CSDH.[47] Compared with traditional surgical methods, interventional therapy causes less damage and facilitates quick recovery. However, it is not cost-effective and the absorption of hematoma takes time.[48] Symptomatic patients and those with minor symptoms are eligible for embolization as the sole treatment. It can be used as an adjuvant treatment for patients with high-risk recurrence after drilling.[49]

Both general and local anesthesia methods are commonly used in CSDH surgery. The anesthesia method is selected based on the patient's condition and surgeon's preference. Hence, recurrence is not associated with the anesthesia method. General anesthesia is safe for elderly patients. However, it is expensive and associated with a longer time to regain consciousness. Some patients with severe ischemic diseases require strict blood pressure control during surgery under anesthesia to prevent secondary ischemic events.[50]

Irrigation is essential for reducing recurrence. It can significantly decrease the persistence of hematoma. At the same time, the formation of local vortex in the lavage cavity can break the fiber strands and capsules and promote the recruitment of brain tissues. In terms of the routine use of normal saline as irrigation fluid, a meta-analysis showed no significant difference between the intraoperative irrigation and non-irrigation groups. However, the intraoperative irrigation group showed a lower recurrence rate than the intraoperative non-irrigation group. A meta-analysis of the types of irrigation fluids revealed that irrigation with artificial cerebrospinal fluid can significantly reduce recurrence compared with normal saline because the composition of artificial cerebrospinal fluid is similar to that of the human cerebrospinal fluid. Hence, brain protective properties are enhanced. Artificial cerebrospinal fluid can reduce edema around traumatic wounds, minimize cerebrovascular permeability and cell damage, and achieve faster hemostasis without interrupting normal coagulation.[12]

Postoperative drainage is extremely necessary. It can reduce the size of the remaining hematoma, promote brain tissue recruitment, and reduce recurrence. However, the appropriate drainage timing remains unclear. In general, the effect of drainage on the surgical cavity is correlated with drainage time.[51] Extending the drainage time increases the risk of infection. Drainage tubes will restrict patient's activities and prolong bedtime among elderly patients, thereby increasing the incidence of complications. It is usually safe and effective to remove the drainage 24–48 h after surgery.[52]

Results showed no significant difference between the placement of the drainage tube in the hematoma cavity below the bone hole and the subperiosteal drainage effect. Drainage tube indwelling under the periosteum can effectively prevent injury and facilitate easier and safer surgery.[53]

Nakaguchi showed that when patients with CSDH lie flat on their backs after surgery, air accumulates in the frontal convexity and that the drainage catheter on the top or side is not effective in expelling air from the subdural space. The tip of the drainage catheter must be accurately placed on the anterior lobe to remove subdural air, and this is the most effective method to prevent CSDH recurrence.[22,54]

Patients are commonly placed in the supine position after surgery. Results showed that postoperative bedside elevation was not associated with patient outcome and recurrence. However, an upright posture immediately after surgery is advantageous because it reduces postoperative complications, including atelectasis, bedsores, and ulcers.[55]

The perioperative imaging characteristics of CSDH are closely correlated with recurrence. The present study assessed the imaging characteristics during the perioperative period, whereas most studies focused on the analysis of preoperative imaging characteristics, including the internal structure of the hematoma,[56] maximum width of the hematoma, volume of the hematoma, and distance of the midline shift.[57] The width, volume, and center displacement distance of the hematoma directly or indirectly reflect the volume of the hematoma. Moreover, the recurrence rate increases significantly when the volume of the hematoma exceeds the cutoff point.[58]

CT imaging characteristics are closely associated with the pathological characteristics of CSDH.[56] Based on the classification of hematoma density, hematomas with high and mixed densities on CT imaging were associated with higher recurrence rates. On CT, a high-density area indicates new or active bleeding, whereas a low-density area suggests chronic hematoma.[59] When there is a new pathological blood vessel proliferation in the hematoma adventitia, the ruptured red blood cells infiltrate the hematoma cavity, manifesting as fresh bleeding and causing an inflammatory reaction in the subdural space. Previous studies have found that marker expression in the outer membrane of CSDH and hematoma fluid are closely associated with imaging characteristics. Weigel et al. first showed that the concentration of VEGF in the hematoma fluid of CSDH is significantly correlated with the exudation rate of the hematoma cavity observed on CT.[59] Pripp et al. revealed that the proinflammatory factors IL-6 and IL-8 in the CSDH hematoma fluid are correlated with CT imaging findings.[60] These conditions cause CSDH to be more active, and they play a role in persistent hematoma, rebleeding, and recurrence.

Nakaguchi classified the internal structure of the hematoma. The homogeneous hematoma type has three subtypes (hypodense, isodense, and hyperdense). The separated type has a higher density component under a lower density component, and there is a clear boundary between them. If two components are mixed together without a boundary, it is referred to as the gradation type. The laminar type is defined as a hematoma

with a dense layer that runs along the inner membrane. The trabecular type is defined as a hematoma with a low isodensity component and a high-density septum separating the inner and outer membranes. Results showed that hyperdense, laminar, separated, and grading hematomas are associated with a higher recurrence rate.

The present study analysis showed that the above-mentioned characteristics are closely associated with hematoma recurrence, and the level of evidence is high. The postoperative imaging features include effusion density in the hematoma cavity, maximum width and effusion volume, distance of the postoperative midline shift, clearance rate of the hematoma, and rate of brain recruitment.[61] Although the number of studies is limited, the positivity rate is high. Therefore, imaging characteristics in the perioperative period play a vital role in evaluating prognosis.

This meta-analysis provides the most comprehensive analysis of evidence about the risk factors of postoperative CSDH recurrence to date. In total, 32 risk factors were investigated. Among them, 21 were significantly associated with the postoperative recurrence of CSDH. Three risk factors (male, bilateral hematoma, and no drainage) had convincing evidence. Our research is of great significance for the clinical evaluation of the postoperative recurrence of CSDH. However, further research should be conducted to confirm the findings of the current and previous studies.

Contributors

L.B. designed the study. FL.Z., WC.L., S.H., JY.Y., CY. Z., ZA.L., GY.F., M.N., and XH.L. collected and analyzed the data and prepared the manuscript. FL.Z. edited the manuscript. All the authors approved the final manuscript.

Funding

No funding was received.

Data sharing statement

The all data of the current study would be obtained from the corresponding author on reasonable request.

Declaration of interests

The authors declare no conflicts of interest related to this study.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.eclinm.2021.101234.

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