

Relationship of Bern Score, Spinal Elastance, and Opening Pressure in Patients With Spontaneous Intracranial Hypotension

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Abstract

Background and Objectives

Existing tools to diagnose spontaneous intracranial hypotension (SIH), namely spinal opening pressure (OP) and brain MRI, have limited sensitivity. We investigated whether evaluation of brain MRI using the Bern score, combined with calculated craniospinal elastance, would aid in diagnosing SIH and provide insight into its pathophysiology.

Methods

A retrospective chart review was performed of patients who underwent brain MRI and pressure-augmented dynamic CT myelography (dCTM) for suspicion of SIH. Two blinded neuroradiologists assigned Bern scores for each brain MRI. OP and incremental pressure changes after intrathecal saline infusion were recorded to calculate craniospinal elastance. The relationship between Bern score, OP, and elastance and whether a leak was found were analyzed.

Results

Seventy-two consecutive dCTMs were performed in 53 patients. Twelve CSF-venous fistulae, 2 ruptured meningeal diverticula, 2 dural defects, and 1 dural bleb were found (17/53, 32%). Among patients with imaging-proven CSF leak/fistula, OP was normal in all but 1 patient and was not significantly different in those with a leak compared with those without (15.1 vs 13.6 cm H₂O, $p = 0.24$, $A = 0.40$). The average Bern score in individuals with a leak was significantly higher than that in those without (5.35 vs 1.85, $p < 0.001$, $A = 0.85$), even when excluding pachymeningeal enhancement from the score (3.77 vs 1.57, $p = 0.001$, $A = 0.78$). The average elastance in those with a leak was higher than that in those without, but this difference was not statistically significant (2.05 vs 1.20 mL/cm H₂O, $p = 0.19$, $A = 0.40$). Increased elastance was significantly associated with an increased Bern score (95% CI -0.55 to 0.12 , $p < 0.01$) and was significantly associated with venous distention, pachymeningeal enhancement, prepontine narrowing, and subdural collections, but not a narrowed mamillopontine or suprasellar distance.

Discussion

OP is not an effective predictor for diagnosing CSF leak and if used in isolation would result in misdiagnosis of 94% of patients in our cohort. The Bern score was associated with a higher diagnostic yield of dCTM. Elastance was significantly associated with certain components of the Bern score.

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Glossary

CVF = CSF-venous fistula; **dCTM** = dynamic CT myelography; **DSM** = digital subtraction myelography; **ICHD** = International Criteria for Headache Disorders; **OP** = opening pressure; **PVI** = pressure volume index; **SIH** = spontaneous intracranial hypotension.

Spontaneous intracranial hypotension (SIH) is a syndrome resulting from the leakage of the CSF through a spinal dural defect, meningeal nerve root sleeve diverticulum, or CSF-venous fistula (CVF).¹ Prior work has shown that with an increased duration of a CSF leak, head pain is less likely to be orthostatic, opening pressure (OP) is less likely to be low, and brain MRI is less likely to show obvious features of intracranial hypovolemia.²⁻⁸ As these imaging and clinical features become less conspicuous, delayed or misdiagnosis of SIH is more likely to occur, which can lead to significant morbidity, including both delays in effective treatments and exposure to inappropriate treatments and procedures.⁹

In this setting, the tools used to detect CSF leak are evolving. A probabilistic scoring system—termed the Bern score—has shown predictive validity for positive findings of a CSF leak on subsequent conventional CT myelograms.¹⁰ These criteria assign a probability of finding a leak based on subtle brain MRI measurements, which qualitatively might have previously been overlooked or interpreted as normal. Simultaneously, data on optimal spinal imaging and invasive diagnostic testing have rapidly advanced because it is now understood that conventional CT myelography and spinal MRI do not identify CVF, which require decubitus digital subtraction myelography (DSM) or dynamic decubitus CT myelography (dCTM) for their localization.^{11,12} The Bern criteria have been shown to predict the likelihood of finding a CVF on DSM; however, these findings have not yet been replicated nor extended to dCTM.¹³

Spinal OP, previously considered the gold standard for diagnosing SIH, may actually be of limited diagnostic value. Two prior reports have shown that most patients with CSF leaks visible on conventional CT myelogram will have OP that is either normal or even elevated.^{14,15} Despite this, the current International Criteria for Headache Disorders (ICHD) diagnostic criteria for “low-pressure” headache requires the presence of positive imaging or low OP.¹⁶ In addition, many parts of the world without ready access to MRI or advanced myelography might, in light of the current ICHD-3 criteria, rely on OP to affirm or exclude the diagnosis of SIH and CSF leak. Thus, both neurologists and patients have significant unmet needs for tests with better predictive validity and increased sensitivity for symptomatic SIH.

Infusion of intrathecal saline has long been recognized for its therapeutic value in cases of severe SIH leading in obtundation or coma; however, it may also increase the visibility of leaks by raising the CSF pressure, while simultaneously providing

valuable information regarding the elastance of the craniospinal compartment.¹⁷⁻¹⁹ Elastance refers to the change in pressure of a compartment in response to a known change in volume and has been shown in prior work to be associated with the presence of an underlying CSF leak or fistula, adding a potential biomarker to the existing armamentarium of advanced diagnostic testing for SIH, inclusive of CTM, DSM, and radioisotope cisternography.^{6,20,21}

We hypothesized that abnormalities in spinal elastance might drive specific anatomic brain changes in SIH measured by the Bern score and that changes in elastance would be predictive of the Bern score. If so, spinal elastance could provide an important adjunctive measure of underlying leak pathology in patients with SIH and at the same time provide data to support a mechanistic physiologic underpinning of the anatomic changes seen in SIH. In addition, we sought to understand whether the predictive validity of the Bern score would persist if pachymeningeal enhancement was ignored, which might extend its applicability to patients who have received non-contrast brain MRI.

Methods

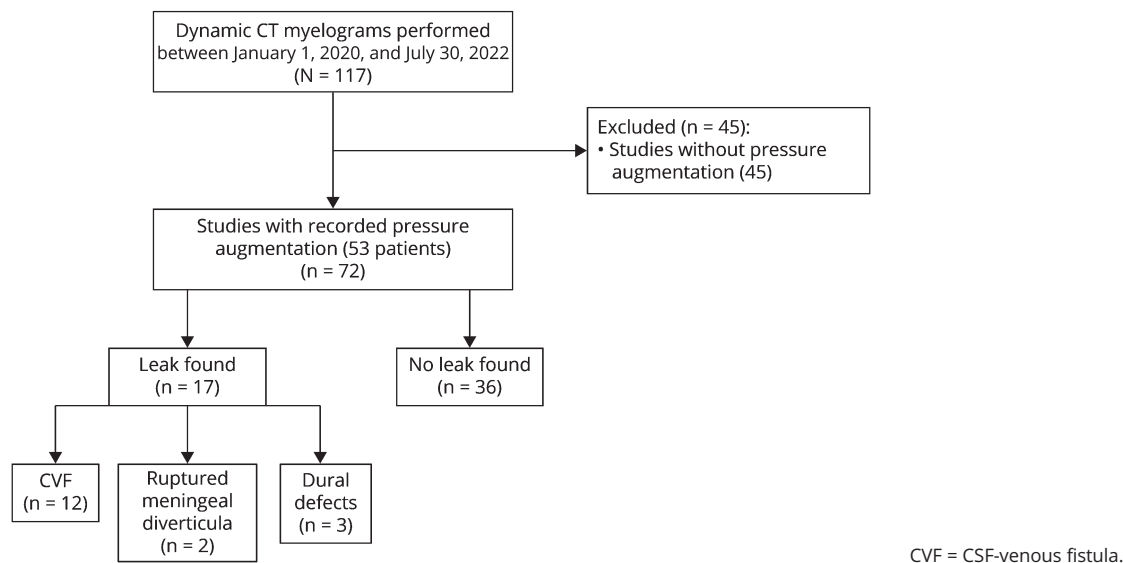
Standard Protocol Approvals, Registrations, and Patient Consents

Approval from an ethical standards committee to conduct this retrospective study was obtained, which did not require participant consent post hoc.

Data Acquisition and Patient Selection

Medical records of consecutive patients between November 2020 and July 2022 who underwent dCTM with pressure augmentation (with recorded OP and postaugmentation pressure) to localize a suspected CSF leak or CVF were retrospectively reviewed. Individuals who did not receive pressure augmentation or received pressure augmentation but did not have pressure measurements recorded were not included (Figure 1). “Pressure augmentation” refers to the infusion of incremental aliquots of sterile saline through a spinal needle.²² Imaging reports of dCTM studies were collected using a report search engine tool through the electronic medical record (Primordial Prism), which identified all reports associated with dCTM procedures in the specified period. When pressure augmentation was performed, the OP, volumes of saline infusion, and incremental pressure measurements were recorded in a standardized format in the body of the procedural report by the proceduralist. This information was then transposed from the reports by the primary investigator.

Figure 1 Flowchart Illustrating Patients Selected for Analysis



All patients were at least 18 years of age, were referred from neurologists with specialty expertise in headache disorders for concern for SIH, and had an MRI brain and spine before myelography. Patients were referred for headaches with a current or past positional component, with or without red flags for secondary headache disorders including sudden onset, age older than 50 years at onset, recent onset of a new type of headache precipitated or exacerbated by sneezing, coughing, or exercise, and was not better accounted for by an alternate ICHD-3 diagnosis.^{16,23}

Dynamic CT Myelography Technique

All dCTMs were performed by 1 of 3 experienced neuroradiologists (A.L.C., A.A.T., and V.M.T.). Our institution's dCTM procedural technique has been previously published.²² In brief, if the MRI spine demonstrated an epidural fluid collection, the patient was placed in the prone or decubitus position with hips elevated to evaluate for a ventral or lateral dural defect, respectively.^{23,24} If the MRI spine did not demonstrate an epidural fluid collection, patients were placed in the lateral decubitus position on a HoverMatt inflatable device (Hovermatt Air Transfer System, Hovertech International) to evaluate for a CVF. Access to the thecal sac was obtained using a 22-gauge Whitaker spinal needle. Once the needle tip was confirmed to be within the subarachnoid space, OP was measured using a digital manometer (Compass Digital Manometer; Centurion Medical Products, Williamston, MI). As long as pressure was either within normal range or low, pressure augmentation was incrementally performed with 5 mL aliquots of sterile saline. Between each aliquot, OP was remeasured and recorded using the digital manometer. Infusion continued after performing this measurement without any other standardized time delay. Once pressure reached 25–30 cm water, 5–10 mL 300 mg/mL iodinated contrast was

administered through the needle. If the initial OP was high, saline augmentation was not performed, but rather a second pressure might be measured after administration of 10 mL contrast alone. Immediately after contrast injection, the HoverMatt was inflated for 10 seconds to facilitate the cranial passage of contrast, 2 serial scans were performed in rapid succession, and in the case of suspected CVF, the patient was repositioned to the contralateral decubitus side, and 1 final scan was performed. If there was inadequate cephalad extension of contrast material noted on the first scan, the scan was terminated, the HoverMatt was reinflated for an additional 5–10 seconds, and scanning was reinitiated.

Whether pressure augmentation was performed was determined by the proceduralist for any given patient. In general, our practice is to perform pressure augmentation during dCTM for increased sensitivity in the context of suspected CVF more so than in the context of a fast leak with an associated longitudinal epidural fluid collection. Therefore, most included patients who received pressure augmentation were believed to have CVF, except in cases where it was believed to have potential adjunctive therapeutic benefit and where those pressures were recorded in the clinical record. In patients with particularly high clinical suspicion and/or Bern scores, and a negative first dCTM, a repeat dCTM might be pursued.

Spinal Elastance Calculation

OP, serial augmented pressures, and infusion volumes were recorded and used to generate spinal elastance curves, as described by Caton et al.²⁰ The pressure volume index (PVI) was calculated using the log transformation of the exponential CSF elastance curve. The total elastance was calculated as the reciprocal of the line of best fit of the linear regression of the

pressure-volume curve. If the same patient had more than 1 pressure-augmented dCTM, OP and total elastance measurements were averaged for each patient.

Brain MRI Assessment

The Bern criteria assess venous distension, pachymeningeal enhancement, subdural collections, and suprasellar, prepontine, and mamillopontine distances to assign a probabilistic score for the presence of SIH^{10,13} (eTable 1, links.lww.com/WNL/C727). Each patient's brain MRI was retrospectively scored by 2 board-certified neuroradiologists with subspecialty expertise in SIH, blinded to the outcome of the patient's dCTM. Individual radiologist scores were averaged for the final score.

Statistical Analysis

Wilcoxon rank sum tests were performed to assess the pairwise relationship between the presence of a leak and Bern score, OP, and elastance, with effect size estimates reported as Vargha and Delaney A.²⁵ Six univariable logistic regression models were estimated to assess the association of the Bern score components with whether a leak was found. Univariable linear regression models were estimated to assess the pairwise association of the Bern score with elastance and OP. Six univariable linear regression models were estimated to assess whether elastance or OP was associated with the individual components of the Bern score. Cohen κ coefficient was calculated for each component of the Bern score to determine inter-reader variability. All data analyses were performed using R version 4.1.2.

Data Availability

Anonymized data not published within this article will be made available by request from any qualified investigator.

Results

Patient Characteristics

Within the study period, a total of 72 consecutive dCTMs in 53 patients were performed with recorded pressure augmentation

and thus were included in the analysis. Two patients had 3 dCTMs, 10 patients had 2 CTMs, and 41 patients had a single dCTM. Patient characteristics are summarized in Table 1. The mean patient age was 54.5 years (SD 13.3 years) and 50.6 years (SD 15.4 years) in the leak found and no leak found groups, respectively; 67.9% of patients were women. Leaks were found in 17/53 (32%) of patients. Symptom duration in the leak found group on average was 3.3 years (SD 2.8 years) compared with 8.5 years (SD 11.1 years) in the no leak found group (95% CI 1.10–9.23, $p = 0.014$). Of all localized leaks, there were 12 CVF (71%), 2 ruptured meningeal diverticula (12%), 2 ventral dural defects (12%), and 1 dural bleb (6%). Other than clinical suspicion by the referring neurologist, patients without localized leaks did not have other evidence of confirmed spinal CSF leak on any other diagnostic testing. Of the 17 patients with a confirmed leak, 8/17 (41%) had received an epidural blood patch before dCTM.

Forty patients underwent 45 total dCTMs without pressure augmentation during the study period and thus were excluded from primary analysis. In this subgroup, the mean patient age was 43.8 (SD 12.6 years), and 33/40 (83%) were women. Leaks were found in 15/40 patients (37.5%). Of all localized leaks in this subgroup, there were 7 ventral dural defects (47%), 4 ruptured meningeal nerve root sleeve diverticula (27%), 1 dural bleb (7%), 1 leaking cranioplasty (7%), and 1 CVF (7%).

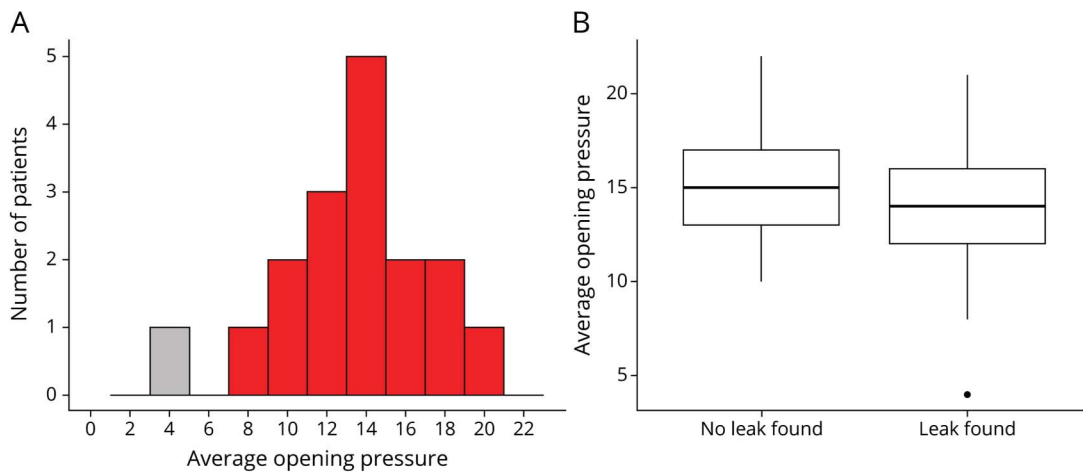
Opening Pressure

Sixteen of 17 patients with a confirmed leak had a normal OP (greater than 6 cm H₂O) (sensitivity 6%; 95% CI 0.3%–31%) (Figure 2). All patients (100%) with CVF had a normal OP. The average OP in those in whom a leak was found was 13.6 cm H₂O (SD 4.22 cm H₂O), compared with 15.1 cm H₂O (SD 2.84 cm H₂O) in those in whom no leak was found (Wilcoxon rank sum test $p = 0.24$, $A = 0.40$). Within those in whom a leak was found, the average OP in CVF was 13.5 cm H₂O (SD 3.74 cm H₂O), in ruptured diverticulae 20.0 cm H₂O (SD 1.41 cm H₂O), and in dural defects 10.0 cm H₂O

Table 1 Patient and CSF Leak Characteristics

	Pressure augmented (N = 53)	Nonpressure augmented (N = 40)	<i>p</i> Value
Male, n (%)	17 (32.1)	7 (17.5)	0.18
Female, n (%)	36 (67.9)	33 (82.5)	
Age, y, mean (SD)	51.9 (14.8)	43.8 (12.6)	0.003
No leak found, n (%)	36 (67.9)	25 (62.5)	0.75
Leak found, n (%)	17 (32.1)	15 (37.5)	
CSF-venous fistula, n (%)	12/17 (71)	1/15 (7)	
Ruptured meningeal diverticulum, n (%)	2/17 (12)	4/15 (27)	
Dural defect, n (%)	2/17 (12)	7/15 (47)	
Dural bleb, n (%)	1/17 (6)	1/15 (7)	

Figure 2 Histogram (A) Illustrating the Distribution of Spinal Opening Pressures in Individuals in Whom a Leak Was Localized and Boxplot (B) Illustrating the Average Opening Pressure in Individuals in Whom a Leak Was Found Compared With That in Those in Whom No Leak Was Found



The mean opening pressure was slightly higher in the no leak found group; however, this difference was not statistically significant (mean 15.1 cm H₂O (SD 2.8 cm H₂O) compared with mean 13.6 cm H₂O (SD 4.2 cm H₂O), Wilcoxon rank sum test: $p = 0.24$). Notably, only 1 patient (gray bar) had an opening pressure less than 6 cm H₂O, while the remainder of patients (red bars) had opening pressures in the normal range.

(SD 2.83 cm H₂O). The 1 patient with a dural bleb had an OP of 10 cm H₂O.

Spinal Elastance

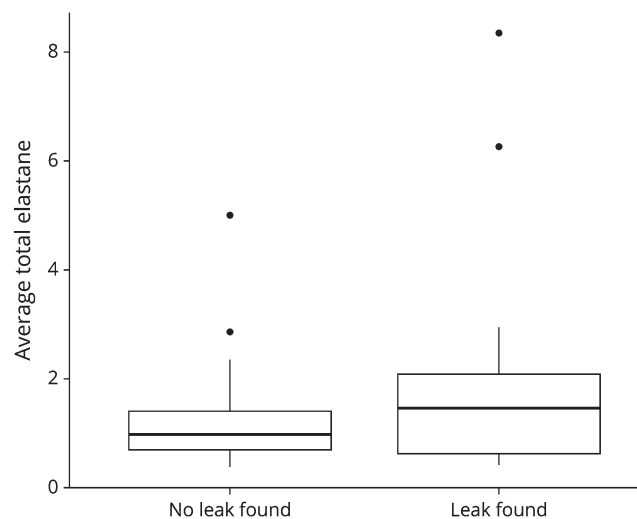
Pressure augmentation was performed successfully in all patients, without any associated adverse side effects. The average total elastance in those in whom a leak was found was 2.05 mL/cm H₂O (SD 2.14 mL/cm H₂O), compared with

1.20 mL/cm H₂O (SD 0.87 mL/cm H₂O) in those in whom no leak was found ($p = 0.19$, $A = 0.61$) (Figure 3). The average total elastance in CVF was 1.33 mL/cm H₂O (SD 0.71), in ruptured diverticulae was 0.69 mL/cm H₂O (SD 0.31), in dural defects was 7.29 mL/cm H₂O (SD 1.47), and in the 1 patient with a dural bleb was 2.94 mL/cm H₂O.

Bern Score

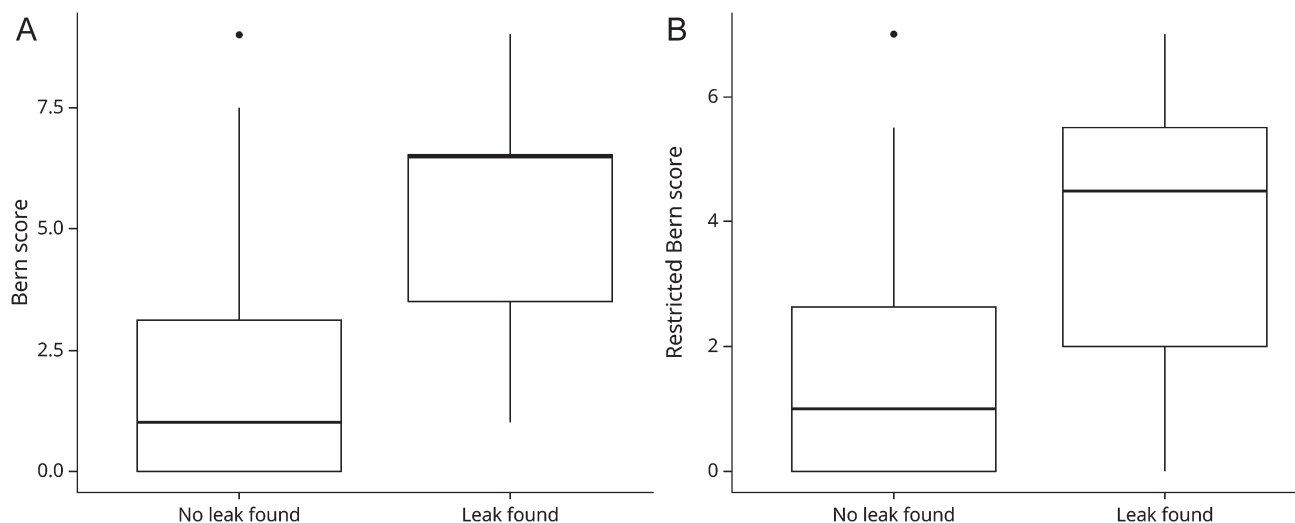
The average Bern score between the 2 blinded neuroradiologists was used to evaluate for associations between whether a leak was found and measures of OP and elastance. Cohen κ coefficient reflecting inter-rater variability for each component of the Bern score was 0.79 for pachymeningeal enhancement, 0.71 for venous distention, 0.77 for suprasellar distance, 0.93 for subdural collections, 0.43 for prepontine distance, and 0.64 for mamillopontine distance. The average Bern score in individuals with a leak found was 5.35 (SD 2.54), statistically significantly larger than that in those without a leak found [1.85 (SD 2.17)] (Wilcoxon rank sum $p < 0.001$, $A = 0.85$). When pachymeningeal enhancement was excluded from the composite Bern score, the mean score in those with a leak found remained statistically significantly larger than that in those without (3.77 (SD 2.31) vs 1.57 (SD 1.79) $p = 0.001$, $A = 0.78$) (Figure 4). Within those who had a leak found, the average Bern score in CVF was 5.63 (SD 2.41), in ruptured diverticulae 2.25 (SD 1.17), and in dural defects 7.5 (SD 2.12). The Bern score in the patient with a dural bleb was 4. Logistic regression assessing the association of Bern score components with whether a leak was found demonstrated that pachymeningeal enhancement, venous sinus distention, a narrowed suprasellar distance, and the presence of a subdural collection were significantly associated with leak found status, whereas narrowed prepontine and mamillopontine distances were not (Table 2).

Figure 3 Boxplot Illustrating the Average Total Elastance in Individuals With No Leak Found Compared With That in Those With a Leak Found



The average total elastance was higher in those with a leak found, but this difference was not statistically significant (median 1.46, mean 2.05 mL/cm H₂O, vs median 0.97, mean 1.20 mL/cm H₂O, Wilcoxon rank sum: $p = 0.19$).

Figure 4 Boxplots Illustrating the Average Total and Restricted Bern Score in Individuals With a Leak Found Compared With Those in Individuals With No Leak Found



(A) Boxplot illustrating the average Bern score in individuals with a leak found (median 6.50, mean 5.35, SD 2.54), compared with that in those without a leak found (median 1.00, mean 1.85, SD 2.17). This difference was statistically significant (Wilcoxon rank sum test $p < 0.001$). (B) Boxplot illustrating restricted Bern score (minus pachymeningeal enhancement) in individuals with a leak found (median 4.5, mean 3.77, SD 2.31) compared with those without a leak found (median 1.0, mean 1.57, SD 1.79). This difference was statistically significant (Wilcoxon rank sum test $p = 0.001$).

Relationship of Bern Score to OP and Spinal Elastance

Univariate regression demonstrated that both spinal elastance and OP were significantly associated with the Bern score ($\beta = 0.80$, 95% CI 0.30, 1.30, $p = 0.002$ vs $\beta = -0.33$, 95% CI -0.55 to -0.12 , $p = 0.003$, respectively). Figure 5 illustrates the relationship of OP by whether a leak was found.

Linear regression assessing whether spinal elastance or OP was associated with the individual components of the Bern score demonstrated that both were strongly associated with venous distention, pachymeningeal enhancement, and a subdural fluid collection. By contrast, suprasellar interval and mamillopontine interval showed no association with either OP or elastance (Table 2).

Neither OP nor total elastance correlated with a large portion of the variability of the Bern score between patients. OP accounted for 14 percent of the variance in the Bern score ($R^2 = 0.14$; $p = 0.003$). The average total elastance accounted for 15 percent of the variance in the Bern Score (adjusted $R^2 = 0.15$; $p = 0.002$).

Discussion

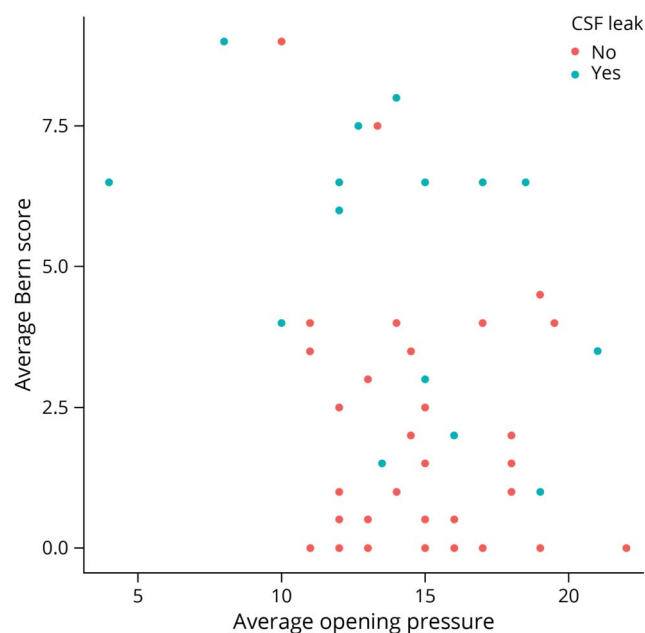
In this retrospective cohort study, we evaluated the Bern score, craniospinal elastance, and OP in a group of consecutive patients who underwent pressure-augmented dCTMs for suspicion of underlying SIH. We found that neither OP nor elastance predicted the detection of a leak, replicated the findings that the Bern score predicted the presence of an

Table 2 Results of Logistic Regression Investigating the Relationship of Individual Components of the Bern Score to Whether a Leak Was Found, Opening Pressure, and Elastance

Bern score component	Leak found?			Opening pressure			Elastance		
	Odds ratio	<i>p</i> Value	95% CI	β	<i>p</i> Value	95% CI	β	<i>p</i> Value	95% CI
Pachymeningeal enhancement	6.48	2.7e-05	2.92-17.28	-0.074	0.048	-0.15 to -0.001	0.238	0.005	0.073 to 0.402
Venous sinus distention	5.38	2.0e-4	2.39-14.58	-0.108	0.001	-0.17 to -0.047	0.269	0.000	0.13 to 0.41
Suprasellar distance	2.13	0.022	1.13-4.22	-0.041	0.289	-0.12 to 0.036	0.058	0.520	-0.12 to 0.24
Subdural fluid	11.73	7.1e-3	2.26-95.85	-0.048	0.001	-0.075 to -0.02	0.097	0.005	0.031 to 0.16
Prepontine distance	1.48	0.58	0.37-6.00	-0.040	0.020	-0.073 to -0.007	0.090	0.025	0.012 to 0.17
Mamillopontine distance	1.87	0.35	0.51-7.00	-0.020	0.286	-0.056 to 0.017	0.047	0.279	-0.039 to 0.13

β coefficient estimates should be interpreted as the change in the Bern score component associated with a 1-unit increase in the exposure (either opening pressure or elastance).

Figure 5 Scatterplot Illustrating the Relationship of Bern Score to Opening Pressure in Those With and Without a Leak



Pearson correlation coefficient reflecting the relationship between the average opening pressure and average Bern score is -0.4 .

underlying CVF or leak, and showed that the Bern score retains its predictive strength even when excluding the consideration of pachymeningeal enhancement. We also found that both OP and elastance were statistically significantly related to some specific brain MRI changes associated with CSF leak but not others.

OP was normal in 16 of 17 patients who had confirmed leaks (sensitivity 6%; 95% CI 0.2–29). Furthermore, 12 of 12 (100%) patients with CVF had OP within the normal range. Thus, OP alone would result in misdiagnosis in 94% of patients. These data from a consecutive sample validate initial concerns about OP, first reported in 2 prior retrospective analyses in 2016, which evaluated individuals with type 1 and 2 leaks.^{5,14} Of importance, we extend this concept to apply to CVF, an entity that was only first reported in 2014, and for which such data has not been previously reported.¹¹ CVFs are not detected by conventional neuroimaging, and we note that for much of the world, which may have limited access to advanced diagnostic imaging tests, it may be tempting to use OP to evaluate patients for underlying CSF leak, particularly because it remains embedded in the ICHD-3 diagnostic criteria for low-pressure headache. Given the relatively small sample size of this study, these data need to be reproduced in a larger prospective sample.

Our work investigating craniospinal elastance builds upon recent work by Beck et al.,²⁶ who suggested that there may be valuable information encoded in advanced spinal pressure

measurements.^{6,26} Using computer-controlled intrathecal infusions through a 20-gauge indwelling needle, they demonstrated that it is possible to measure not only the OP but the plateau pressure reached with ongoing instillation of volume, the cyclic pressure changes elicited by the cardiac cycle, and to calculate the elastance of the craniospinal compartment.²⁶ While conceptually enlightening, their computer-controlled infusion technique has seen limited adoption, perhaps because it remains beyond the practical capabilities of most physicians in the clinical setting. Furthermore, this work was reported before it was known that CVF might account for up to 75% of spinal CSF leaks among patients with symptomatic SIH and negative spinal imaging and their report of the Bern criteria.^{10,11} We extend their work in this study in 2 major respects. First, we report a practical method for the computation of intrathecal elastance using routine lumbar puncture and a 22-gauge Whitaker needle. Second, we show that intrathecal elastance is correlated with the Bern score, tying specific brain anatomic findings to spinal pressure volume parameters for the first time and further validating the Bern score by tying it to a specific element of altered spinal CSF physiology in CSF leak.

Pressure augmentation through intrathecal saline injection during myelography remains a clinical practice in need of further empirical support. Pressure augmentation has at least 2 posited advantages: the measurement of craniospinal elastance possibly useful as a diagnostic biomarker of CSF leak and possible enhanced sensitivity of dCTM for CVF. We found that the measurement of elastance permitted by pressure augmentation did not predict the detection of a CSF leak. This lack of association may reflect the lack of a true biomechanistic correlation or alternatively reflect the lack of power related to sample size. These results diverge from those reported by Caton et al.²⁰ who detected a significant association of elastance with the presence of CVF in a smaller sample. Future work should therefore continue to evaluate the role of measuring elastance, which might still play an important role such as identifying candidates for repeat invasive testing or potentially increase sensitivity for radiographically detecting CVF. This potential role deserves further study, and our data support the safety of further pursuing the utility of this approach.

In our cohort, logistic regression demonstrated that pachymeningeal enhancement, venous sinus distention, a narrowed suprasellar distance, and the presence of a subdural collection were significantly associated with the detection of CSF leak, whereas narrowed prepontine and mamillopontine distances were not. These findings parallel the original report proposing the Bern criteria scoring system, in which prepontine distance and mamillopontine distances also had the smallest associated odds ratios for predicting the detection of CSF leak by conventional CT myelogram among the Bern criteria components.¹⁰ This concordance of results suggest that these brain measures are truly more weakly associated with an underlying CSF leak than the other Bern criteria components. Future

work should continue to evaluate the relative predictive validity of each Bern score component in CSF leaks and CVF.

In our cohort, OP and spinal elastance did not predict the detection of a CSF leak. However, the Bern score did strongly predict the detection of a CSF leak, and it is therefore somewhat surprising that OP and spinal elastance were associated with the Bern score. This discrepancy is accounted for by the fact that OP and elastance accounted for only a small minority of the variance in the Bern score (14% and 15%, respectively). The remainder of unexplained variance in the Bern score thus seems to be mediated by yet undetermined physiologic variables that are separate and distinct. Previous authors have hypothesized that there exist 2 main pathophysiologic set of variables in SIH: (1) those arising from increased intracranial vascular volume replacing lost CSF consistent with the Monro-Kellie postulate—consisting of pachymeningeal enhancement, subdural fluid collections, venous engorgement, and pituitary hyperemia and (2) those distinct, sometimes subtle, structural changes reflecting caudal displacement of the brain—consisting of reduced mamillopontine distance, pontomesencephalic angle, and others.²⁷ Our data provide further insights and partial empiric support for this hypothesis. In our cohort, the OP and average total elastance were associated with pachymeningeal enhancement, venous distension, and subdural collections, but not a reduced suprasellar or mamillopontine distance (Table 2). The former set of variables are the same ones hypothesized by Choi et al.²⁷ to be part of the Monro-Kellie–driven changes and, in our data, seem to be related to OP and elastance. The second set of variables related to caudal descent have been previously hypothesized to be reflecting a “loss of buoyancy.” Whether these variables are in fact accounted by buoyancy or some other pathophysiologic variable—perhaps related to spinal CSF/venous dynamics—remains to be determined by future research.²⁷ Overall, these data provide a very preliminary empiric underpinning to support the clinical observations and hypothesis articulated by Mokri⁴ as far back as 1999 that some other component of CSF volume loss, and not reductions in CSF pressure, best explain the clinical and imaging heterogeneity seen in patients with CSF leak.

In exploratory subanalysis, a restricted Bern score—in which the presence or absence of pachymeningeal enhancement was excluded from the scoring criteria—continued to be strongly associated with the presence of a leak. This has tremendous practical utility because most patients undergoing imaging evaluation of headache will have brain MRI without gadolinium contrast. Reporting a restricted Bern score may obviate the need for repeat brain MRI in patients with high clinical suspicion for SIH. The research relevance of this finding is that it opens for analysis the various cohorts with linked noncontrast-enhanced brain MRI imaging data such as the cohorts collected under NIH’s FITBIR database (fitbir.nih.gov). In addition, we note that the original cohort of patients from which the Bern score was derived and the cohort

reported by Kim et al., both represent ideal existing cohorts with data amenable to verifying our finding because they contain results of both scored brain MRI and results of invasive spinal imaging.^{10,13} If this finding is validated in other cohorts, a restricted Bern score may prove useful to identify candidates previously unsuspected of having an underlying CSF leak.

In our cohort, an increased Bern score was associated with the discovery of leak or CVF when using dCTM. These results validate similar findings first reported last year by Kim et al., that the Bern score predicted CVF when investigated by DSM and extend their results by showing that the Bern score is also predictive of the ability to find CVF using dCTM.^{10,13} Both dCTM and DSM are used at quaternary SIH referral centers, and each modality has specific strengths and weaknesses, which have been previously described.²² Our data support the growing use of dCTM as an alternative to DSM in patients with brain changes associated with an elevated Bern score. Given the Bern score’s repeatedly proven predictive validity for the presence of not only an underlying dural defect but also an underlying CVF, we feel that this scoring system should be incorporated into routine clinical practice in patients with suspected SIH, perhaps in a standardized radiology reporting template. By doing so, risk stratification could inform the pretest probability for a patient and referring provider tasked with weighing the associated radiation and potential procedural complications of dCTM with the likelihood of localizing a leak or CVF. Conversely, a high Bern score may also be used to encourage a repeat study in a patient with initial negative testing.

In our cohort, individuals in whom a leak was found had a statistically significantly shorter duration of symptoms compared with those in whom no leak was found. Prolongation of CSF leak has previously been shown to decrease the frequency of 3 core clinical findings that would otherwise facilitate a correct diagnosis of CSF leak: the occurrence of orthostatic features in the accompanying headache; the occurrence of abnormally low OP, and the detection of pachymeningeal enhancement on brain MRI.^{2,4-8} In this context, our finding that patients in whom a leak was found by dCTM had statistically significantly shorter symptom duration raises the question of whether the sensitivity of dCTM has a similar time-dependent function with decreasing sensitivity over time or if the longer duration of symptoms among patients with a negative dCTM reflects a true association between symptom duration and lower probability of ongoing CSF leak. Future work should address these clinically relevant questions.

Our study has several limitations. Our sample size was modest, and our total number of individuals with non-CVF leaks was low. This was mostly accounted for by the relative lack of use of pressure augmentation, and thus elastance calculation, when performing dCTM on a patient with spine MRI findings suggestive of a type 1 or type 2 leak. Our results should be considered not yet validated in this subpopulation of patients

with suspected CSF leaks. Whether to augment pressure was left to the discretion of the physician performing the procedure, and variables such as OP, patient discomfort, and pretest probability were considered in each case. We believe that these data are thus in line with the real-world experience of radiologists evaluating patients for CSF leak or CVF. A further limitation of this study is that in our cohort, 8/17 patients with confirmed leak had previously received epidural blood patching before dCTM, which could alter measured OP and elastance. The large number of patients in our study who did not eventually have a leak localized may reflect a combination of true negative cases and potentially occult CVF, noting that the sensitivity and specificity of dCTM has yet to have been reliably quantified. This positivity rate reflects the clinical practice of a single institution and neurology department's referral patterns and may not be generalizable to the population at large. Finally, the generalizability of our data is further limited by the fact that our cohort's mean age was greater than 50 years, and prior work has shown that craniospinal elastance is altered in patients older than 50 years, likely due to age-related volume loss.²⁸

In this study, the Bern score was predictive of the presence of an underlying spinal CVF or CSF leak even when excluding the assessment of pachymeningeal enhancement. OP was not significantly associated with the presence of an underlying CVF or leak and should not be used to exclude patients from further diagnostic testing when there is clinical suspicion for SIH. OP and spinal elastance were statistically significantly associated with specific components of the Bern score. Future work should continue to explore the use of pressure augmentation and spinal elastance in the evaluation of SIH.

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Appendix (continued)

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