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Intervention for Elevated Intracranial Pressure Improves Success Rate After Repair of Spontaneous Cerebrospinal Fluid Leaks

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Objectives/Hypothesis: Spontaneous cerebrospinal fluid (CSF) leaks are associated with increased intracranial pressure (ICP) and considered a manifestation of idiopathic intracranial hypertension. Although postoperative acetazolamide and placement of CSF shunt systems are considered valuable interventions for elevated ICP, the impact on recurrence rate remains unclear. The objective of this study was to systematically review evidence from reported literature to evaluate whether postoperative ICP management reduces recurrence rates after primary endoscopic repair.

Study Design: Prospective case series and systematic review.

Methods: Demographics, defect location, success rates, and ICP management in spontaneous CSF leak patients were prospectively collected over 8 years. A search was also conducted in PubMed to identify studies reporting cases of spontaneous CSF rhinorrhea.

Results: Fifty-six articles with nonduplicated data were identified and combined with a prospective series of 108 patients for a total of 679 patients treated for spontaneous CSF rhinorrhea. Average age was 50.4 years with 77% female. Average body mass index was 35.8 kg/m^2. Defects were most commonly located in the sphenoid sinus (n = 334) followed by the ethmoid (n = 318) and the frontal sinus (n = 46). Successful primary repair was 92.82% in patient cohorts where ICP evaluation and intervention with acetazolamide or CSF shunt systems was performed, but was significantly decreased to 81.87% in series with no active management of elevated ICP ($P < .001$).

Conclusions: Evaluation and intervention for elevated ICP in spontaneous CSF leaks is associated with significantly improved success rates following primary endoscopic repair.

Key Words: Spontaneous cerebrospinal fluid leak, cerebrospinal fluid leak, cerebrospinal fluid rhinorrhea, spontaneous cerebrospinal fluid rhinorrhea, idiopathic cerebrospinal fluid rhinorrhea, idiopathic cerebrospinal fluid leak, endoscopic cerebrospinal fluid leak repair, endoscopic sinus surgery, encephalocele.

Level of Evidence: 4.

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INTRODUCTION

Cerebrospinal fluid (CSF) leaks are an uncommon pathological entity that are most often classified based on the etiology of the skull base defect: spontaneous, trauma, tumor, or congenital.[1] Timely and effective closure of defects is critical to avoid potentially serious consequences including brain abscess and meningitis. Endoscopic repair of CSF leaks has been a mainstay of treatment for nearly 30 years; however, understanding the etiology of the defect is integral to achieving successful primary repair. Spontaneous CSF leaks are defects that arise in patients with seemingly no identifiable cause. However, mounting evidence indicates spontaneous CSF leaks are associated with increased intracranial pressure (ICP) and are thought to be due to preexisting idiopathic intracranial hypertension (IIH).[2,3]

IIH commonly presents clinically in obese (body mass index [BMI] >30) females with a wide variety of symptoms including headache, visual disturbances, and balance problems. Previous studies have shown that the vast majority of patients with spontaneous CSF leaks also have concomitant IIH.[4–10] Elevated ICP is generally demonstrated by radiographic evidence or direct measurement through lumbar tap. Radiographic signs of increased ICP include encephalocele, empty sella, dilated Meckel's caves, and vertical tortuosity of dilated optic nerve sheaths on magnetic resonance imaging as well as skull base attenuation on computed tomography scan often with multiple erosions (Fig. 1).[4,5,7,9,11,12] Lumbar puncture has also been used to directly measure opening pressure in numerous studies.[2–4,6–9,13–20] Endoscopic repair is the preferred surgical intervention for spontaneous CSF leaks, but reported success rates vary widely in the literature ranging from 33% to 100%.[9,10,14,16,21,22] Presumably, higher success rates are thought to reflect short- and long-term mitigation of elevated ICP in this patient population, with ventriculoperitoneal shunting, acetazolamide, and other measures such as weight

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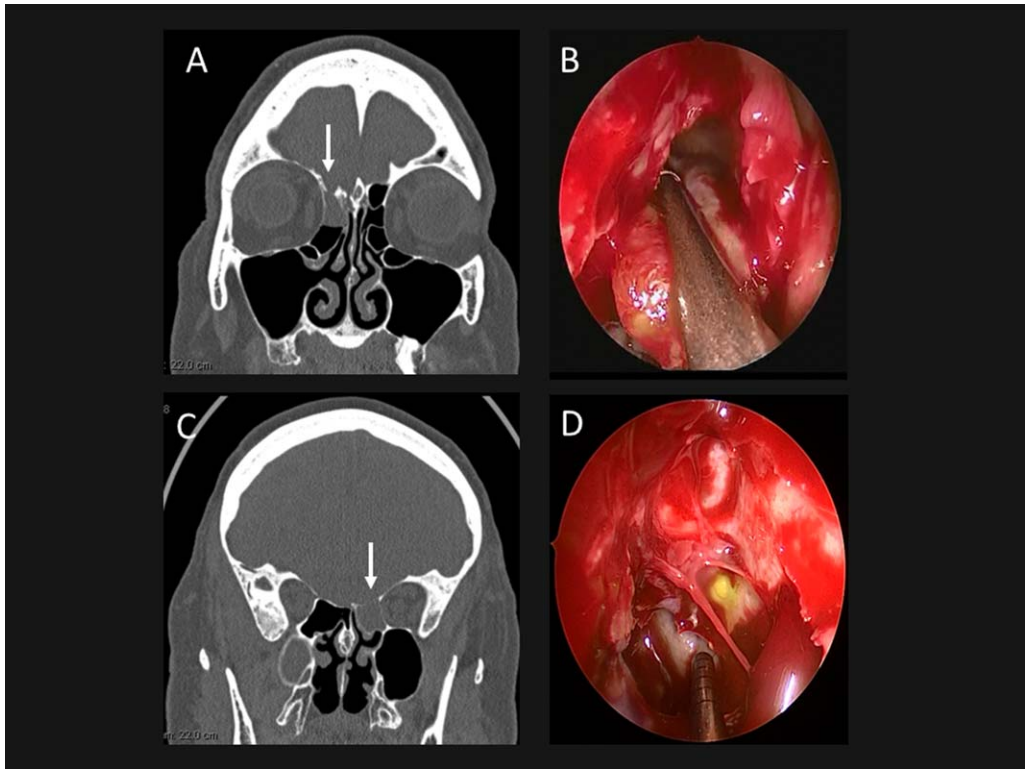

Fig. 1. Coronal CT scan (A) and corresponding 70° nasal endoscopic view (B) of a 52-year-old female with spontaneous CSF leak and encephalocele of the right anterior ethmoid roof. This patient was noted to have seven skull base defects/erosions. Suspicion for contralateral CSF leak in the left posterior ethmoid roof by coronal CT scan (C) was confirmed with corresponding 0° nasal endoscopic view (D). Green color represents CSF stained with intrathecal fluorescein. CSF =- cerebrospinal fluid; CT = computed tomography. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

loss.[3,8,10,16,23,24] At this time, there is no consensus regarding the importance of active management of ICP in patients treated for spontaneous CSF leaks despite a plethora of literature describing this phenomenon.

The objective of the current study was to systematically review evidence from reported literature to evaluate whether active intervention for elevated ICP reduces recurrence rates after primary endoscopic repair.

MATERIALS AND METHODS

Prospective data collection for 108 patients treated for spontaneous CSF rhinorrhea at the University of Alabama at Birmingham was performed. All patients were treated by the senior author (B.A.W.) over an 8-year period. Demographics, defect location, success of treatment, and ICP management data were collected. Relevant data concerning signs of increased intracranial pressure were also gathered. Additionally, a systematic review using PubMed was conducted to identify studies that reported cases of spontaneous CSF rhinorrhea repair. The studies identified were evaluated for the same data. For the purposes of this review, case series with active intervention were defined as those where ICP was measured with either lumbar puncture, lumbar drain, or ventriculostomy for the purposes of documenting intracranial hypertension and obtaining long-term control with acetazolamide or permanent CSF diversion (ventriculoperitoneal or lumboperitoneal shunt).[8] Lumbar drain alone was not considered an intervention for ICP management if the purpose of the drain was only to provide short-term diversion rather than assessment for long-term intervention.

A systematic PubMed search was completed for studies published up to July 2016 using the search terms "spontaneous CSF leak," "CSF leak," "CSF rhinorrhea," "spontaneous CSF rhinorrhea," "idiopathic CSF rhinorrhea," "endoscopic CSF leak repair," and "endoscopic sinus surgery." Articles containing spontaneous lateral recess CSF leaks were included even if inappropriately labeled congenital Sternberg's canal leaks, because defects lateral to the maxillary nerve cannot be from a Sternberg's canal defect.[6,14,25] Inclusion criteria included the following: 1) spontaneous leak etiology, 2) endoscopic repair. Exclusion criteria applied to the results included the following: 1) articles written in any language other than English, 2) non-spontaneous leak etiologies, 3) articles where data were not delineated by etiology, and 4) lack of patient outcomes data regarding success and clinical follow-up. The literature was reviewed, and studies were identified according to the inclusion and exclusion criteria by two authors (W.T. and B.A.W.). When an author combined data from previously published case series, only the patients from the most current article were included in the data analysis. The results of the literature search and prospective case series were then combined. A full meta-analysis was not performed due to study heterogeneity from a mix of comparisons of different treatments with different comparators (e.g., use of Diamox vs. lumboperitoneal vs. ventriculoperitoneal shunt). In series where pressure was checked and measures to control the pressure initiated, all patients in a given series of spontaneous leaks were not subjected to the same pressure-lowering measures. Some patients were identified as not having high pressure, and no measures were instituted yet still included in the active intervention group.

TABLE I.
Demographics and Success Rates.

Author	Age, yr	Mean BMI, kg/m^2	No. of Males	No. of Females	No. Treated	No. of Failures	Success Rate, %	ICP Control
Woodworth	51.4 ± 11.4	38.2 ± 9	18	90	108	4	96.30	Yes
Seltzer et al.[28]	44	36.5	0	1	1	0	100.00	No
Pagella et al.[29]	60.3 (36-91)	26.85 (21-35)	0	6	6	1	83.33	No
Tomazic and Stammberger[30]	51.2	31.9 (20.5-50.4)	1	4	5	2	60.00	No
Castelnuovo et al.[31]	60.3 ± 9.3 (34-75)	30.1 (22.3-41.6)	6	9	15	0	100.00	No
Bibas and Skia [21]	46 (43-52)	N/A	0	3	3	2	33.33	No
Warade and Misra [32]	26	N/A	1	0	1	0	100.00	No
Matsubara et al.[33]	34	34.1	0	1	1	0	100.00	Yes
Sanjari et al.[34]	45.1 (34-66)	N/A	0	1	1	1	0.00	No
Schmidt et al.[35]	58	N/A	0	2	2	0	100.00	Yes
Schmitt et al.[36]	59	33	0	1	1	1	0.00	No
Wise et al.[37]	59	N/A	0	1	1	0	100.00	Yes
Stangherlin et al.[27]	45	48	0	1	1	1	0.00	No
Lescanne et al.[38]	26	N/A	0	1	1	1	0.00	Yes
Gendeh et al.[39]	38.1 (14-53)	N/A	0	7	7	2	71.43	No
Van Zele et al.[40]	52.6 (37-78)	N/A	1	5	6	0	100.00	Yes
Bhalodiya et al.[41]	38.3 (35-40)	N/A	0	3	3	2	33.33	Yes
Perez et al.[42]	41.3 (32-49)	N/A	1	2	3	0	100.00	Yes
Rosenfeld et al.[43]	41.6 (35-48)	35.3 (25-42)	0	3	3	0	100.00	Yes
Carrau et al.[44]	49 (15-65)	N/A	2	7	9	0	100.00	Yes
El-Tarabishi et al.[45]	40.1 (30-51)	36.3 (32.2-39.5)	2	5	7	0	100.00	Yes
Deenadayal et al.[46]	42.7 (28-58)	N/A	2	5	7	0	100.00	No
Xie et al.[17]	49.2 ± 12.5	38.5 ± 11.7	1	24	25	0	100.00	Yes
Schlosser et al.[3]	49.6 (32-65)	35.9 (29.8-55.6)	3	13	16	0	100.00	Yes
Mirza et al.[47]	N/A	31 (21-49)	15	14	29	6	79.31	No
Seth et al.[24]	57.7	38.5	6	33	39	5	87.18	Yes
Cassano and Felippu[22]	N/A	N/A	N/A	N/A	43	7	83.72	No
Banks et al.[7]	51.4	35.4	20	57	77	7	90.91	Yes
Tomaszewska et al.[48]	69 (66-72)	N/A	0	2	2	0	100.00	No
Safavi et al.[49]	41	N/A	0	5	5	2	60.00	No
Minak and Carmody[50]	67	N/A	1	0	1	0	100.00	No
Sannareddy et al.[51]	N/A	N/A	2	9	11	2	81.82	Yes
Virk et al.[26]	50.4	34	9	27	36	4	88.89	Yes
Ozturk et al.[52]	33.0 (19-47)	N/A	2	0	2	0	100.00	No
Kirtane et al.[53]	46.3 (15-67)	N/A	6	7	13	0	100.00	No
Maselli et al.[54]	45.1 (34-66)	N/A	0	1	1	0	100.00	No
Roehm and Brown[55]	74	N/A	1	0	1	0	100.00	No
Bendersky et al.[56]	59.5 (46-73)	N/A	0	2	2	2	0.00	No
Gilat et al.[57]	47.8	N/A	1	6	7	0	100.00	No
Giannetti et al.[58]	50.3	N/A	2	24	26	10	61.54	No
Forer and Sethi[59]	49.1 (40-54)	N/A	2	5	7	1	85.71	No
Muscatello et al.[60]	57 (50-67)	N/A	1	2	3	1	66.67	No
Tabaee et al.[61]	57.1 ± 14.3 (36-78)	N/A	5	8	13	2	84.62	No
Sautter et al.[62]	49.7 (37-57)	38.7 (32-46.3)	0	4	4	1	75.00	No
Schuknecht et al.[63]	51.1	N/A	17	10	27	5	81.48	No
Ismail et al.[64]	45.1 (34-66)	N/A	3	9	12	2	83.33	No
Meco et al.[65]	33.3 (24-40)	N/A	1	2	3	0	100.00	No
Chatrath and Saleh[66]	46.3 (40-58)	N/A	0	3	3	0	100.00	No
Silva et al.[67]	40.2 (10-54)	N/A	1	5	6	0	100.00	No
Dunn et al.[68]	N/A	N/A	2	13	15	3	80.00	No

TABLE I.
(*Continued*)

Author	Age, yr	Mean BMI, kg/m^2	No. of Males	No. of Females	No. Treated	No. of Failures	Success Rate, %	ICP Control
Al-Sebeih et al.[69]	42.9 (25-62)	N/A	3	5	8	1	87.50	No
Lindstrom et al.[70]	N/A	33	N/A	N/A	12	2	83.33	No
Lopatin et al.[71]	N/A	N/A	6	15	21	1	95.24	No
Gendeh et al.[72]	51.3 (47-59)	N/A	0	3	3	2	33.33	No
Rahgavan et al.[73]	72	N/A	0	1	1	1	0.00	No
Castelnuovo et al.[74]	47.6 (32-63)	N/A	2	7	9	1	88.89	No
Casiano and Jassir[75]	N/A	N/A	N/A	N/A	4	0	100.00	No

BMI = body mass index; ICP = intracranial pressure; N/A = not available.

RESULTS

The search identified 2,048 potentially relevant articles that were then screened by title and abstract to 98 studies. Full-text review yielded the final total of 56 articles for inclusion in the review. The 56 articles were identified according to the search criteria and were combined with a prospective case series of 108 patients, leading to a total of 679 patients treated for spontaneous CSF rhinorrhea. The demographic data for the studies included are located in Table I. The mean age among articles reporting was 50.4 years, and mean BMI was 35.8 kg/m^2. Seventy-seven percent of patients treated were female. Defect locations were classified based on three locations: sphenoid, ethmoid, and frontal sinuses as seen in Table II. The most common defect location among studies reporting site was the sphenoid sinus (n = 334), followed by ethmoid sinus (n = 318) and frontal sinus (n = 46). The primary success rate of our case series of 108 patients was 96.30%. The overall average primary success rate among all patients analyzed in this systematic review was 89.11%. Success rates by study are reported in Table I.

Studies were separated by active (defined by ICP evaluation and measures instituted for patients identified as having high pressure with acetazolamide or permanent CSF diversion through lumboperitoneal or ventriculoperitoneal shunt), and no intervention for ICP. In the active intervention group, 348 patients were identified. The primary success rate from the active intervention combined cohort was 92.82%. In the no-intervention cohort, 331 patients were identified. The primary success rate of the cohort of patients without active ICP management was found to be significantly lower at 81.87% ($P < .001$) (Table III).

DISCUSSION

The focus of this review was to evaluate the impact that intervention for ICP control in patients surgically treated for spontaneous CSF rhinorrhea had on successful primary repair of skull base defects. There is currently no consensus in the literature on whether active ICP management should be standard in treatment of spontaneous CSF rhinorrhea, despite several authors demonstrating the association of spontaneous CSF leaks and increased ICP.[3,8,13] The results of this review suggest that active ICP management in patients being treated for spontaneous CSF rhinorrhea is associated with significant improvement in successful primary closure rate when compared to patients who do not undergo intervention for elevated ICP.

In this review, 17 authors described management of ICP as part of the treatment plan for endoscopic repair of spontaneous CSF rhinorrhea, whereas 40 authors did not. In total, 348 patients were treated with active ICP management in the postoperative period, with 25 failures in this patient group. The primary repair success rate for this cohort was 92.82%. Three hundred thirty-one patients were treated for spontaneous CSF rhinorrhea with no ICP management, and 60 patients had failure of the primary repair. The primary repair success rate for the cohort of patients not undergoing ICP management was 81.87%. The mean follow-up for the ICP intervention cohort was 24.1 ± 2.9 months, and the mean follow-up for the no-ICP intervention cohort was 26.9 ± 3.7 months.

Normal CSF pressure ranges from 5 to 15 cm H_2O on opening measurement via lumbar puncture.[8] In previously reported cohorts of patients with spontaneous CSF leaks, CSF pressures preoperatively have been well above the normal range.[14] There are many reported methods of ICP management in the literature including the standard treatments of acetazolamide or permanent CSF diversion as well as diet, serial lumbar punctures, and bariatric surgery.[8,10,26,27] The management of elevated ICP in patients being treated for spontaneous CSF rhinorrhea in

TABLE II.
Skull Base Defect Locations.

Sphenoid Sinus	Ethmoid Sinus	Frontal Sinus
334	318	46

TABLE III.
Comparison of ICP Intervention.

Patient Cohort	No. Treated	No. of Failures	Success Rate	Mean Follow-up, mo
ICP intervention	348	25	92.82%	24.1 ± 2.9
No ICP intervention	331	60	81.87%	26.9 ± 3.7

ICP = intracranial pressure.

our prospective case series was accomplished either with acetazolamide, a diuretic that decreases CSF production, or permanent CSF diversion via ventriculoperitoneal shunt. Some authors reported temporary use of lumbar drains in the postoperative period, but did not measure ICPs or utilize methods for long-term control of elevated ICP. Previous studies have shown that immediately after closure of the skull base defect, ICP significantly increases during the postoperative period when measured by lumbar drain or ventriculostomy.[8] Although temporary use of lumbar drainage will decrease this pressure, ICP will remain elevated if no intervention is performed, subjecting the patient to both early and late failures.

Patients presenting with spontaneous CSF rhinorrhea are classically obese (BMI >30) females, largely due to the coexistence of IIH in this population.[3] In this review, 77% of patients were women, and the average BMI among all patients treated was 35.8 kg/m^2.[9,14] Additionally, 43.5% of patients reviewed in this study had documented signs of increased ICP on imaging or through lumbar tap. Although the amount of patients determined to have increased ICP is lower than found in other studies, many authors, especially those who did not manage intracranial hypertension, did not report ICP data.[2,11] There were very limited data on specific ICP pressure values available in the literature despite the previously documented association between IIH and spontaneous CSF leaks. Furthermore, some authors do not monitor or measure ICP levels regardless of therapeutic intervention for increased ICP.

There are a number of limitations of the current study. First, as in any systematic review, there is the possibility of failing to include studies with relevant data because they did not match the chosen search terms. Additionally, many studies that fit preliminary inclusion material had to be excluded because the data were presented in a way that did not allow separation of spontaneous etiologies from other etiologies reported within the series. There is also variability in both surgeon skill and institutional experience with managing spontaneous CSF leaks. Larger case series with high success rates where ICP is monitored could reflect better technical proficiency rather than pressure lowering measures. Most importantly, the length of follow-up of studies in the review was roughly 2 years for both groups; however, failure of repair is still possible beyond this time frame, especially with the chronic erosive process compatible with longstanding intracranial hypertension. This is especially true for patients who did not have ICP management as part of their treatment protocol and long-term pressure-lowering measures. Future analysis would benefit from longer follow-up to ensure all primary failures for both cohorts are included.

CONCLUSION

This study demonstrates a significant difference in the primary repair success rate of spontaneous CSF rhinorrhea in patients who receive active ICP management compared to no treatment. ICP measurements and active intervention for intracranial hypertension should be a routine part of the management of spontaneous CSF leak patients.

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