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Brain Spontaneous Intracranial Hypotension Score for treatment monitoring after surgical closure of the underlying spinal dural leak

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Abbreviations

bSIH score	brain spontaneous intracranial hypotension score
CSFVF	CSF venous fistula
CT	computed tomography
FLAIR	fluid-attenuated inversion recovery
IQR	interquartile range
MPD	mamillopontine distance
MPR	multiplanar reconstruction
NRS	numeric rating scale
ntEBP	non-targeted epidural blood patch
SD	standard deviation
SE	spin echo
SIH	spontaneous intracranial hypotension
SSS	superior sagittal sinus

Key words: spontaneous intracranial hypotension, CSF loss, CSF leak, SIH score

Abstract

Background: Spontaneous intracranial hypotension (SIH) is a debilitating condition requiring effective treatment. However, objective data on treatment response are scarce.

Purpose: To assess suitability of the brain MRI-based, SIH score (bSIH) for therapy success monitoring of SIH patients with a proven spinal CSF leak after microsurgical closure of the underlying dural breach.

Methods: This retrospective cohort study included consecutive SIH patients with a proven spinal CSF leak, investigated at our department from January 2012 to March 2020. The bSIH score integrates 6 imaging findings; 3 major (2 points) and 3 minor (1 point), and ranges from 0 to 9, with 0 indicating low and 9 high probability of spinal CSF loss. The score was calculated using brain MRI before and after surgical treatment of the underlying CSF leak. Headache intensity was registered on a numeric rating scale (NRS) (range: 0–10).

Results: Fifty-two SIH patients (35 [67%] female; mean age, 45.3 years) with a proven spinal CSF leak were included. The mean bSIH score decreased significantly from baseline to after surgical closure of the underlying dural breach (6.9 vs 1.3, $P < .001$). A decrease in the NRS score was reported (8.6 vs 1.2, $P < .001$).

Conclusions: The bSIH score is a simple tool which may serve to monitor treatment success in SIH patients after surgical closure of the underlying spinal dural leak. Its decrease after surgical closure of the underlying spinal dural breach indicates restoration of an equilibrium within the CSF compartment.

Introduction

Spontaneous intracranial hypotension (SIH) is a debilitating medical condition resulting from the disturbance of a well-regulated equilibrium within the CSF compartment.

Most patients present with orthostatic headache; however, atypical headache phenotypes including thunderclap, non-positional, exertional, and "second-half-of-the-day" headache have also been reported.[1–4]

Despite being termed intracranial hypotension, only 34–38% of SIH patients present with an opening pressure of <6 cm H_2O.[5,6] Since continuous CSF loss is associated with typical spine and brain imaging findings, neuroimaging plays a crucial role in the diagnostic work-up.[7] Various brain imaging findings have been described in SIH patients; however, none is pathognomonic. Recently, a brain MRI-based SIH score (bSIH), predicting the likelihood of a spinal CSF leak in patients with clinical suspicion of SIH, has been proposed[8] (Figure 1a). The bSIH score incorporates the 6 most relevant brain imaging findings and ranges from 0 to 9. According to the final score patients may be classified as having low (score ≤ 2), intermediate (3–4), or high probability (≥ 5) for a CSF leak (Figure 1b).

Therapy in SIH patients widely varies among institutions. The clinical presentation after treatment can pose diagnostic difficulties and a standardized and objective tool for treatment follow-up is lacking.

The main goal of our study was to compare the change in the bSIH score between baseline and follow-up after microsurgical closure of the underlying spinal CSF leak, as well as its correlation with the clinical course.

Material and Methods

We obtained approval from the local ethics committee for this study (Project ID 2020-00645). Informed consent for further use of health care data was provided by the patient or next-of-kin using the general consent form.

Study cohort

All consecutive patients with a clinical suspicion of SIH who underwent clinical work-up at our institution between January 2012 and March 2020 were eligible for this retrospective study (n = 215). The exclusion criteria were: no proof a spinal CSF leak or CSF venous fistula (CSFVF) on multimodal imaging (spine MRI, dynamic myelography, postmyelography computed tomography (CT)) (n = 123); inadequate brain MRI (missing or acquired >6 months) or recent lumbar puncture (n = 37), previous spinal surgery due to CSF loss (n = 2), and age younger than 18 years (n = 1) (flowchart see Figure 2).

The final study population comprised 52 patients who met the following criteria: (1) clinical work-up due to suspicion of SIH, (2) baseline brain MRI performed prior to lumbar puncture and CSF leak surgery, (3) spinal CSF leak proven on multimodal imaging (spine MRI, dynamic myelography, and postmyelography CT), (4) treated with primary surgery, or secondary surgery after failed non-targeted epidural blood patch (ntEBP), and (5) follow-up brain MRI performed after spine surgery.

Brain MRI

MRI before and after treatment was performed on a 1.5 or 3 Tesla scanner (Magnetom

Avanto/Aera and Magnetom Verio/Trio, Siemens, Erlangen, Germany). The MRI included native and gadolinium-enhanced sequences.

Since brain MRI was performed for clinical reasons and not as part of a dedicated study protocol, the acquired sequences were not identical.

bSIH score

This recently proposed score is based on brain MRI and integrates the 6 most reliable imaging findings in SIH patients:[8] 3 major (2 points each) – pachymeningeal enhancement, engorgement of venous sinus, and effacement of the suprasellar cistern (≤4.0 mm), and 3 minor (1 point each) – subdural fluid collection, effacement of the prepontine cistern (≤5.0 mm), and mamillopontine distance (≤6.5 mm) (Fig. 1). Patients with a score of ≤2, 3–4, or ≥5 have a low, intermediate, or high probability of spinal CSF loss (Fig. 1b). The score was calculated at baseline and after treatment. In patients for whom multiple MRIs were available the most recent before therapy was considered baseline. For patients who underwent secondary surgery after a failed ntEBP, the baseline MRI was considered to be the exam after ntEBP. If patients had records of multiple follow-up examinations, all were scored separately to evaluate the long-term evolution of the bSIH score.

Image analysis

The MRI studies of all subjects were assessed by one board-certified neuroradiologist (T.D., 9 years of experience), and a medical student with a special interest and training in this field (R.R.) blinded to clinical presentation, other imaging studies, and type of therapy.

Engorgement of the venous sinuses was evaluated on post-gadolinium T1-weighted images based on the shape of the outer contour of the superior sagittal sinus and of the dominant transverse sinus. Briefly, under normal circumstances, the inferior border of the middle portion of the transverse sinus and lateral border of the SSS usually exhibit a concave or straight border, which usually becomes convex in case of intracranial hypotension. Abnormal pachymeningeal enhancement, which was defined as a thickened smooth and diffuse line around both hemispheres and was assessed on post-gadolinium T1-weighted images. Subdural fluid collection(s) was assessed on transversal and coronal FLAIR images.

All quantitative measures were assessed on sagittal T1-weighted post-gadolinium images. The suprasellar cistern - distance between the inferior surface of the optic chiasm and the superior surface of the pituitary gland. The prepontine cistern - between the anterior aspect of the midportion of the pons and the clivus. The mamillopontine distance - between the inferior border of the mammillary body and the upper surface of the pons.

When a disagreement between readers in any of the qualitative signs was identified, the finding was reviewed together to reach consensus. All quantitative signs, which all have been previously demonstrate to have a high interrater agreement, were measured by one reader only. Only patients with data on all 6 variables required for the calculation of the score were considered for the bSIH score analysis (SIH complete). Patients with any missing variables were excluded from bSIH score analysis, and the available variables were analyzed separately.

Additionally, the height of the pituitary and the time interval between each imaging study and treatment was recorded.

Surgical closure of spinal dural CSF leak

This technique has been previously described.[9,10] Briefly, after interlaminar fenestration or hemilaminotomy, the ligamentum flavum was removed. In the case of a ventral dural leak, a dorsal or slightly paramedian durotomy and release of the dentate ligaments were performed in order gain access to the anterior dura. The ventral osseous microspur penetrating the dura was removed, the dura was sutured and a small intra- and epidural patch placed for augmentation. In the case of a tear in the nerve root sleeve diverticulum access was gained via foraminotomy, the diverticulum was reduced and the nerve root was then clipped or the dura sutured before being wrapped with an external dura graft.

In most patients, surgery was the primary treatment. For patients who did not respond to ntEBPs, it was the secondary treatment.

Clinical investigation

Patients were followed in the outpatient clinic for 6 to 8 weeks after surgery. Patients living abroad, who came to our institution for surgical treatment of SIH, were followed up by phone interview. Additionally, a standardized questionnaire was sent to all patients several months after treatment. The questionnaire asked about headache intensity according to the numeric rating scale (NRS) before and after treatment, whether there was complete, partial, or no resolution of SIH symptoms after treatment, and general satisfaction with treatment. When available, clinical follow-up data were derived from the questionnaire (n = 38; 73%). Otherwise, clinical data were extracted from the chart review of the regular postoperative follow-up visits (n = 14; 27%). No clinical follow-up information was available for 2 patients who lived abroad and were not contactable.

Statistical analysis

Statistical analysis was performed using R (R Core Team (2019); R: A language and environment for statistical computing.

Descriptive analysis used frequencies and percentages for categorical variables and mean (± standard deviation [SD]) or median (interquartile range [IQR]) for continuous variables. Chi-square tests and t-tests or Wilcoxon tests were used to compare categorical and continuous variables, respectively. The results enabled comparisons of the bSIH score and the NRS score at baseline and after surgery.

The main analysis focused on the patients for whom information on all the variables was available to compute the bSIH scores pre- and post-surgery.

Data Availability Statement

Where not in conflict with constraints of the original ethical approval under which the data were collected, pseudo-anonymized data will be made available for appropriate collaborative research, subject to appropriate ethical approval being gained for such use.

Results

The final study cohort included 52 SIH patients with a confirmed CSF leak. Mean age was 45.3 years (SD ± 11.4, range: 25–73); 35 patients were female and 17 male. The duration of clinical symptoms varied from a few days to several years. Mean duration of clinical follow-up was 631 days.

Baseline characteristics of the CSF leak

In 38/52 cases (73%), a ventral microspur originating from an intervertebral disc or an endplate osteophyte, and in 11/52 cases (19%) a tear in the nerve root diverticulum, was the underlying pathology. In 3 patients, a ventral dural tear with epidural CSF was demonstrated in the absence of a microspur, presumably due to a resorbed spur. No patient with a CSFVF was identified. The site of CSF leakage was in the cervical, thoracic, and lumbar spine in 4, 47, and 1 patient, respectively.

Imaging and clinical follow-up:

The mean time interval between the baseline MRI and surgery was 49 days (±63), and between surgery and the first follow-up MRI, it was 149 days (±242).

Records of clinical follow-up were available for 50 patients, while 2 were lost to follow-up. Complete symptom regression, clinical improvement with residual symptoms, or no clinical change was reported in 29, 18, and 3 patients, respectively. The NRS score decreased from baseline to first follow-up after surgery (8.6 vs 1.2, $P<.001$).

Prior to surgery orthostatic headache was reported by 32 patients, denied by 9 patients and not specified by 11 patients. Other, non-orthostatic headache types were reported by 18 patients, denied by 20 patients and not specified by 14 patients. Furthermore, at baseline visual impairment was reported by 18 patients, declined by 23 patients, and could not be specified by 11 patients. Additional auditory symptoms (impairment or tinnitus) was reported by 24 patients, declined by 17 patients, and could not be specified in 11 patients at baseline.
After surgery orthostatic headache was reported by only 3 patients, denied by 35 patients and not specified by 14 patients. Other, non-orthostatic headache types were reported by 13 patients, denied by 25 patients and not specified by 14 patients. The most frequently reported non-headache symptom after surgery was tinnitus (n=5), dizziness (n=4), local discomfort at the surgical access site (n=4).

Low correlation between bSIH and NRS was found pre-surgery 0.299, and post-surgery, respectively 0.381.

bSIH score analysis (n=31)

In patients with a complete MRI work-up for calculation of the bSIH score (n = 31), the value decreased significantly between baseline and the first follow-up after surgery (6.9 vs 1.3, $P<.001$) (Fig. 3). This was paralleled by a decrease in the NRS score which is demonstrated in figure 4. All of these patients demonstrated decrease in qualitative SIH signs from baseline to first follow-up: pachymeningeal enhancement (83.9% vs 0%, $P<.001$), engorgement of venous sinus (80.6% vs 3.2%, $P<.001$), and subdural fluid collection (54.8% vs 19.4%, $P=.009$) (Table 1). (Fig. 5). The number of patients with abnormal quantitative variables as defined by previously published cut-off values significantly decreased from baseline to first follow-up after surgery, indicating a normalization within the CSF compartment: suprasellar cistern (cut-off 4 mm) (74.2% vs 29.0%, $P<.001$), prepontine cistern (cut-off 5 mm) (77.4% vs 25.8%, $P<.001$), and mamillopontine distance (cut-off 6.5 mm) (80.6% vs 16.1%, $P<.001$)

In patients who had multiple MRI examinations (n = 8) after treatment, the bSIH score decreased over time or remained stable at a low level; no patient had an increase in the bSIH score (Fig. 6).

After treatment five patients demonstrated an intermediate (n=4 bSIH 3; n=1 bSIH 4), and one patient a high (bSIH 5) probability for a CSF leak. In all of these patients there was an average drop in bSIH from baseline to first follow-up brain MRI of 4.8 (min -3, max. -6). One patient each demonstrated a bSIH of 5 or 4 on follow-up. In both of them follow-up MRI was acquired only 3 days after surgery which might not be enough for the imaging signs to completely normalize. In the remaining four patients, follow-up imaging was acquired later after surgery (mean: 84 days). One patient had a 5-year history of SIH prior to surgery; thus, in long-standing history of imaging signs might not completely normalize. Three further patients with a bSIH of 3 on follow-up demonstrated a subtle effacement of the prepontine and suprasellar cistern; just above the proposed cut-off value.

Analysis of single imaging signs in the entire cohort (n=52)

Twenty-one patients had a missing MRI sequence (T1weighted imaging after gadolinium) meaning that calculation of the bSIH score could not be performed. In all patients (n = 52), whether or not a complete bSIH score was available, a significant improvement in each imaging variable between baseline and after surgery was statistically significant. A significant increase ($P<.001$) in all quantitative variables from baseline to first follow-up after surgery, indicating a normalization within the CSF compartment, was demonstrated: suprasellar cistern (3.3 vs 5.8 mm), prepontine cistern (4.3 vs 5.7 mm), and mamillopontine distance (5.8 vs 7.4 mm)

The height of the pituitary decreased from baseline to follow-up after surgery (7.4 vs 5.7 mm, $P<.001$).

Discussion

Our study demonstrates a significant decrease in the bSIH score after surgical closure of the dural breach in SIH patients with a proven spinal CSF leak. This shift implies restoration of an equilibrium within the CSF compartment by sealing the CSF leak. In the cohort with a proven spinal CSF leak, the bSIH score seems a robust diagnostic tool to objectively quantify treatment success after surgical closure of a spinal dural CSF leak.

Reestablishing the equilibrium within the well-regulated CSF compartment, which is disturbed by the continuous CSF loss in SIH patients, is the common aim of all therapeutic approaches. Depending on the type of therapy and local expertise, different medical disciplines may be involved in treating patients, including neurologists, neuroradiologists, anesthesiologists or neurosurgeons. This leads to considerable heterogeneity between studies in SIH patients with regard to their design and outcome measures. The lack of a standardized and objective follow-up tool makes comparison between therapies challenging. Moreover, the level of evidence on treatment outcome in SIH patients is poor, mostly based on small retrospective studies.

SIH patients typically present with orthostatic headache caused by traction on pain-sensitive fibers within the dura mater and the walls of venous sinuses. In addition, cranial nerve palsy, due to sagging of the brain, which leads to nerve stretching or compression, may occur. These phenomena are the result of an increased spinal CSF loss when in the upright position leading to decreased brain buoyancy. However, clinical presentation may vary and various headache phenotypes have been reported in SIH patients. [1–4] Rebound intracranial hypertension (RIH), which may occur after successful treatment of a CSF leak may further compound the problem.[11] This is because headache associated with RIH may resemble that caused by intracranial hypotension, and this makes clinical discrimination challenging, albeit essential, since therapy for SIH and RIH is different.[12,13]

Given that the clinical presentation is variable and subjective, and the opening pressure is unreliable for diagnosis, it may likewise be considered inadequate for follow-up.[14] Relying merely on these 2 factors is inadequate for objective monitoring of SIH patients. Brain MRI may provide a valuable additional tool for standardized therapy monitoring and may complement the clinical presentation.

Although imaging plays a pivotal role during the diagnostic work-up, it is often neglected during follow-up. Most studies reporting on the change in brain MRI after treatment focus on single imaging findings.[15–17] This may be inadequate, since none of the signs is pathognomonic, and, in our experience, some signs are subject to poor interobserver agreement.[8] As previously reported, the bSIH score is a reliable and objective tool to assess the likelihood of spinal CSF loss in patients with orthostatic headache at baseline. The findings of the present study indicate that the bSIH score may also serve as a reliable and quantitative tool for monitoring treatment success.

Our data indicate that improvement in bSIH score and each of the included imaging variables after surgical closure of a dural CSF leak is paralleled by a clinical improvement in orthostatic headache, visual and auditory symptoms. On the other hand, other non-orthostatic headache symptoms seem to be less likely to regress after surgery. SIH patients have often gone through a grueling ordeal, particularly when the true diagnosis and underlying cause has been missed. These patients may experience considerable psychological distress and even despair. Thus, successful treatment that can be confirmed not only by improved clinical findings, but also by the SIH score has tremendous value in reassuring these patients.

Of note, only low correlation between the bSIH score and headache intensity was demonstrated before and after surgery. Consequently, higher bSIH score is not necessarily indicative of more severe case of SIH. This may underline the fact that individual perception of symptoms is variable and subjective. However, as previously reported by our group the bSIH score was proposed to correlate with the probability of a spinal CSF leaks and not clinical severity.

Our study is subject to the weaknesses common to monocentric case series. It was retrospective, and did not include a control group. Because of a less standardized imaging and clinical follow-up in the beginning of the study period the follow-up time-point varies among patients and is a limitation of the current study. In addition, due to the absence of patients with a CSFVF in the utility of the bSIH score has not been tested in this cohort. However, Brinjikji et al. have recently reported similar decrease in the bSIH in patients with a CSFVF.[18] A small number of patients was lost to follow-up, as they were referred to our institution from abroad, and follow-up imaging was performed in their home countries.

A larger prospective study is required for confirmation of the proposed score and its utility for treatment follow-up. Use of the proposed bSIH score in future studies could increase transparency in the field of SIH research, limit the heterogeneity in patient selection, and reduce bias.

Conclusion

Our results show that the bSIH score is a simple tool which may serve to monitor treatment success in SIH patients after surgical closure of the underlying spinal dural leak. An improvement in the score indicates a successful surgical closure of the underlying spinal CSF leak, and implies restoration of the equilibrium within the CSF compartment. Its routine application could lead to more standardized follow-up and patient reassurance, instead of relying merely on clinical findings, which may be nonspecific or difficult to interpret. Lastly, it may be useful in the design of future clinical trials.

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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Tables:

	Before Surgery (n=31)	After Surgery (n=31)	*P* Value
NRS score (mean ± SD)	8.64 (±1.60)	1.20 (±1.78)	<.001
bSIH score (mean ± SD)	6.90 (2.43)	1.26 (1.37)	<.001
Score grades			
Low (0–2)	3 (9.7%)	25 (80.6%)	<.001
Intermediate (3–4)	3 (9.7%)	5 (16.1%)	
High (5–9)	25 (80.6%)	1 (3.2%)	
Score variables			
Venous engorgement	25 (80.6%)	1 (3.2%)	<.001
Pachymeningeal enhancement	26 (83.9%)	0 (0%)	<.001
Suprasellar cistern (≤4 mm) (mean ± SD)	3.0 (2.1)	6.2 (2.6)	<.001
Subdural collection	17 (54.8%)	6 (19.4%)	<.009
Prepontine cistern (≤5 mm) (mean ± SD)	4.0 (1.8)	6.0 (1.1)	<.001
MPD (≤6.5 mm) (mean ± SD)	5.4 (2.5)	7.7 (1.4)	<.001
Pituitary height	7.9 (1.5)	5.9 (1.6)	<.001

Table 1. All Patients with a Complete bSIH Score (n=31)

A total of 6 patients underwent secondary surgery after ntEBP failed to lead to long-term clinical improvement. In those patients, the brain MRI examination performed after ntEBP was considered the baseline for this evaluation. The bSIH score ranges from 0–9, with 0 indicating very low and 9 very high probability of spinal CSF loss. Headache intensity was registered according to a numeric rating scale (NRS) (range: 0–10).

Figures:

Fig. 1. The bSIH Score

Upper row: Scoring system based on brain MRI for patients with CSF loss syndrome. It is calculated by summation of 3 major criteria (2 points each) and 3 minor criteria (1 point each).

Lower row: The bSIH score ranges from 0 to 9, with 0 indicating very low probability of spinal CSF loss and 9, very high probability. Patients with a score of ≤2, 3–4, or ≥ 5 have a low, intermediate, or high probability of spinal CSF loss, respectively.

		Score
Major	Engorgement venous sinus	2
	Pachymeningeal enhancement	2
	Suprasellar cistern (≤ 4 mm)	2
Minor	Subdural fluid collection	1
	Prepontine cistern (≤ 5 mm)	1
	Mamillopontine distance (≤ 6.5 mm)	1

Fig. 2. Study Flowchart

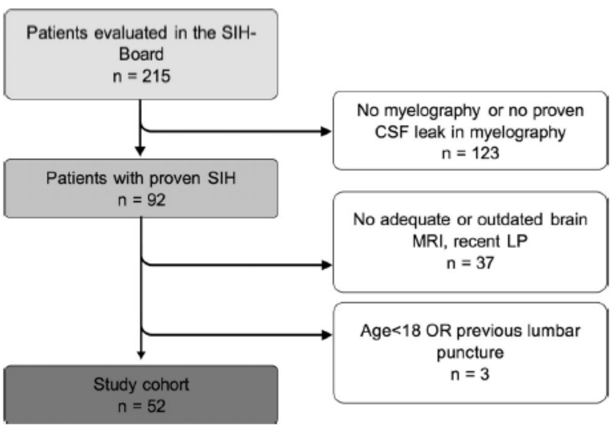


Fig. 2 Study flowchart. *CSF* cerebrospinal fluid, *MRI* magnetic resonance imaging, *LP* lumbar puncture, *SIH* spontaneous intracracranial hypotension

Fig. 3. bSIH Score Before and After Treatment

The distributions of scores on the bSIH scale before and after surgery are shown. The bSIH score ranges from 0 to 9. Patients with a score of ≤2 (green) have a low, 3–4 (orange) an intermediate, and ≥ 5 (red), a high probability of spinal CSF loss.

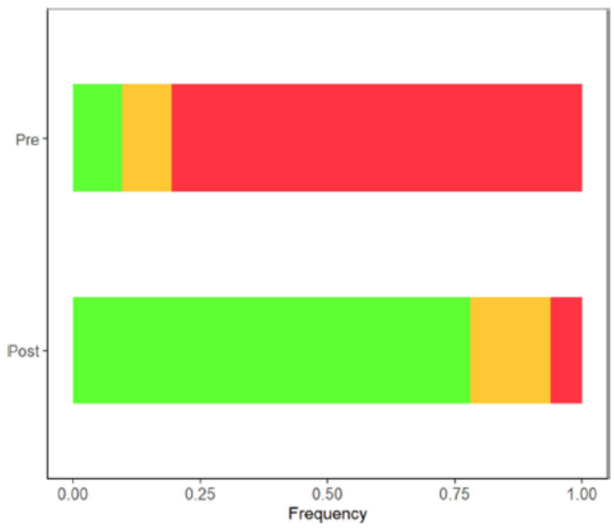


Fig. 4 Pre- and postsurgical bSIH score and the NRS score

The y-axis denotes the bSIH score and NRS score; Scores are standardized and set on the same scale.

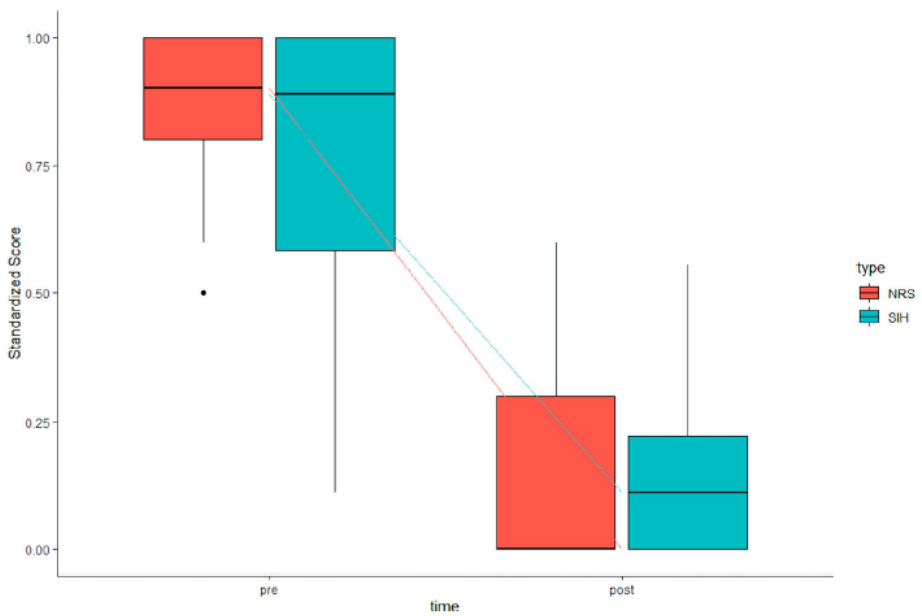
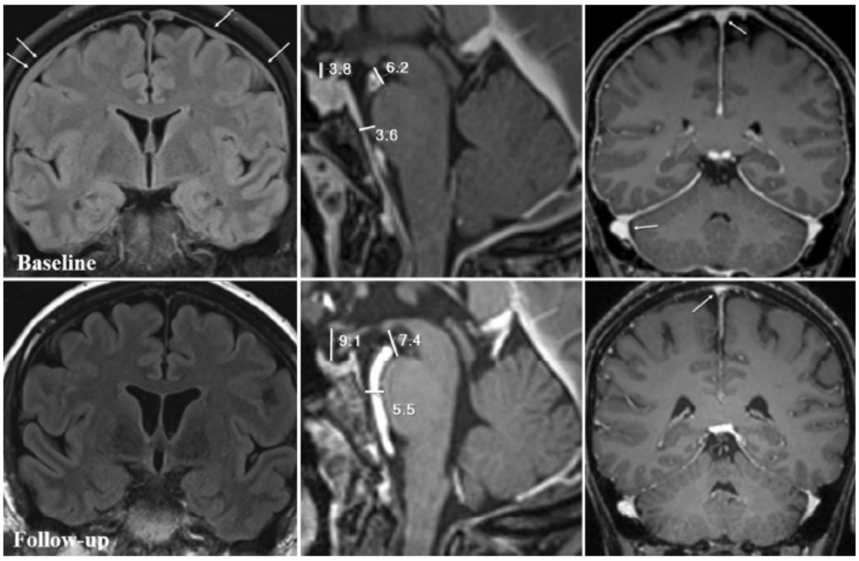
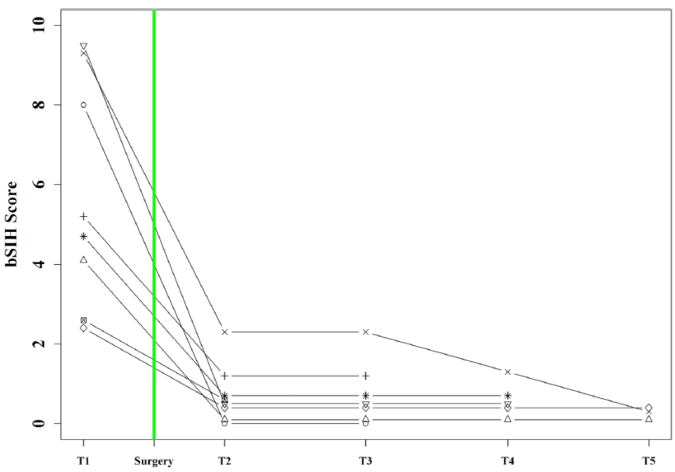


Fig. 5. Female Patient with a Myleographically Proven Spinal CSF leak due to a Microspur at Level C 2/3



Upper row: MRI performed before spinal surgery demonstrates typical findings of intracranial hypotension; bSIH score 9: pachymeningeal enhancement (2 points), engorgement of venous sinus (2 points), effacement of the suprasellar cistern (≤4.0 mm, 2 points), subdural fluid collection (1 point), effacement of the prepontine cistern (≤5.0 mm, 1 point), and mamillopontine distance (≤6.5 mm, 1 point). Lower row: MRI performed after surgery demonstrates almost complete resolution of all findings; bSIH score 0. Note also the striking decrease in pituitary size. Pain level before surgery, NRS 9; after surgery, NRS 0.

Fig. 6. Longitudinal evolution of the bSIH Score in Patients with Multiple MRI Exams



The y-axis denotes the bSIH score and the x-axis the timeline, with T1, T2, T3, and T4 representing consecutive brain MRI studies. The time of follow-up was not standardized and ranges from 1 year to 3 years. The green vertical line represents the time of surgery. Different time points represent different MRI exams.