Retrospective Study

Bed Rest as a Protective Factor for Subdural Hematoma in Spontaneous Intracranial Hypotension: A Retrospective Study

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Background: Subdural hematoma (SDH) is a potentially life-threatening complication in patients with spontaneous intracranial hypotension (SIH). Though bed rest is the basis of conservative treatment, no clear evidence exists regarding the association between bed rest and the later complication of SDH in these patients.

Objectives: This study aimed to evaluate the association between bed rest and SDH development in patients with SIH.

Study Design: A retrospective study was conducted from March 2013 through December 2019. Four hundred twenty adult patients diagnosed with SIH were enrolled. Clinical presentations and radiographic findings were recorded. The cumulative duration of bed rest in hours was used to measure the bed rest length. The clinical outcomes during follow-up were assessed.

Methods: Categorical data were compared using χ^2 tests; continuous data were compared using the Mann-Whitney U test or Kruskal-Wallis test. A backwards stepwise Cox proportional hazard regression model adjusted with confounders which differed between SDH and non-SDH in univariate analysis was used to estimate the risk of cumulative duration of bed rest for SDH. A stratified Cox regression was performed to exclude the effect of the treatment algorithm.

Results: Of the 420 patients with SIH, 88 (21%) were in the SDH Group and 332 (79%) were in the non-SDH (NSDH) Group. The cumulative duration of bed rest in hours was a protective factor for SDH in SIH (Hazard Ratio [HR] = 0.997; $P < 0.001$). A stratified Cox regression analysis showed that the cumulative duration of bed rest remained a protective factor for SDH both in patients who received conservative treatment before admission (HR = 0.997; $P < 0.001$) and in those who did not (HR = 0.996; $P = 0.061$). Age (HR = 1.029, 95% CI, 1.009-1.050; $P = 0.004$) and orthostatic headache (HR = 4.770, 95% 95% CI, 2.177-10.450; $P < 0.001$) were risk factors for SDH in SIH. The clinical outcomes, including length of hospital stay, epidural blood patch (EBP) therapy, and repeated EBP therapy, were higher in the SDH Group. The revisit rate was similar between the 2 groups.

Limitations: Retrospective studies are susceptible to different radiological procedures and therapeutic strategies. A bed rest score based on a patient's memory is susceptible to recognition and reporting bias. This is a single-center study and the sample size is not large. The validity of the bed rest scale has not been previously evaluated in any other study.

Conclusions: Bed rest was a protective factor for SDH in patients with SIH. With more time and proper treatment, patients with SIH who have an SDH can achieve good prognosis in the long term.

Key words: Spontaneous intracranial hypotension, complication, subdural hematoma, bed rest, protective factor, conservative treatment, epidural blood patch, prognosis

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Spontaneous intracranial hypotension (SIH), with orthostatic headache as the typical presenting symptom, occurs due to spontaneous spinal cerebrospinal fluid (CSF) leakage (1). The core pathogenic mechanism of SIH involves a decrease in CSF volume. Low CSF volume may lead to compensatory enlargement of the subdural/subarachnoid spaces, resulting in subdural fluid collection and brain descent, which may produce tears in bridging veins and cause subdural hematoma (SDH). SDH is a potentially life-threatening complication in patients with SIH, with an incidence of approximately 20% (2,3). Some patients with severe SDH may develop neurological deficits, disturbed consciousness, and even cerebral herniation (4). Thus, timely detection and rapid response are important; determination of the risk factors for an SDH in SIH may contribute to better prediction and early screening of SDH.

Despite numerous publications, studies on the risk factors for SDH in patients with SIH differed from one another. Clinical course duration (5), advanced age, male gender, the recurrence of severe headache, and neurological deficits (6) may be related to SDH. Nevertheless, as the majority of studies have been case series, the small number of patients and poor design without proper controls have limited their results. Besides, detailed clinical presentations, like orthostatic headache, or unconsciousness, have not been studied before.

Some patients with SIH enjoy resolution of symptoms with only conservative treatment. Given enough time, conservative treatment consisting of bed rest and hydration is probably effective in many patients with SIH. However, some patients require injections of autologous blood in the spinal epidural space, known as an epidural blood patch (EBP) (7). Strict bed rest is the basis of nonsurgical conservative treatments (3), because it is believed that being supine reduces CSF pressure at the site of leakage, allowing healing of the underlying meningeal defects (8). However, the mechanism remains unclear and has not been evaluated by randomized clinical trials. Also, no clear evidence exists regarding the association between inadequate bed rest and the later complication of an SDH in patients with SIH.

Herein, we retrospectively reviewed 420 patients with SIH in our hospital, 88 of whom had an SDH. The purpose of this study was to investigate the association between bed rest and SDH development in patients with SIH. We hypothesized that bed rest may be a protective factor for an SDH in SIH.

Methods

Patient Population

This single center retrospective study was conducted at Sir Run Run Shaw Hospital. From March 2013 through December 2019, 540 patients with SIH were admitted. Only adult patients (≥ 18 years old) meeting the diagnostic criteria for SIH according to the second edition of the International Classification of Headache Disorders (ICHD-2) were included; we retrospectively applied ICHD-3 for confirmation (9). Only patients experiencing their first SIH episode were included; patients admitted due to an SIH recurrence were excluded. Patients with incomplete medical records, and those with an unconfirmed diagnosis of SIH due to their refusal to undergo definitive diagnostic tests were excluded. Patients who were lost to follow-up or refused to complete the bed rest questionnaire were also excluded. Patients who had an SDH after an EBP treatment were excluded (Fig 1). For patients who were admitted more than once because of SIH in our hospital, data at the first visit was used.

Each included patient first underwent a cranial computed tomography (CT) scan. Brain magnetic resonance imaging (MRI) with gadolinium enhancement was performed for diagnosing SIH. For patients suspected of having SIH, at least one of the following imaging modalities was performed to identify the CSF leakage sites: computed tomography myelography (CTM), magnetic resonance myelography (MRM), or intrathecal gadolinium MR myelography (Gd-MRM),.

One or more SDHs were diagnosed if the subdural fluid showed hyperintensity on both T1- and T2-weighted images and isodensity or hyperdensity on CT scans (5,6,10). All patients with an SDH received an EBP. Neurosurgical drainage was done in patients with an SDH with neurological deficits or disturbed consciousness or failure to reduce the volume of large hematomas (> 1 cm) by EBP. For those without SDHs, an EBP was carried out in those who failed 2 weeks of conservative treatments. The Medical Ethics Committee of Sir Run Run Shaw Hospital approved this study (ID of the approval: 20210329-31). All patients gave written informed consent and written permission for publication of their medical images.

Clinical Data Collection

Data on demographic factors such as age and gender, as well as the clinical course of an SIH (the days from symptom onset to diagnosis of an SDH or to admission in our hospital), headache location, associ-

ated symptoms, physical examinations, CSF opening pressure, length of hospitalization, and EBP times were recorded. For patients who received repeated lumbar punctures before their diagnosis, the first CSF opening pressure was recorded. Recurrence was defined as a revisit of patients to our hospital due to similar characteristics of headache.

Cumulative Bed Rest Duration

A bed rest scale was assessed on the return visit or via telephone call after the patients with SIH were discharged to reveal the bed rest length. The scale was defined as follows: one = strict bed rest (100% of awake time, about 16 hours per day); 2 = bed rest almost all of the time (about 95% of awake time, about 15.2 hours per day); 3 = bed rest most of the time (about 75% of awake time, about 12 hours per day); 4 = bed rest sometimes (about 25% of awake time, about 4 hours per day); and 5 = no bed rest during time spent awake (0 hours per day).

Since patients received strict bed rest as medical advice after admission in our hospital, we only measured bed rest in the period between the onset of symptoms and the occurrence of an SDH or admission to our hospital. For patients who were admitted to our hospital, the scale was assessed once. For patients who were transferred from other hospitals with an SDH diagnosis, the scale was assessed twice: once before the patient was admitted to another hospital and once after the patient was admitted to other hospitals before the occurrence of an SDH. For patients who were transferred from other hospitals without an SDH, the scale was assessed 3 times: once before the patient was admitted to other hospitals, once after the patient was admitted to other hospitals, and once before the patient was admitted to our hospital. The duration in days of each period was recorded. The final cumulative duration of bed rest in hours was calculated as follows: ∑duration of each period (days) * bed rest per day (hours).

Radiographic findings

Brain MRI was performed using a 3.0-T System (Siemens) and included T1-weighted sagittal, axial, and coronal sequences with gadolinium enhancement; and T2-weighted axial sequences and axial fluid attenuation inversion recovery sequences. CTM/MRM/Gd-MRM were performed to detect the sites of CSF leakage. The leakage sites were categorized on the basis of their location in the cervical, thoracic, lumbar, and sacral segments. All radiological images were reviewed by at least one board-certified neuroradiologist and one board-certified neurologist. They reviewed all images to evaluate the characteristic features of an SIH (3), to document the presence or absence of SDHs, and to determine the number and locations of CSF leakage sites.

EBP and Analysis of Outcomes

All patients who had an SDH or failed with two weeks of conservative treatments received a targeted EBP (7) or blind EBP if the leakage site could not be

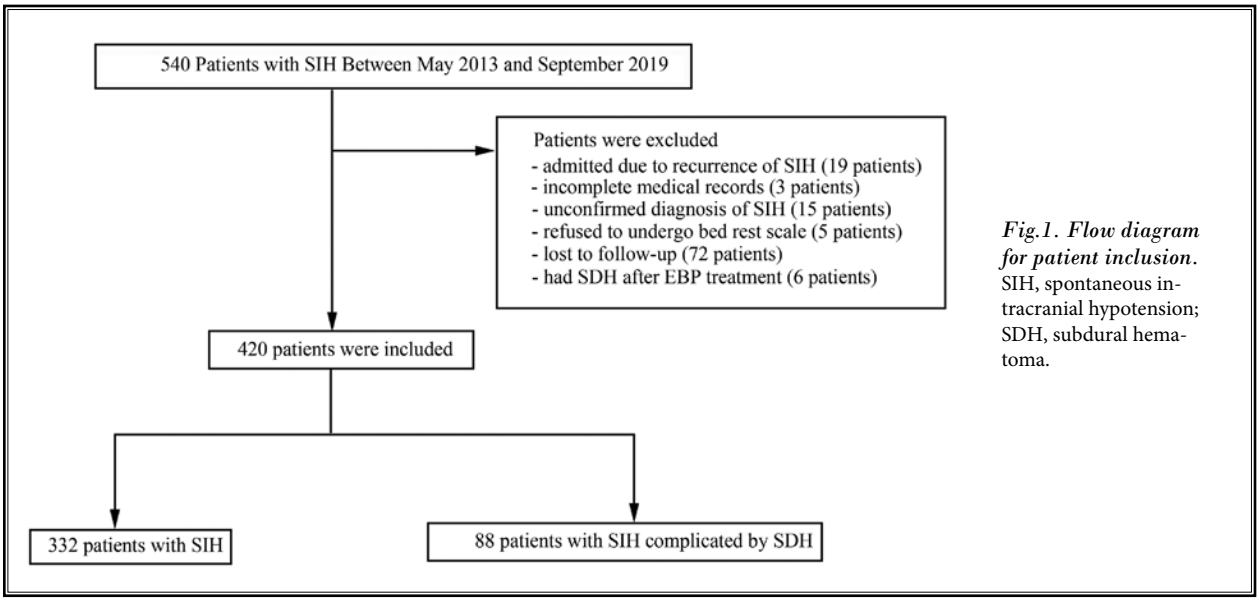

Fig.1. Flow diagram for patient inclusion. SIH, spontaneous intracranial hypotension; SDH, subdural hematoma.

identified. If patients still had persistent symptoms, or CSF leakage signs were seen on imaging after the first EBP, they received repeated EBPs. Some patients were even readmitted due to the recurrence of an SIH after discharge. The numbers of readmission (in total and within 3 months) were recorded.

Statistical Analyses

Statistical analyses were performed using IBM SPSS Statistics 24.0 software (IBM Corporation). Continuous variables were expressed as medians with interquartile ranges (IQRs). Categorical variables were reported as numbers and percentages. In univariate analysis, the Mann-Whitney U test or Kruskal-Wallis test was used to compare the values of nonnormally distributed continuous variables. A χ^2 test or Fisher's exact test was applied for categorical variables. A backwards stepwise Cox proportional hazard regression model was used to estimate the risk of cumulative duration of bed rest for an SDH.

Other potential confounders, including age, gender, orthostatic headache, nausea or vomiting, and unconsciousness which were significantly different ($P < 0.05$) in univariate analysis were included in the model as explanatory variables. Adjusted HRs and 95% CIs were estimated. To exclude the effect of the treatment algorithm, a Cox regression stratified by medical advice of strict bed rest before admission were performed. For all analyses, a 2-sided P value of < 0.05 was considered to indicate a statistically significant difference.

Results

From March 2013 through December 2019, 540 patients with SIH were admitted to our hospital. Patients who were admitted due to the recurrence of SIH were excluded (n = 19, 9 with SDH). Patients who had incomplete medical records (n = 3), had an unconfirmed diagnosis of SIH due to their refusal to undergo a definitive diagnostic test (n = 15, all without SDH), refused to complete a bed rest questionnaire (n = 5, one with SDH) or were lost to follow-up (n = 72, 12 with SDH) were excluded. Patients who had an SDH after EBP treatment were excluded as well (n = 6). Thus, we enrolled 420 patients with SIH, who were divided into 2 groups: an SDH Group (n = 88, 21%) and a non-SDH (NSDH) Group (n = 332, 79%), according to their manifestations on CTs or MRIs. Of the 88 patients with an SDH, only 29 underwent neurosurgical drainage.

Table 1 shows the demographic and clinical characteristics of the patients in the SDH and NSDH groups. The demographic data on the 420 patients, consisting of 275 (65.5%) women and 145 men (34.5%), were retrospectively reviewed; their median age was 40 (IQR, 33.00–49.75). The patients in the SDH Group were older than those in the NSDH Group, median age, 45.00 (IQR, 36.00-55.00) vs 39.00 (IQR, 32.25-47.00), $P < 0.001$. There were more men in the SDH Group than the NSDH Group (55.7% vs 28.9%, $P < 0.001$).

There were no significant differences in headache location between the 2 groups ($P = 0.245$). Patients in the SDH Group had fewer orthostatic headaches than those in the NSDH Group (90.9% vs 98.8%, $P < 0.001$). No significant differences in associated symptoms, except for nausea or vomiting ($P = 0.013$) and unconsciousness ($P < 0.001$), were found between the 2 groups. The 2 groups showed a similar percentage of patients with positive physical examination findings ($P = 0.707$) and meningeal irritation signs ($P = 0.436$). There were no significant differences between the SDH and NSDH Groups in cumulative duration of bed rest ($P = 0.814$). A backward stepwise Cox regression showed that significant predictor variables for SDH were: cumulative duration of bed rest in hours (HR = 0.997, 95% CI, 0.996-0.998; $P < 0.001$), age (HR = 1.029, 95% CI, 1.009-1.050; $P = 0.004$), and orthostatic headache (HR = 4.770, 95% CI, 2.177-10.450; $P < 0.001$) (Table 2).

Bed rest duration may be affected by medical advice. The differences in demographic and clinical characteristics of the patients who received conservative treatment (bed rest and hydration) before being admitted to our hospital or not admitted are shown in Supplemental Table 1. More patients were found to have received conservative treatment (27.2% vs. 5.7%, $P < 0.001$). The cumulative duration of bed rest in hours was longer in patients who received conservative treatment than those did not (median 255.2 [IQR, 149.6-425.6]) vs 120.0 [IQR, 54.0-319], hours; $P < 0.001$). With the consideration of the treatment algorithm, a backward stepwise Cox regression model showed that conservative treatment was a protective factor (HR = 0.437, 95% CI, 0.268–0.713; $P = 0.001$) and the interaction between the treatment algorithm and cumulative duration of bed rest was significant (HR = 1.001, 95% CI, 1.000–1.001; $P = 0.042$). Age (HR = 1.031, 95% CI, 1.011-1.052; $P = 0.002$) and orthostatic headache (HR = 5.419, 95% CI, 2.537-11.572; $P < 0.001$) remained significant predictors. Further analysis using a Cox regression model stratified by treatment algorithm showed that the HR for SDH was 0.997 (95% CI, 0.996–0.998; $P < 0.001$) in patients who received conservative treatment

Table 1. *Clinical characteristics of patients with SIH in the study.*

	Total (n = 420)	NSDH Group (n = 332)	SDH Group (n =88)	*P* Value
Age	40.00 (33.00-49.75)	39.00 (32.25-47.00)	45.00 (36.00-55.00)	< 0.001
Gender (men)	145 (34.5%)	96 (28.9%)	49 (55.7%)	< 0.001
Headache location				0.245
Frontal	84 (20.0%)	68 (20.5%)	16 (18.2%)	
Occipital	86 (20.5%)	69 (20.8%)	17 (19.3%)	
Temporal	24 (5.7%)	15 (4.5%)	9 (10.2%)	
Parietal	69 (16.4%)	58 (17.5%)	11 (12.5%)	
Diffuse (≥ 2 locations)	157 (37.4%)	122 (36.7%)	35 (39.8%)	
Orthostatic headache	408 (97.1%)	328 (98.8%)	80 (90.9%)	< 0.001
Associated symptoms				
Nausea or vomiting	207 (49.3%)	174 (52.4%)	33 (37.5%)	0.013
Hearing disturbance/tinnitus	100 (23.8%)	79 (23.8%)	21 (23.9%)	0.989
Stiffness	87 (20.7%)	68 (20.5%)	22 (21.2%)	0.819
Neck pain	19 (4.5%)	15 (4.5%)	4 (4.5%)	0.991
Dizziness	34 (8.1%)	30 (9%)	4 (4.5%)	0.170
Diplopia	3 (0.7%)	3 (0.9%)	0 (0.0%)	> 0.999
Decreased visual acuity	14 (3.3%)	11 (3.3%)	3 (3.4%)	0.964
Photophobia	0 (0.0%)	0 (0.0%)	0 (0.0%)	*
Seizure	3 (0.7%)	1 (0.3%)	2 (2.3%)	0.113
Trachyphonia	1 (0.2%)	1 (0.3%)	0 (0.0%)	> 0.999
Unconsciousness	8 (1.9%)	1 (0.3%)	7 (8.0%)	< 0.001
Positive physical examination findings	108 (25.7%)	84 (25.3%)	24 (27.3%)	0.707
Meningeal irritation sign	84 (20.0%)	69 (20.8%)	15 (17.0%)	0.436
Cumulative duration of bed rest (hours)	240.0 (107.4-400.0)	240.0 (120.0-385.4)	240.8 (60.8-453.0)	0.814

Values are expressed as median with interquartile range and n (%).
NSDH, no subdural hematoma; SDH, subdural hematoma; SIH, spontaneous intracranial hypotension.
*No statistics are computed because photophobia is a constant.

and 0.996 (95% CI, 0.992–1.000; $P = 0.061$) in patients who did not, respectively.

The results of diagnostic tests, including brain MRI, CTM/MRM/Gd-MRM, and CSF opening pressure analysis are summarized in Table 3. We found that 22.0% of the patients in the NSDH Group but no patients in the SDH Group showed normal features on brain MRIs ($P < 0.001$). Some characteristic findings in the NSDH Group and SDH Group, respectively, were: subdural fluid collection (5.1% vs 22.7%; $P < 0.001$), enhancement of the pachymeninges (74.4% vs 95.5%; $P < 0.001$), and sagging of the brain (6.9% vs 14.8%; $P = 0.019$).

Some studies have suggested that MRM itself is not a reliable means for localizing spinal CSF leaks, reporting CSF leakage in 48% to 76% of cases (11). So we only analyzed those who underwent CTM or Gd-MRM together with MRM to confirm the presence of a perineural leak. In total, 194 patients underwent successful CTM (n = 28) or Gd-MRM (n = 166) after MRM. Among those patients, the CSF leakage location ($P = 0.199$) and the number of leakage locations ($P = 0.252$) did not differ significantly between the 2 groups (Table 3). Overall, 337 patients had measured CSF opening

Table 2. *Multivariable analysis using a Cox regression Model for patients with SIH complicated by SDH.*

Variables	Hazard Ratio	95% CI	*P* Value
Age	1.029	1.009-1.050	0.004
Orthostatic headache	4.770	2.177-10.450	< 0.001
Cumulative duration of bed rest (hours)	0.997	0.996-0.998	< 0.001

NSDH, no subdural hematoma; SDH, subdural hematoma; SIH, spontaneous intracranial hypotension.

Table 3. *Diagnostic tests between the NSDH and SDH Groups in SIH.*

	Total (n = 420)	NSDH Group (n = 332)	SDH Group (n = 88)	*P* Value
Brain-enhanced MRI				
Normal features	73 (17.4%)	73 (22.0%)	0 (0.0%)	< 0.001
Subdural fluid collection	37 (8.8%)	17 (5.1%)	20 (22.7%)	< 0.001
Enhancement of the pachymeninges	331 (78.8%)	247 (74.4%)	84 (95.5%)	< 0.001
Small lateral ventricle	161 (38.3%)	125 (37.6%)	36 (40.9%)	0.735
Engorgement of venous structures	94 (22.4%)	80 (24.1%)	14 (15.9%)	0.101
Pituitary hyperemia	114 (27.1%)	92 (27.7%)	22 (25.0%)	0.611
Sagging of the brain	36 (8.6%)	23 (6.9%)	13 (14.8%)	0.019
Number of leak locations*				0.252
No clear site	13 (6.7%)	13 (8.0%)	0 (0.0%)	
Single site	84 (43.3%)	69 (42.6%)	54 (61.4%)	
Multiple sites	97 (50%)	80 (49.4%)	34 (38.6%)	
Locations				0.199
Cervical	13 (6.7%)	12 (7.4%)	1 (3.1%)	
Thoracic	28 (14.4%)	22 (13.6%)	6 (18.8%)	
Lumbar	10 (5.2%)	9 (5.6%)	1 (3.1%)	
Cervical+Thoracic	105 (54.1%)	87 (53.7%)	18 (56.3%)	
(Cervicothoracic junction)	32 (30.4%)	26 (29.9%)	6 (33.3%)	
Cervical+Lumbar	1 (0.5%)	0 (0.0%)	1 (3.1%)	
Thoracic+Lumbar	12 (6.2%)	10 (6.2%)	2 (6.3%)	
Cervical+Thoracic+Lumbar	12 (6.2%)	9 (5.6%)	3 (9.4%)	
No clear location	13 (6.7%)	13 (8.0%)	0 (0.0%)	
CSF opening pressure (mm H_2O) †	45 (17.5-80)	45 (15-75)	50 (25-95)	0.250
Patients with CSF opening pressure < 60 mm H_2O†	219 (52.1%)	186 (37.4%)	33 (40.0%)	0.218

Values are expressed as median with interquartile range and n (%).
CSF, cerebrospinal fluid, EBP, epidural blood patch; MRI, magnetic resonance imaging; NSDH, no subdural hematoma; SDH, subdural hematoma; SIH, spontaneous intracranial hypotension.
* In total 194 patients underwent successful computed tomography myelography (n = 28) or intrathecal gadolinium MR myelography (n = 166) after magnetic resonance myelography to confirm the presence of a perineural leak.
†CSF analysis was performed for 337 patients (280 patients in NSDH Group and 57 patients in SDH Group).

pressure (280 in the NSDH Group and 57 in the SDH Group) as 83 patients did not receive lumbar puncture. The CSF opening pressure was similar between the 2 groups (45, [IQR, 15-75] vs 50 [IQR, 25-95], mm H_2O, P = 0.250). The percentage of patients whose CSF opening pressure was below 60 mm H_2O, was similar between the 2 groups (37.4% vs 40.0%, P = 0.218).

Regarding clinical outcomes shown in Table 4, the length of hospital stay was longer in SDH Group patients than in NSDH Group patients (median, 22 [IQR, 16-31] vs 14 [IQR, 11-18] days; P < 0.001). More patients in the SDH Group received an EBP (97.7% vs 85.5%, P = 0.002) and repeated EBP than patients in the NSDH Group (60.5% vs 33.8%, P < 0.001). The median EBP times were 2 (IQR, 1-2) in patients in the SDH Group and one (IQR, 1-2) in the NSDH Group (P < 0.001). Among all patients, 14.3% were readmitted due to an SIH recurrence after hospital discharge. The recurrence of an SIH after discharge occurred mostly in the first 3 months (73.3% of all cases of recurrence). There were no significant differences in the readmission times due to an SIH recurrence (overall and within 3 months) between the 2 groups (P = 0.845 and P = 0.760, respectively.

Discussion

The incidence of SDHs in patients with SIH in our cohort was 21.0%, which is in agreement with reported data (3,6,12). We found the cumulative duration of bed rest in hours was a protective factor for an SDH in SIH (HR = 0.997, 95% CI, 0.996-0.998; P < 0.001). With the

Table 4. *Clinical outcomes of patients with SIH between the NSDH and SDH Groups.*

	Total (n = 420)	NSDH Group (n = 332)	SDH Group (n = 88)	*P* Value
Length of hospitalization (days)	15 (12-20)	14 (11-18)	22 (16-31)	<0.001
EBP	370 (88.1%)	284 (85.5%)	86 (97.7%)	0.002
Repeated EBP	148 (40.0%)	96 (33.8%)	52 (60.5%)	< 0.001
EBP times	1 (1-2)	1 (1-2)	2 (1-2)	< 0.001
Readmission due to recurrence of SIH after discharge (in total)	60 (14.3%)	48 (14.5%)	12 (13.6%)	0.845
Readmission due to recurrence of SIH after discharge (< 3 months)	44 (10.5%)	34 (10.2%)	10 (11.4%)	0.760

Values are expressed as median with interquartile range and n (%).
EBP, epidural blood patch; NSDH, no subdural hematoma; SDH, subdural hematoma; SIH, spontaneous intracranial hypotension.

consideration of treatment, cumulative duration of bed rest was associated with SDH development in patients who received conservative treatment before admission (HR = 0.997, 95% CI, 0.996–0.998; $P < 0.001$) and in patients who did not (HR = 0.996, 95% CI, 0.992–1.000; $P = 0.061$), respectively. We also found that age (HR = 1.029, 95% CI, 1.009-1.050; $P = 0.004$) and orthostatic headache (HR = 4.770, 95% CI, 2.177-10.450; $P < 0.001$) were risk factors for an SDH in SIH. Clinical short-term outcomes, including length of hospital stay, EBP therapy, and repeated EBP therapy, were higher in the SDH Group. Long-term outcomes, i.e., revisit rates, were similar between the 2 groups.

To the best of our knowledge, the present report is the first to evaluate the association of bed rest with later development of an SDH in SIH. We found that the cumulative duration of bed rest was a protective factor for an SDH in SIH in the adjusted model. Though only patients with a diagnosis of SIH were included, our cohort had 2 sources of patients, i.e., those who were admitted in our hospital, and those who had received conservative treatment in other hospitals and transferred to our hospital.

Since bed rest durations would be affected by medical advice, we included conservative treatment in the Cox regression model and found that conservative treatment was a protective factor for an SDH and that there was interaction between the cumulative duration of bed rest and conservative treatment. Further stratified Cox analysis showed that the cumulative duration of bed rest remained associated with SDH development in patients who received conservative treatment and in patients who did not, suggesting that bed rest, no matter whether before or after medical consultation, contributes to a lower risk of SDH development in SIH. It is generally believed that being supine reduces CSF pressure at the site of leakage. Bed rest can diminish hydrostatic pressure against defects in the dural membrane and allow the defect to heal (13).

We postulated that inadequate bed rest may decrease the rate of CSF pressure reconstruction, leading to longer compensation by venous engorgement resulting in subdural fluid collection, which may produce tears in bridging veins and cause an SDH. Bed rest is considered a purely conservative approach for SIH, but has not been evaluated by randomized clinical trials. Our study, which illustrates that the cumulative duration of bed rest is a protective factor for SDH in SIH, providing evidence for bed rest therapy as the basis of conservative treatments.

We found that advanced age is associated with an SDH, in accordance with previous studies (5,14). Older people are thought to have a higher tendency to develop an SDH due to brain atrophy (15,16). We found that orthostatic headache occurs less frequently in an SDH, but further multivariable analysis illustrated that orthostatic headache was a risk factor for SDH. This is probably because the orthostatic headaches may illustrate severe CSF leakage and produce more tears in bridging veins and cause SDH. Other symptoms were not associated with an SDH in the multivariable analysis, in accordance with previous findings (3,5,12). We are the first to demonstrate that the positive physical examination findings, and meningeal irritation sign, were similar between the NSDH and SDH Groups.

Patients with SIH have been known to exhibit certain characteristic features on brain MRI (3,17). We found patients in the SDH Group more frequently showed subdural fluid collection, enhancement of the pachymeninges, and sagging of the brain, whereas patients in the NSDH Group showed more normal features on brain MRI, in accordance with previous studies (5,18).

Our study failed to identify any differences between the SDH and NSDH Groups in CSF leakage loca-

tions and the number of leakage locations, probably because the size of the leakage site and the velocity of leakage rather than the number of leakages are directly correlated with SIH, consistent with previous observations (5,18).

The CSF opening pressure did not differ significantly between the 2 groups. Previous studies are controversial with some finding an increased CSF opening pressure (19,20), while others did not (21,22). Thus, we speculate that elevated intracranial pressure may not be related to SDHs in SIH.

Many reports describe SIH as having a benign course after surgical or conservative management. We revealed that 11.9% of patients recovered after conservative treatment. We found that more patients with an SDH failed conservative management. A meta-analysis reported the success of conservative treatment in 28% of patients with SIH (11). Our failure rate was likely higher because our center is the largest center for SIH in the Chinese mainland, and admits patients with more severe SIH, especially those who failed to heal after conservative treatment in other hospitals.

Notably, we demonstrated that 60% of patients with SIH recovered with the first EBP, in accordance with a previous meta-analysis (11). Patients in the SDH Group received more repeated EBPs than patients in the NSDH Group. We speculate that more EBPs may be given to patients with an SDH due to severe CSF leakage. We found that the length of hospital stay was longer for patients in the SDH Group, probably due to receiving more EBPs or even surgery.

The total recurrence rate of SIH was 14.3% and was comparable between the SDH and NSDH Groups. The recurrence rates in previous studies varied, ranging from 0% to 28% (3,18,23-25). However, the small number and specific nature of the patients limited the generalization of their findings. Moreover, we found that readmission due to the recurrence of SIH after discharge occurred mostly in the first 3 months, probably because of incomplete healing of the previous CSF leakage. We found that the recurrence of SIH were similar between the SDH and NSDH Groups, illustrating that SIH with an SDH can have good outcomes with proper and in-time treatment.

Limitations

This study has some limitations. First, this was a retrospective study. The retrospective collection of data, especially spanning a long period of time, meant that our patients were assessed by different radiological procedures, particularly to identify CSF leakages, and were managed using different therapeutic strategies. In addition, the bed rest scores were based on the patient's memory; therefore, due to memory distortion or incompleteness, their accuracy and reliability may be biased. In addition, this was a single-center study. Multicenter studies using a larger sample size are needed to validate any decision algorithm. Moreover, the validity of the bed rest scale, which was first designed by our team, has not been evaluated in a prospective study.

Conclusions

In summary, cumulative duration of bed rest is a protective factor for the development of an SDH in SIH. With more time and proper treatment, patients with SIH with an SDH can achieve a good prognosis.

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Suppl. Table 1. ***Comparison between SIH patients received conservative treatment or not.***

	Patients without conservative treatment (n = 122)	**Patients with conservative treatment (n =298)**	***P* value**
SDH number (%)	7 (5.7%)	81 (27.2%)	< 0.001
Age	39.5 (32-48.25)	41 (33-50)	0.264
Gender (male)	46 (37.2%)	99 (33.2%)	0.380
Headache location			0.922
Frontal	24 (19.7%)	60 (20.1%)	
Occipital	5 (4.1%)	61 (20.5%)	
Temporal	25 (20.5%)	19 (6.4%)	
Parietal	21 (17.2%)	48 (16.1%)	
Diffuse (≥ 2 locations)	47 (3%)	110 (36.9%)	
Orthostatic nature	120 (98.4%)	288 (96.6%)	0.338
Associated symptoms			
Nausea or vomiting	63 (51.6%)	144 (48.3%)	0.537
Hearing disturbance or tinnitus	25 (20.5%)	75 (25.2%)	0.307
Stiffness	22 (18.0%)	65 (21.8%)	0.386
Neck pain	4 (3.3%)	15 (5.0%)	0.432
Dizziness	15 (12.3%)	19 (6.4%)	0.043
Diplopia	1 (0.8%)	2 (0.7%)	> 0.999
Decreased visual acuity	7 (5.7%)	7 (2.3%)	0.079
Photophobia	0 (0.0%)	0 (0.0%)	ǂ
Seizure	2 (1.6%)	1 (0.3%)	0.203
Trachyphonia	0 (0.0%)	1 (0.3%)	> 0.999
Unconsciousness	2 (1.6%)	6 (2.0%)	0.799
Positive physical examination findings	32 (26.2%)	76 (25.5%)	0.877
Meningeal irritation sign	23 (18.9%)	61 (20.5%)	0.707
CSF opening pressure (mmH_2O)*	52 (9.25-120)	45 (20-70)	0.158
Patients with CSF opening pressure < 60 mmH_2O	54 (56.3%)	165 (68.5%)	0.034
Cumulative duration of bed rest (hours)	120.0 (54.0-319.2)	255.2 (149.6-425.6)	< 0.001
Time from symptom to SDH or last assessment (days)	17.5 (7.0-30.0)	30.0 (16.0-40.0)	< 0.001

Values are expressed as median with interquartile range and n (%).
SDH, subdural hematoma; SIH, spontaneous intracranial hypotension.
*CSF analysis was performed for 337 patients (96 patients without conservative treatment and 241 patients with conservative treatment).