Factors Influencing Wait and Watch Management for Primary Chronic Subdural Hematoma: A Retrospective Case–control Study

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Abstract

Prognostic factors in patients with primary chronic subdural hematoma (CSDH) taking the natural course are unclear. To identify independent influencing factors of wait-and-watch management, a case–control study of moderate CSDH patients using wait-and-watch as monotherapy in a single center from February 2014 to November 2021 was conducted. A total of 39 patients who responded to wait-and-watch management (cases) and 24 nonresponders (controls) matched for age, sex, height, weight, MGS-GCS (Markwalder grading scale and Glasgow Coma Scale), and bilateral hematoma were included. Demographics, blood cell counts, serum biochemical levels, imaging data, and relevant clinical features at baseline were collected. **S**ignificant differences between cases and controls were found in the hematoma volume, ability to urinate, maximal thickness of the hematoma, and hypodensity of the hematoma in univariate analysis. Hypodense hematoma and hematoma volume were independently associated with the outcome in multivariate analysis. Combining these independently influencing factors revealed an area under the receiver operator characteristic curve of 0.741 (95% CI: 0.609-0.874, sensitivity = 0.783, specificity = 0.667). **T**hese findings may contribute to the early detection of patients with moderate CSDH who may respond to wait-and-watch strategies. Although wait-and-watch tactics could work sometimes, medical interventions, including drug treatment, should be recommended in the clinic.

Introduction

CSDH is the result of a series of complex mechanisms thought to be initiated by a separation of the border cell layer in the dura, which triggers healing responses, including cell proliferation in the dura border, granulation tissue formation, and macrophage deposition[1]. The accumulation of blood within the subdural space incites an inflammatory response involving fibroblast proliferation, granulation tissue formation, and the release of angiogenic factors, which results in the formation of a neomembrane[1–3].

Burr-hole drainage with or without rinsing is the first choice of treatment. However, the incidence of recurrent CSDH may reach 25%, regardless of the type of surgery. Furthermore, most CSDHs occur in older patients, who carry a high risk of perioperative infection, pneumonia, and high-surface-tension pulmonary edema[4,5]. An overall mortality rate of 38.4% is reported for patients 90 years or older, independent of the treatment approach[6]. Thus, it is occasionally difficult to choose between surgical and conservative treatments when the patients have no neurological symptoms or have only mild symptoms.

Although many neurosurgeons are aware of spontaneously resolving subdural hematoma, it is reported only in case reports or very small case series with interactions between many confounding factors, such as pharmacotherapy and surgical elements [7–12]. In particular, some of these patients were receiving anticoagulant or antiplatelet medications, representing a large subgroup of CSDH cases[13]. To date, the factors predictive of success with only wait-and-watch management of CSDHs have not been adequately described in the literature[9–12,14–19]. In the current study, we aimed to investigate the predictive factors of hematoma stability and hematoma progression among cases under wait-and-watch management and to provide more insights into how to select the most appropriate treatment strategy for primary mild CSDHs.

Materials And Methods

Study design and patients

From February 2014 to November 2021, a total of 734 subjects were retrospectively reviewed with a diagnosis of a mild primary CSDH in the Department of Neurosurgery, Tianjin Medical University General Hospital. This study complied with the Declaration of Helsinki and was approved by the Ethics Committee of Tianjin Medical University General Hospital (approval number IRB2022-WZ-035). The requirement for informed consent was waived by the Committee due to its retrospective nature. The inclusion criteria were as follows: (a) treated by a wait-and-watch/close observation strategy without any special medications; (b) the presence of supratentorial CSDH on imaging examination; (c) MGS-GCS grade of 0–2 (Supplementary Table 1); (d) acceptance of an 8-week follow-up; (e) normal liver and kidney function; (f) no diagnosis of cancer; (g) no treatment with prophylactic antiplatelet medications; (h) age 18 or older; and (i) no previous CSDH surgery. Mild CSDH was defined when a brain computed tomography (CT) scan revealed slight compression of the brain parenchyma by the hematoma and the patients had no neurological symptoms or had only moderate symptoms with an MGS-GCS score of 0–2. Special medications include those that could affect hematoma resolution, such as mannitol, steroids, tranexamic acid, and angiotensin-converting enzyme inhibitors. Among the 734 total patients, 671 were ultimately excluded, 465 due to drug treatment, 43 due to surgery, 84 due to relapse after surgery, 27 due to taking anticoagulant medications, 42 due to an incomplete medical record, 5 due to incomplete follow-up, and 5 due to failure to complete imaging (Fig. 1).

Wait-and-watch therapy

The patients were treated with a wait-and-watch strategy without special medications due to no/mild symptoms, no medical comorbidities, and/or refusal of surgery. Depending on the patient’s condition, we closely observed the patients’ neurological status and performed a routine follow-up assessment. All patients and their family members were thoroughly informed of the risks and benefits of wait-and-watch treatment. The control group was defined as those who accepted wait-and-watch treatment plus surgery/drug intervention because of any worsening of symptoms, deterioration in the GCS, new focal neurological deficits, or if CT indicated an increase in the size of the CSDH during the follow-up period. The case group was defined as patients with improvements of their neurological state and/or a spontaneously resolving or stable hematoma volume that did not necessitate a change in therapy. An extensive literature search found that none of the concurrent medications affected CSDH development.

Data collection

Regular follow-up visits were recommended, while complete blood cell counts and serum levels of alanine aminotransferase, aspartate transaminase, gamma-glutamyl transpeptidase, urea nitrogen, and creatinine were measured at baseline and at the 4th and 8th weeks. The demographic, imaging and clinical data were collected regarding the patients' age, sex, weight, height, blood pressure, duration from the symptoms to head trauma, location of the CSDH (unilateral or bilateral), cause of the traumatic brain

injury (TBI), headache scale, Activities of Daily Life-Barthel Index scale (ADL-BI), American Society of Anesthesiologists Physical Status classification system (ASA-PS), volume of the hematoma (VOH, ml), distance from the midline shift (MLS, mm), basal cistern compression (BCC), initial maximal thickness of the subdural hematoma (MTH, mm) and the presence of an organized hematoma. The ADL-BI evaluates the ability of a patient to dine, bathe, groom (face washing, tooth brushing, shaving, and combing), dress (tying shoes and fastening buttons), defecate, urinate (self-cleaning, adjusting clothing, and washing up), go to bed and move to a chair, walk on a flat floor, and go up and down a flight of stairs[20].

The subdural hematoma density was classified into the 4 following groups based on the CT findings: hypodense (< 25 Hounsfield units [HU]), isodense (25–35 HU), hyperdense (> 35 HU) and mixed dense[21] (Fig. 2). A hematoma volume was calculated based on the Coniglobus Formula given as hematoma volume (ml) = 1/2 × the longest diameter of the hematoma layer with the largest area (cm) × the longest diameter perpendicular to the longest diameter (cm) × the thickness of the hematoma (cm). If a patient had more than one hematoma, the total volume of the multiple hematomas was calculated[22]. BCC was defined if the basal cisterns were obliterated or compressed on the first CT scan. The MLS was identified as a deviation of the septum pellucidum from the central position[23].

Statistical Analyses

The differences between the case and control groups were analyzed using the chi-square test for categorical variables (TBI history, cause of TBI, duration from symptoms to traumatic history, BCC, bilateral hematoma, density of the subdural hematoma, and organized hematoma), the Mann–Whitney U test for ordinal categorical variables (ADL-BI scoring ASA-PS and headache scale), and Student's t-test for continuous variables (blood pressure, MLS, MTH, VOH, blood cell counts and serum levels). Multivariate logistic regression models were used to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) for the association between independent influencing factors and the response of the CSDH during wait-and-watch management. Variables that were significant in the univariate test were included in the multivariate logistic regression models. The receiver operating characteristic (ROC) curve and the area under the ROC curve (AUC) were used to examine the predictive accuracy of the combination of independent factors for the response to wait-and-watch management. P values less than 0.05 were considered statistically significant. All statistical analyses were performed using SPSS 25.0 (IBM Corporation, Armonk, New York, USA).

Results

A total of 39 mild CSHD patients with a known response (case group) were matched to the control of 24 mild CSHD patients who were nonresponsive (1.6:1 matching) (Fig. 1). The cases and controls were matched by age, sex, height, weight, MGS-GCS, and bilateral hematoma. Among them, 57 patients had a history of apparent head trauma; the median interval between the trauma and the first symptom was 1–2 months. The main symptoms and signs of CSDH were headache, dizziness, slow thinking, unsteady gait,

and slow movement. According to the MGS-GCS scale, 55 and 8 patients were in grades 1 and 2, respectively, at admission.

Twenty-seven patients (43.5%) had concomitant conditions of hypertension (n = 12, 19.4%), hyperlipidemia (n = 7, 11.3%), coronary heart disease (n = 1, 1.6%), gastritis (n = 2, 3.2%), epilepsy (n = 1, 1.6%), interstitial pneumonia (n = 1, 1.6%), atrial premature beat (n = 2, 3.2%), benign prostate hyperplasia (n = 1, 1.1%), diabetes mellitus (n = 4, 6.5%), hyperthyroidism (n = 1, 1.6%), pelvis fracture (n = 1, 1.6%) and mild anemia (n = 1, 1.6%). These patients were classified as independent (31 patients), slightly dependent (19 patients), moderately dependent (5 patients), severely dependent (6 patients), and completely dependent (2 patients) according to their baseline ADL-BI.

The CSDH was bilateral in 37 patients. BCC was observed in 22 patients. The MLS ranged from 0–13 mm (3.2 ± 3.8 mm). The MTH ranged from 4–33 mm (16.4 ± 6.5 mm), and 9 of 62 (14.5%) patients had organized hematoma. The total hematoma volume ranged from 6.9-176.7 ml (79.6 ± 40.0 ml) (Table 1). CSDHs were located in the frontal (n = 1), frontotemporal (n = 1), temporoparietal (n = 2), frontal-parietal and temporal (n = 13), frontoparietal (n = 8), bilateral frontal (n = 2), bilateral frontoparietal (n = 8), bilateral frontal-parietal and temporal (n = 15), lateral cerebral hemispheres (n = 5) and bilateral cerebral hemispheres (n = 8).

Table 1
General characteristics of study participants.

Characteristics	Number of patients (%)
Age, years	65.2 ± 13.3
Male	58 (92.1)
Body height, cm	168.2 ± 6.7
Weight, kg	65.0 ± 9.4
CSDH with TBI history	57 (90.5)
Impact of motor vehicles, bicycles, etc.	19 (30.2)
Fall	13 (20.6)
Bump	15 (23.8)
Raid	1 (1.6)
Drop	2 (3.2)
Other	1 (1.6)
Duration from symptoms to trauma	
≤ 1 month	20(31.7)
1–2 months	25(39.7)
2–3 months	9(14.3)
3–6 months	2(3.2)
>6 months	1(1.6)
MGS-GCS score	
0	0
1	55 (87.3)
2	8 (12.7)
ADL-BI score	
95–100 Independent	31 (49.2)

Abbreviations: ADL-BI, activities of daily living–Barthel Index; CSDH, chronic subdural hematoma; MGS-GCS, Markwalder grading scale–Glasgow Coma Scale; TBI, traumatic brain injury; WBC, white blood cell; INR, international normalized ratio; FIB, fibrinogen; APTT, activated partial thromboplastin time; PT, prothrombin time; RBC, red blood cell; HGB, hemoglobin.

Characteristics	Number of patients (%)
80–90 Slightly dependent	19 (30.2)
65–75 Moderately dependent	5 (7.9)
45–60 Severely dependent	6 (9.5)
0–40 Completely dependent	2 (3.2)
Headache	
None	18 (28.6)
Minor	34 (54.0)
Moderate	11 (17.5)
Severe	0 (0)
The density of the subdural hematomas	
Isodensity	7 (11.1)
Low-density	26 (41.3)
High-density	16 (25.4)
Mixed density	14 (22.2)
Mean total hematoma volume, ml	79.6 ± 40.0
Mean midline shift, mm	3.2 ± 3.8
Mean maximal thickness of hematoma, mm	16.4 ± 6.5
Basal cistern compression	22 (34.9)
Organized hematoma	9 (14.3)
RBC, 10^12/L	4.3 ± 1.0
HGB, g/L	134.0 ± 30.0
WBC, 10^9/L	6.5 ± 2.2
PLT, 10^9/L	216.8 ± 76.0
APTT, s	31.0 ± 9.4

Abbreviations: ADL-BI, activities of daily living–Barthel Index; CSDH, chronic subdural hematoma; MGS-GCS, Markwalder grading scale–Glasgow Coma Scale; TBI, traumatic brain injury; WBC, white blood cell; INR, international normalized ratio; FIB, fibrinogen; APTT, activated partial thromboplastin time; PT, prothrombin time; RBC, red blood cell; HGB, hemoglobin.

Characteristics	Number of patients (%)
PT, s	11.4 ± 3.0
FIB, g/L	3.3 ± 1.3
D-Dimer, mg/L	0.5 ± 0.8
INR	0.9 ± 0.2
Total cholesterol, mmol/l	4.1 ± 1.4

Abbreviations: ADL-BI, activities of daily living–Barthel Index; CSDH, chronic subdural hematoma; MGS-GCS, Markwalder grading scale–Glasgow Coma Scale; TBI, traumatic brain injury; WBC, white blood cell; INR, international normalized ratio; FIB, fibrinogen; APTT, activated partial thromboplastin time; PT, prothrombin time; RBC, red blood cell; HGB, hemoglobin.

In the control group, 10, 5, 3, and 6 patients presented with hyperdense, hypodense, isodense, and mixed-density hematomas, respectively. Twenty-three patients were switched to surgery, and 1 patient was switched to atorvastatin plus corticosteroid drug treatment. In the case group, 6, 21, 4 and 8 patients displayed hyperdense, hypodense, isodense, and mixed-density hematomas, respectively. At the 8 w-radiological follow-up of the case group, the SDH had nearly disappeared in 7 patients but was visible in 32 patients (range, 4.3–119.0 ml; 39.6 ± 30.2 ml), with MTH ranging from 2–20 mm (11.3 ± 4.6 mm). The initial VOH of these disappearing and visible subgroups were 31.3 ± 18.1 ml and 79.0 ± 33.6 ml, respectively, a significant difference between them (P = .001). MLS was visible in 9 patients, ranging from 1–5 mm (2.6 ± 1.6 mm). All patients who were switched to surgery underwent a burr hole craniotomy with drainage. At baseline, there were no significant differences in blood cell counts or hematological and liver function between the case and control groups.

As summarized in Table 2 and Supplementary Table 2, univariate analysis showed that the outcome of a response was significantly associated with hematoma density (P = 0.038), MTH (P = 0.042), VOH (P = 0.025), and urination ability (P = 0.046). Multivariate logistic regression analysis identified hypodense hematoma (odds ratio, 0.104 [0.028–0.385]; P = .001) and VOH (odds ratio, 1.011 [1.000-1.021]; P = 0.047) as independent predicting factors between the two groups (Table 3). AUCs were calculated for the efficacy of the independently associated factor and revealed an area under the curve of 0.741 (95% CI: 0.609–0.874, P = 0.002, sensitivity = 0.783, specificity = 0.667) (Fig. 3).

Table 2
Univariable analyses for factors related to the outcome of wait and watch management.

Factors	Response Not response		*P* Value
Total	39	24	
Sex			0.698
Male	35 (89.7%)	23 (95.8%)	
Age, years	63.9 ± 14.4	67.1 ± 11.4	0.358
Systolic pressure, mmHg	129.5 ± 14.6	135.7 ± 11.4	0.088
Diastolic pressure, mmHg	81.7 ± 10.2	80.5 ± 9.3	0.647
Body height, cm	168.7 ± 6.1	167.4 ± 7.6	0.47
Weight, kg	65.6 ± 10.1	64.0 ± 8.1	0.527
Traumatic brain injury history	36 (92.3%)	21 (87.5%)	0.85
Different causes of TBI			0.667
Impact of motor vehicles, bicycles, etc.	9 (23.1%)	4 (16.7%)	
Fall	14 (35.9%)	11 (45.8%)	
Bump	10 (25.6%)	5 (20.8%)	
Raid	0	1 (4.2%)	
Drop	2 (5.1%)	0	
Other	1 (2.6%)	0	
Headache	29 (74.4%)	16 (66.7%)	0.133
None	10 (25.6%)	8 (33.3%)	
Minor	24 (61.5%)	9 (37.5%)	
Moderate	5 (12.8%)	7 (29.2%)	
Severe	0	0	
RBC, 10^12/L	4.2 ± 1.1	4.4 ± 0.5	0.523

Abbreviations: ADL-BI, activities of daily living–Barthel Index; CSDH, chronic subdural hematoma; MGS-GCS, Markwalder grading scale–Glasgow Coma Scale; WBC, white blood cell; INR, international normalized ratio; FIB, fibrinogen; APTT, activated partial thromboplastin time;

PT, prothrombin time; RBC, red blood cell; HGB, hemoglobin; ASA-PS, American Society of Anesthesiologists Physical Status classification system; TBI, traumatic brain injury.

*$P < 0.05$.

Factors	Response	Not response	*P* Value
HGB, g/L	131. 2 ± 35.0	139.2 ± 17.0	0.344
WBC, 10^9/L	6.2 ± 2.2	6.9 ± 2.0	0.244
PLT, 10^9/L	218.2 ± 86.5	214.1 ± 53.0	0.845
APTT, s	30.9 ± 10.6	31.3 ± 6.7	0.871
PT, s	11.2 ± 3.5	12.0 ± 1.1	0.338
FIB, g/L	3.1 ± 1.2	3.6 ± 1.3	0.206
D-Dimer, mg/L	0.5 ± 0.9	0.6 ± 0.6	0.788
INR	0.9 ± 0.3	1.0 ± 0.1	0.306
Total cholesterol, mmol/l	4.0 ± 1.5	4.4 ± 1.0	0.301
ASA-PS			0.333
1	26 (66.7%)	14 (54.2%)	
2	13 (33.3%)	10 (41.7%)	
3	0	1 (4.2%)	
Duration from trauma to symptoms			0.884
≤ 1 month	20(33.9%)	6(28.6%)	
1–2 months	24(30.7%)	10(47.6%)	
2–3 months	10(16.9%)	4(19.0%)	
3–6 months	4(6.8%)	1(4.8%)	
>6 months	1(1.7%)	0	
MGS-GCS scale			0.258
0	0	0	
1	36 (92.3%)	19(79.2%)	
2	3 (7.7%)	5 (20.8%)	

Abbreviations: ADL-BI, activities of daily living–Barthel Index; CSDH, chronic subdural hematoma; MGS-GCS, Markwalder grading scale–Glasgow Coma Scale; WBC, white blood cell; INR, international normalized ratio; FIB, fibrinogen; APTT, activated partial thromboplastin time;

PT, prothrombin time; RBC, red blood cell; HGB, hemoglobin; ASA-PS, American Society of Anesthesiologists Physical Status classification system; TBI, traumatic brain injury.

*$P < 0.05$.

Factors	Response	Not response	*P* Value
ADL-BI scoring	89.7 ± 14.8	83.5 ± 24.3	0.727
Midline shift (mm)	2.6 ± 3.5	4.2 ± 4.3	0.118
Basal cistern compression	13 (33.3%)	9 (37.5%)	0.948
Bilateral hematoma	22 (37.9%)	11 (52.2%)	0.899
The density of the subdural hematomas			0.038*
High-density	6 (15.4%)	10 (41.7%)	
Low-density	21 (53.8%)	5 (20.8%)	
Isodensity	4 (10.3%)	3 (12.5%)	
Mixed density	8 (20.5%)	6 (25.0%)	
Organized hematoma	7 (17.9%)	2 (8.3%)	0.491
Volume of hematoma (ml)	70.0 ± 36.6	93.2 ± 42.2	0.025*
Maximal thickness of hematoma (mm)	15.1 ± 5.9	18.5 ± 7.0	0.042*
Abbreviations: ADL-BI, activities of daily living–Barthel Index; CSDH, chronic subdural hematoma; MGS-GCS, Markwalder grading scale–Glasgow Coma Scale; WBC, white blood cell; INR, international normalized ratio; FIB, fibrinogen; APTT, activated partial thromboplastin time;			
PT, prothrombin time; RBC, red blood cell; HGB, hemoglobin; ASA-PS, American Society of Anesthesiologists Physical Status classification system; TBI, traumatic brain injury.			
*$P < 0.05$.			

Table 3
Multivariable analysis outcomes

Factors†	OR (95%CI)	*P*-value
Density of hematoma		
High-density	Reference	NA
Isodensity	0.327 (0.057–1.875)	0.210
Low-density	0.104 (0.028–0.385)	0.001*
Mixed density	0.313 (0.079–1.247)	0.100
Volume of hematoma, ml	1.011 (1.000-1.021)	0.047*
Maximal thickness of hematoma, mm	NA	0.351
Systolic pressure, mmHg	NA	0.463
Urinating	NA	0.053
†Factors predictive in univariate analyses were entered into multivariate analyses.		
**P* < 0.05.		
Abbreviations: NA, not available; OR, odds ratio; CI, confidence interval.		

Case illustration

A 69-year-old man in the control group had primary hypertension, which was diagnosed 40 years ago and treated with nifedipine. He presented with dizziness, headache, and a feeling of left eye puffiness after minor head trauma. The initial brain CT scan showed a high-density CSDH without any obvious brain parenchyma compression and MLS or perifocal edema (Fig. 4 ABC). The measured volume of the hematoma was 33.1 ml without BCC. Given the imaging manifestations and the moderate symptoms, wait-and-watch treatment was performed in the outpatient department after informed consent was obtained from the patient and his relatives. However, his neurological status was aggravated on the 13th day of observation, and a brain CT scan revealed a remarkable increase in hematoma volume (88.1 ml) with a significant MLS (Fig. 4 DEF). Therefore, we recommended statin (20 mg/day) and corticosteroid (2.5 mg/day) treatment and immediate hospitalization. His symptoms improved gradually starting on the 7th day of therapy, and brain CT revealed a markedly decreased volume of hematoma (34.8 ml) and a reduced mass effect (Fig. 4 HIJ). He was discharged and has not experienced any recurrence of symptoms or hematoma as observed during outpatient follow-up.

Discussion

CSDH is common and more prevalent in the aged population. Surgical treatment might generally be indicated in conditions of a large hematoma width (> 10 mm) or a shift of the midline (> 5 mm) on CT scan, and surgical intervention has been accepted as the treatment of choice[24]. However, invasive treatment for CSDH in advanced-age patients who take long-term anticoagulation/antiplatelet medications or have poor physical health carries a considerable risk of complications, such as subdural empyema, tension pneumocephalus, brain contusion, subdural or epidural hematoma, intracerebral hemorrhage, catheter penetration to the brain and even death[10,25]. In particular, when a brain CT scan reveals slight compression of the brain parenchyma caused by hematoma and the patients have no/mild neurological symptoms, a surgical decision cannot be justified.

From the literature, it is apparent that observation therapy for CSDH could be used in some appropriately selected patients with asymptomatic, small-volume CSDH, patients refusing surgery, or those for whom surgery carries a high risk, which might result in potential health cost savings and eliminate perioperative risks, such as but not limited to general anesthesia[9,10,12,14,19]. What kind of patients are prone to spontaneous resolution of CSDH is unknown, and there are few studies in the literature concerning the natural course of CSDHs. Kim, H. C. found that 13/16 CSDH patients undergoing simple wait-and-scan management experienced spontaneous total resolution. These patients had an MGS that ranged from grade I to grade II at admission. These results suggest that close watching could be chosen when the hematoma volume or thickness was less than 43 ml or 13 mm, respectively, and the MLS was less than 5 mm on brain CT scan (n = 16)[19].

However, in a review, the rate of spontaneous resolution of CSDH with or without medical therapy ranged from 2.4–18.5%[13,26]. This variability likely stems from heterogeneous disease severity, small sample sizes, and differences in conservative measures. In addition, in most of the patients above, the evaluated conservative treatments were given as adjuvants after surgery, which may affect the evaluation of the real efficacy of each treatment alone. Therefore, we conducted this subgroup analysis on primary (not previously treated) mild CSDH. Although many factors were included in our logistic regression model, we found that only hypodense hematoma and VOH were independent predictors of the efficacy of wait-and-watch management in our study.

Hematoma stability varies depending on the stage of the bleeding cycle[27], namely, bleeding, coagulation, and rebleeding[28]. In clinical cases, CT is the preferred radiological tool for making a CSDH diagnosis. CT-confirmed CSDH may present a variety of imaging characteristics, and it is well known that the radiological subtype of CSDH may change over time[29]. The radiological subtypes that can present at the time of diagnosis possibly represent different pathophysiological stages of CSDH[30]. Different hematoma densities relative to the brain parenchyma on CT images represent the proportion of fresh blood, with hypodense areas representing hematoma of an older age and hyperdense components of more recent or active bleeding[31–34].

Not only is “wait and watch” or “wait and scan” management more appropriate for patients with no or minor symptoms, but some authors also advocate that patients who have small lesions with low density on CT have a greater chance for spontaneous resolution of their hematoma[16]. Nomura et al. suggested that the mixed-density type has a high tendency to rebleed, while a low-density hematoma is stable with a low tendency to rebleed or exhibit fibrinolytic abnormalities[35]. When the interstitial hematoma matrix changes from an isodense to a low-density signal on CT scans, on surgical inspection it changes from a dark reddish to a xanthochromic translucent liquefied hematoma, while it diminishes in volume over time[36]. If a low-density hematoma is considered to be the resolution stage of CSDH, this might explain the significantly higher rate of low-density hematoma in the case group compared with the other three hematoma density groups.

Preoperative VOH and MTH have been reported as prognostic factors of CSDH, consistent with our results in the univariate analysis[37,38]. However, our results only found a significant relationship between VOH and hematoma stability in the multivariate analysis. Additionally, there was a significant difference between the SDH nearly disappearing and the visible subgroups ($P = 0.001$). We hypothesized that the degree of compression from the hematoma might be a result of multiple factors, including hematoma thickness, MLS, patient age, and brain atrophy[39]. In addition, brain atrophy or expandability of the skull may increase the reserve capacity. When the reserve capacity is sufficient, CSDH may be asymptomatic for a longer period, even more than a year[40].

In our present study, under the premise of brain atrophy in the elderly, hematoma volume may contribute more directly to intracranial pressure growth and neurological dysfunction than MTH. With the application of ROC analysis, we estimated the predictive capacity of VOH and hypodensity as a combination in our study. The AUC was under .90, which suggests that the relationship between the predicting factors and treatment outcome is more of an association than a causal relationship. There may be more complex interacting factors that were not included in our analysis, such as physical activity and alcohol use[41]. The mean hematoma volume of the case group in our study was 70.0 ml, which implies not only size but also manifestations of patient-specific factors. In our center, many patients are old and have significant brain atrophy, and sometimes a relatively large hematoma does not necessarily mean that the patient is in poor condition and needs immediate surgery. When a dilemmatic situation is encountered, such as subtle symptomatic patients with a relatively large hematoma or MLS, we require early hospitalization and close monitoring of the patients. If their symptoms worsen and/or their condition deteriorates, we will carry out surgical interventions. In summary, regardless of the selection of treatment (whether it is surgical or not), a close scan/follow-up of these patients is paramount.

A clinical classification might help in deciding which therapy modality might be more appropriate. However, no consensus exists about the best CSDH treatment for each grade. It also seems that there are no clear clinical or radiological signs indicating whether the CSDH will resolve spontaneously. In our study, the ADL-BI score, which measures the daily living activities of patients with neurological diseases, was more sensitive than the MGC-GCS and ASA-PS for predicting the observation treatment outcome in

the univariate analysis. The ASA-PS is a method of characterizing the patient operative risk on a scale of 1–5, with 1 being normal health and 5 being moribund, which has strong, independent associations with postoperative medical complications and mortality[42]. The GCS was originally developed to evaluate the recovery of patients with traumatic brain injury, while the ADL-BI scores measuring the daily living ability, such as being able to defecate and urinate independently, may reveal more subtle information regarding the outcomes of our observation cohort.

Symptoms and neurological deficits from primary and recurrent CSDH arise most often due to the mass effect of the subdural collection. However, observation treatment cannot help reduce this compression and thereby alleviate symptoms and deficits. Furthermore, the prolonged presence of a hematoma on the cerebral surface, as the majority of the patients' hematomas were still present in our study throughout the follow-up, requires longer follow-up periods, which may lead to a lengthy medical procedure and bedridden status. In addition, in some cases in our case group, although the CSDH of the patient had nearly disappeared, there remained the problem of a constant headache, which might seriously affect the patient's quality of life. These arguments suggest that wait-and-watch therapy alone may be less efficient for symptomatic CSDH, especially if the patient is in an anxious mood, while increasing the risk of hematoma enlargement and the duration of disturbing symptoms. In addition, a systematic review found that corticosteroids as either monotherapy or a surgical adjuvant improved the clinical outcomes of adult patients with CSDH[43]; statins are another medication considered a conservative treatment for CSDH. A clinical trial including 200 patients demonstrated that atorvastatin is safe and effective in reducing hematoma volume and improving the neurological function of patients compared to placebo[44]. Therefore, given the above, medical interventions, including drug treatment, should be combined with observational treatment.

Limitations

First, our study has a retrospective design, which usually produces a risk of selection bias. Second, it is unknown whether some patients in the case group may have used traditional herbal medicine to prevent the CSDH increase. Third, the Coniglobus Formula for calculating hematoma measurements can lead to an overestimation of hematoma volume[45,46]. Fourth, our limited follow-up is not the end-point of these patients with CSDH, and there may be some incidence of hematoma recurrence. We have encountered cases with recurrence of a hematoma after strenuous exercise and/or bathing one's feet in hot water. Hence, the results from the patients in the present series are self-limiting, and longer follow-up is needed in the future. Despite these limitations, this study still provides useful information to predict the outcome of CSDH patients receiving observation treatment and can provide more perspectives on CSDH treatment strategies for neurosurgeons.

Conclusions

Mild CSDH patients who are more likely to respond to wait-and-watch treatment may be distinguished from nonresponsive patients via the combined use of hypodensity hematoma and hematoma volume.

The ADL-BI might be more sensitive than the MGS-GCS scale and ASA-PS for predicting the outcomes of mild or moderate CSDH patients. In clinical practice, these findings may contribute to the development of more optimal strategies for mild CSDH management. Although close observation tactics could work sometimes, medical interventions, including drug treatment, should be considered in most cases.

Declarations

Acknowledgments

None

Author Contributions

RJ JZ and JH designed this study. XZ, ZS, and CG carried out this study, collected and analyzed the data, and contributed equally to this study. HW, XL, DW, and YT helped in data collection. TX, CY, and WQ helped to analyze the results. XZ wrote the draft. JZ and RJ revised the final version of the manuscript.

Data Availability Statement

The datasets generated for this study are available on request to the corresponding author.

Competing interests

The authors declare no competing interests.

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Figures

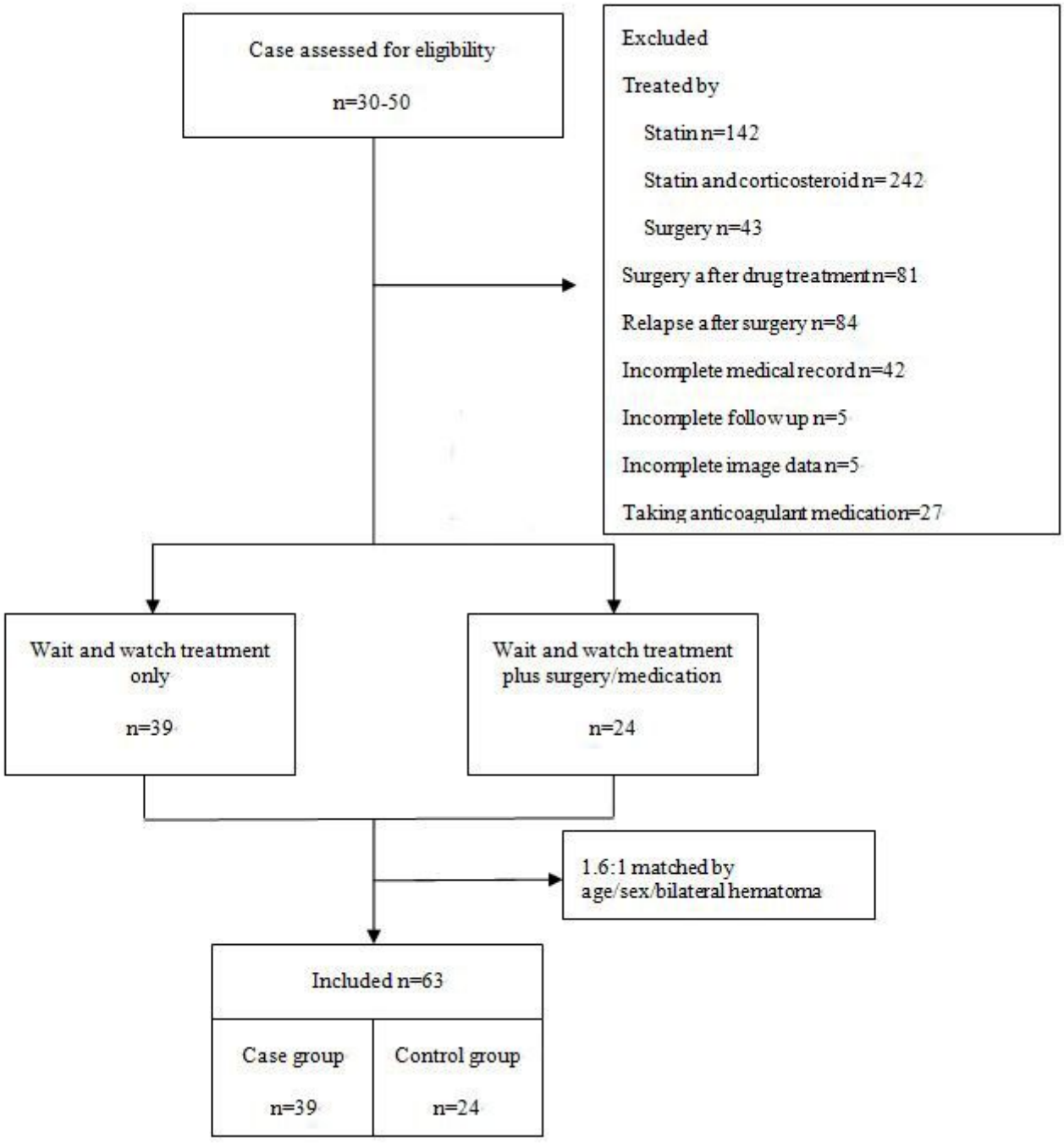

Figure 1

Flow diagram.

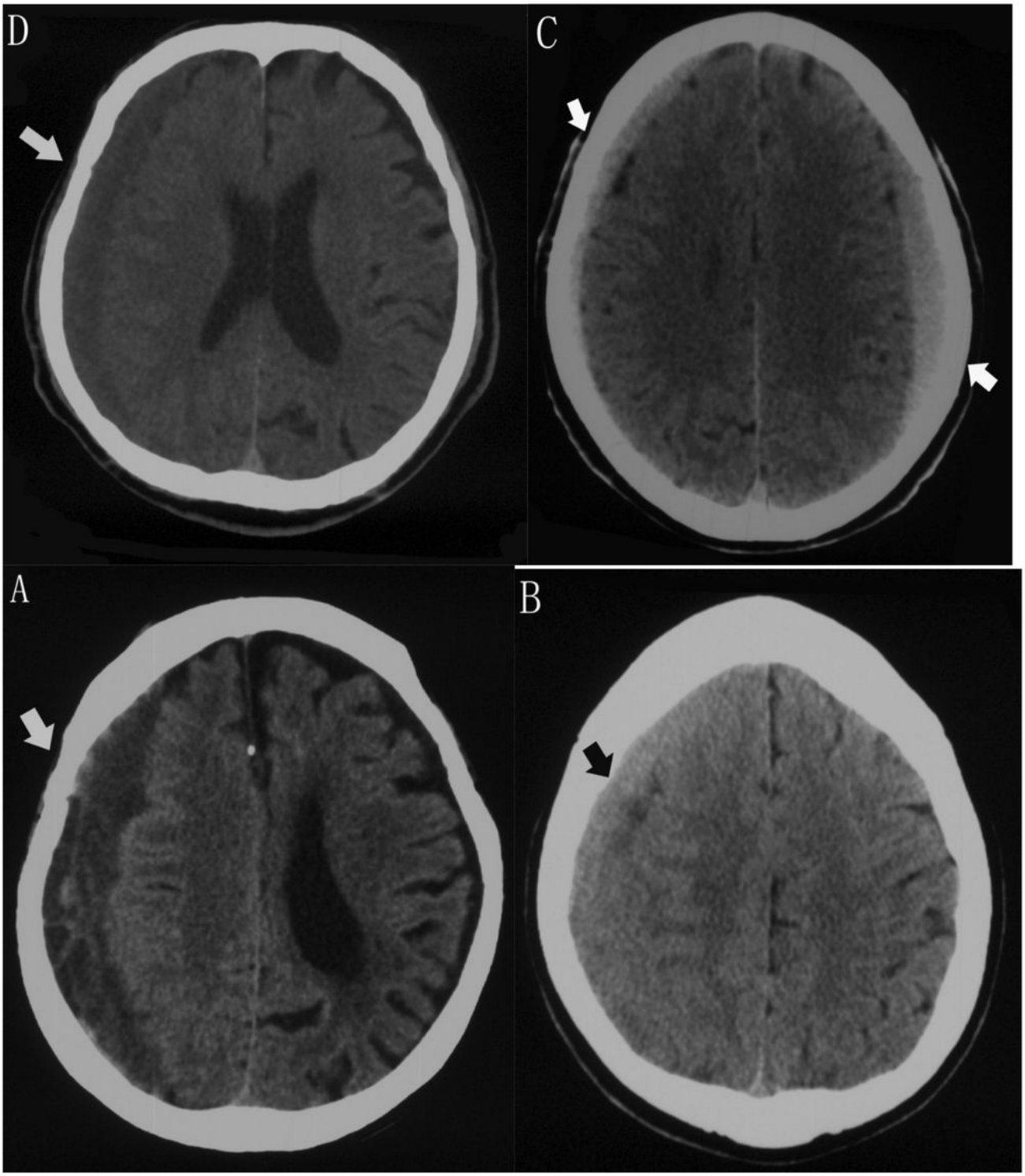

Figure 2

Hematomas of different densities as visualized on computed tomography images.

(A) Mixed density hematoma; (B) Isodensity hematoma; (C) Hyperdensity hematoma; (D) Low-density hematoma. The arrow points to the CSDH.

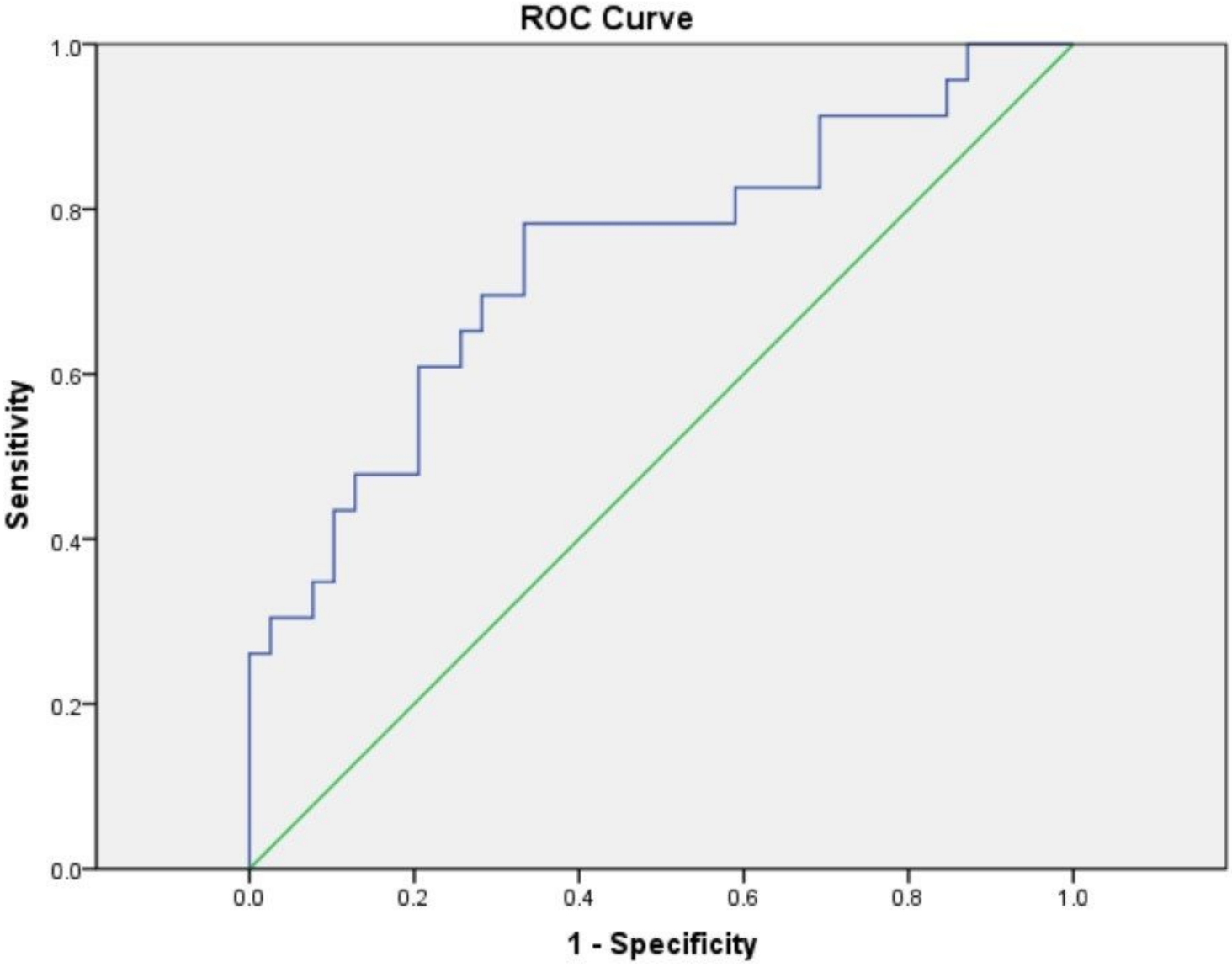

Figure 3

ROC analysis of prognosis outcome to wait and watch strategy.

The results showed that baseline volume of hematoma combined hypo-density have the AUC of 0.741 (95%CI: 0.609-0.874, *P*=0.002, sensitivity = 0.783, specificity = 0.667).

ROC, receiver operating characteristic.

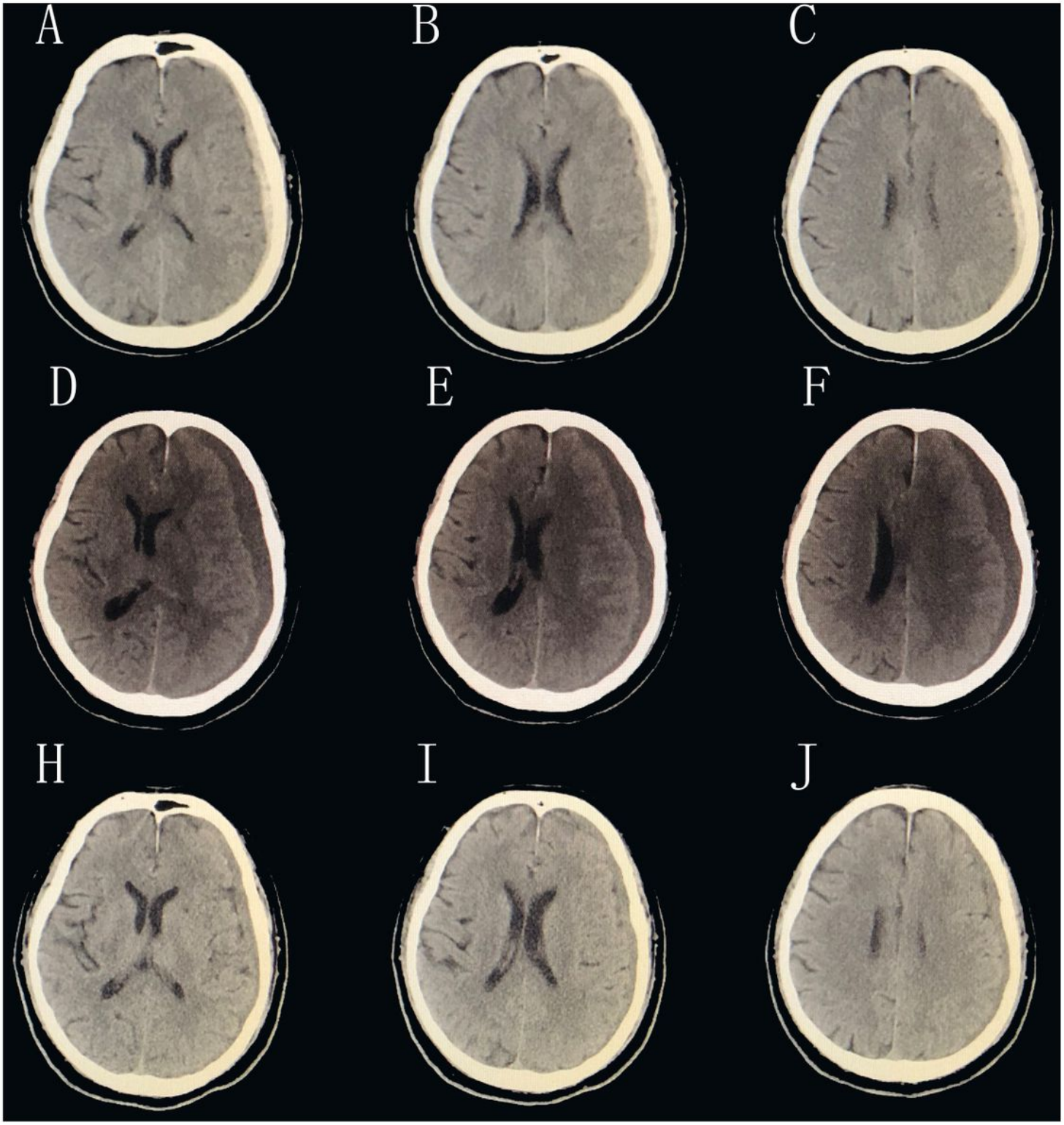

Figure 4

A 59-year-old male complained of dizziness, headache, and feeling of left eye puffy after minor head trauma.

ABC Initial brain CT reveals scanty CSDH in the right hemisphere. DEF Follow-up brain CT scan on the 13th day of observation treatment shows a relatively low-density subdural hematoma that compressed

the brain parenchyma with a midline shift. HIJ Follow-up brain CT scan on the 7th of statin plus corticosteroid therapy shows a remission of mass effect and a remarkably decreased amount of hematoma.

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