The Role of Obesity, Sleep Apnea, and Elevated Intracranial Pressure in Spontaneous Cerebrospinal Fluid Leaks

Cyrus C. Rabbani, MD[1]
Mohamad Z. Saltagi, MD[1]
Rick F. Nelson, MD, PhD[1,2]

Author Affiliations:
[1]Department of Otolaryngology—Head and Neck Surgery
[2]Department of Neurosurgery
Indiana University School of Medicine, Indianapolis, IN, USA

Disclosures: None

Corresponding Author:
Rick F. Nelson, MD, PhD
Indiana University College of Medicine
355 W. 16th St. Suite 3200, Indianapolis, IN 46202
Telephone: 317-963-7073
Fax: 317-963-7085
ricnelso@iupui.edu

Abstract

Purpose of Review:
Spontaneous cerebrospinal fluid (sCSF) leaks often occur in middle age, obese females. Here we investigate the role of obesity, idiopathic intracranial hypertension (IIH) and obstructive sleep apnea (OSA) in the pathophysiology of sCSF leaks.

Recent Findings:
The association of obesity and sCSF leaks has been well established in many studies. It has now been revealed that sCSF leak patients have thinner calvariums along with the skull base. An intracranial process likely leads to calvarium and skull base thinning in sCSF leaks patients since this occurs independent of extracranial bone thinning and independent of obesity. OSA, which is known to cause spikes in intracranial pressure (ICP), has been found to be significantly prevalent in the sCSF population and has been shown to lead to both calvarial and skull base

This is the author's manuscript of the article published in final edited form as:
Rabbani, C. C., Saltagi, M. Z., & Nelson, R. F. (2019). The role of obesity, sleep apnea, and elevated intracranial pressure in spontaneous cerebrospinal fluid leaks. Current Opinion in Otolaryngology & Head and Neck Surgery, 27(5), 349. https://doi.org/10.1097/MOO.0000000000000562

thinning. Chronically elevated ICP (IIH) has also been shown to impact calvarial and skull base thicknesses.

Summary

The incidence of sCSF leaks has increased in recent decades along with an increasing rate of obesity. OSA and IIH, which are obesity-related factors and cause transient and chronic elevations in ICP, have now been implicated as critical factors leading to calvarial and skull base thinning and resultant sCSF leaks.

Key Words: Spontaneous Cerebrospinal Fluid Leak, Obesity, Intracranial Pressure, Obstructive Sleep Apnea, Calvarium Thickness

Abbreviations:

sCSF: Spontaneous Cerebrospinal Fluid Leak
ICP: Intracranial Pressure
IIH: Idiopathic Intracranial Hypertension
BMI: Body Mass Index
OSA: OSA
CI: Cochlear Implant

INTRODUCTION

Spontaneous cerebrospinal (sCSF) fluid leaks occur in the presence of lateral or anterior skull base bone defects in addition to holes in the dura with or without encephalocele. Clinically, lateral leaks lead to hearing loss, persistent ear effusions with or without chronic otorrhea, while anterior leaks lead to chronic clear rhinorrhea. Most importantly, sCSF leaks predispose patients to meningitis, thus prompting surgical repair. It is a spontaneous disease which occurs in patients without known etiology related to trauma, prior skull base surgery, or intracranial tumor [1]. sCSF leaks are most prevalent in middle-aged (average age 45-65 years) and obese (average body mass index, BMI = 35-38 kg/m^2) females (female:male ratio = 70:30) [2*, 3, 4]. Comorbid condition associated with obesity such as elevated intracranial pressure (ICP) and obstructive sleep apnea (OSA) are also common in sCSF leak patients [3, 5*, 6, 7*, 8, 9, 10, 11*]. The rate of sCSF leaks continues to increase over recent decades, mirroring the increasing obesity during this time period, but the pathophysiology and mechanism of sCSF leak are not well understood [3, 7*, 12 , 13].

Increased ICP, whether chronic or intermittent, is suspected to be one of culprits in thinning the skull base and ultimately leading to a defect in the bone and dura. Studies have shown that sCSF leak patients demonstrate isolated skull base defects along with global calvarial thinning, but do not typically have thinning of extracranial bones (zygoma), supporting the notion that an intracranial process is responsible for sCSF leak [2*, 14**]. Recent studies have investigated the role of obesity, idiopathic intracranial hypertension, and OSA in causing transient and chronic elevations in ICP which can lead to skull thinning over time [5*, 6, 7*, 14**, 15**]. These studies have noted that obesity alone does not account for the development of sCSF leaks; rather, obesity related factors such as IIH and/or OSA play a more integral role in the pathophysiology of sCSF leaks [2*, 14**]. The role of OSA has been investigated recently given its association with obesity and its transient effects on ICP. Here we review the recent literature on the association of obesity, ICP, and sleep apnea with the development of spontaneous CSF leaks.

TEXT OF REVIEW

OBESITY

The effect of obesity in the development of sCSF leak has been extensively studied in the past and studies have shown that most patients who undergo sCSF leak repair are obese [7*, 8, 10, 13, 16, 17, 18]. Studies have also demonstrated an association between elevated BMI and elevated ICP [6, 10, 16, 18]. Nonetheless, recent data has begun to suggest that obesity-related factors, rather than obesity itself, are implicated in the development of sCSF leak.

Prevalence of obesity among sCSF leak repair patients

Virtually all studies that have investigated spontaneous CSF leak have noted that most patients are obese. A recent retrospective 10-year review of the University HealthSystem Consortium (UHC) national database found that, of those undergoing craniotomy for CSF leak repair, all patients were overweight (BMI > 25 kg/m^2) and the majority of patients were obese (average BMI = 37.8 kg/m^2) [7*]. In addition, this study found that sCSF leak repair was twice as common in regions of the country with high obesity rates (Midwest) when compared to regions with lower obesity rates (West) [7*]. Other studies in recent years have reported that the average BMI among sCSF leak patients ranges between 32 and 37 kg/m^2 [8, 10, 13, 17, 19]. These studies have conclusively established that obesity is strongly associated with spontaneous CSF leak, prompting further studies on the underlying mechanism of this relationship.

Skull base thickness in obese and non-obese patients

Numerous studies have investigated skull base thickness in obese and non-obese patients. A recent retrospective review compared sCSF leak patients with obese and non-obese controls and measured tegmen thickness in each of these groups; 97 patients were measured overall [20]. The study found that sCSF leak patients had significantly thinner tegmen compared with obese and non-obese controls, and obese patients had thinner tegmen than non-obese patients; BMI was inversely related to tegmen thickness [20]. A similar study compared the tegmen's bone mineral density among obese, non-obese, and sCSF leak patients and concluded that there were no significant differences between the three groups [21*]. Yet another recent study measured the superior semicircular canal and the lateral skull base among obese

and non-obese patients and found that BMI did not correlate with lateral skull base thickness [22*].

Obesity is unlikely to be independently responsible for skull thinning. A study examining calvarium thickness in patients undergoing cochlear implant (CI) surgery sought to examine skull thickness in age-matched obese (BMI ≥ 30 kg/m^2) and non-obese (BMI < 30 kg/m^2) patients in which they measured the squamous temporal bone (**Figure 1**) [2*]. The calvarial thickness was not significantly different when comparing the obese to non-obese CI patients. When comparing both the obese and non-obese CI cohort to patients with lateral skull base sCSF leaks, there was a significant thinning of the calvarium in the sCSF leak patient population (**Figure 1**). The extracranial zygoma bone thickness was then used as a control in this study to control for non-intracranial pathology such as systemic bone disease (e.g. osteopenia). Utilizing the ratio of the squamous temporal bone thickness to the extracranial zygoma thickness, they showed that spontaneous CSF leak patients had a significantly lower ratio than both the obese and non-obese CI patients; and again no difference was found among the two CI cohorts. These data implicate an intracranial process that causes isolated skull thinning and is independent of obesity in the development of sCSF leaks. Thus, it is hypothesized that additional obesity-related factors, such as IIH and OSA, are implicated in the development of sCSF leak, rather than obesity alone [2*, 3, 14**, 15**]. The varying data from the aforementioned studies highlights the potential that obesity alone does not completely account for the development of sCSF leak.

INTRACRANIAL PRESSURE

Studies investigating the association between BMI and ICP in the past have identified a positive linear relationship between BMI and ICP, with an increase of 0.24 mm Hg in CSF pressure per unit of BMI [16]. The mechanism of this linear relationship has been postulated as follows: increased abdominal adiposity can increase intraabdominal and intrapleural pressures and lead to increased cardiac filling pressures and cerebral venous retention, ultimately causing chronically elevated ICP. This in turn is theorized to lead to skull and skull base thinning [6, 9, 10, 16, 18, 23].

Relationship between ICP and sCSF leaks

It has been postulated that sCSF leaks result from chronic or intermittently elevated ICP and may be a type of IIH [23, 24]. Epidemiological studies have revealed obesity as a risk factor for IIH and have identified a relationship between fluctuations in weight and the development of IIH [5*, 11*, 23, 25, 26*, 27, 28, 29, 30]. Furthermore, numerous studies have shown that weight loss, whether by surgical or non-surgical methods, leads to resolution of elevated ICP in the vast majority of patients with IIH [25, 31, 32*, 33, 34, 35, 36*, 37].

Chronic pressure-like forces acting on the skull base and skull are predicted to thin the bone, ultimately leading to dural exposure and tearing. Elevated ICPs have been found on pre-operative ICP measurements in anterior skull base spontaneous CSF leaks, with a reported average opening pressure of 33.0 cm H2O [28]. The nature of anterior skull base CSF leak repair generally warrants the placement of a lumbar drain, whereas this is not generally routine practice in the commonly performed middle cranial fossa approach for lateral skull base leaks [3, 38]. Among those presenting for evaluation and management of sCSF leak, elevated ICP has been observed in 10-66% of patients in studies that were able to perform lumbar puncture [5*, 11*, 39]. Lumbar puncture takes only a single measure of the ICP and it is known that ICP varies with time of day and patient positioning. In addition there are some risks of bleeding, infection and persistent leak with lumbar puncture and many patients defer testing [27]. This makes it difficult to truly know the transient or chronic ICP in many patients with these pathologies.

Imaging findings in IIH

CT scan findings in intracranial hypertension include thinning or attenuation of the skull base and calvarial bone, demonstration of arachnoid pits [40], and the presence of multiple skull base defects in up to 31% [41]. When examining the squamous temporal bone, it was shown that patients with sCSF leak had on average 22% thinner squamous temporal bone thickness than age and BMI matched controls [2*] (**Figure 1**). A similar study examined the relationship between skull thickness and ICP recorded on lumbar punctures; it was revealed that in patients with low or normal ICP, the calvarium thickness increased with aging; while the calvarium thickness decreased with aging in patients with high ICP [42**] (**Figure 2**). The patient cohort was then split into two groups of high and low-normal ICP, revealing a significant difference in

squamous temporal bone thickness. Extracranial zygoma thickness was measured and utilized as a control which revealed no effect from ICP. Furthermore, the skull base was measured above the internal auditory canal revealing decreased thickness in patients in this same cohort with elevated ICP. As with this study and many others, the limitation remains that the methods in which the ICP was measured is at a single timepoint rather than over multiple timepoints or a distinct time period. This highlights the notion that patients with sCSF leaks may not have *chronically* elevated ICP; *transient* spikes in ICP may also be implicated. OSA is known to cause transient elevations in ICP during apnea overnight and thus is central to this discussion [43*, 44].

OBSTRUCTIVE SLEEP APNEA

Sleep apnea has a strong association with obesity [45, 46] and is known to cause transient intracranial hypertension during apneic episodes when patients are asleep [43*, 44]. Recent studies examining the relationship between OSA, sCSF leak, and calvarium and skull base thickness have identified OSA as an important factor strongly associated with this clinical pathology.

Prevalence of OSA in sCSF leak patients

The first prospective study to investigate the prevalence of OSA among sCSF leak patients has been published. This was performed by obtaining level 1 polysomnography (PSG) on every patient who presented for repair of spontaneous CSF leak during a three-year period [15**]. A total of 21 spontaneous CSF leak patients (average BMI 35.3 kg/m^2) presented for evaluation, and 18 of them ultimately obtained a PSG; 15 of 18 patients were found to have OSA (83.3%) [15**]. This prevalence is much higher than expected based on previously reported retrospective studies [6, 7*, 47, 48]. This study established a strong association between OSA and sCSF leak, prompting further research into skull and skull base findings in OSA patients.

Calvarial and skull base thickness in OSA and sCSF leak patients

Numerous studies have investigated skull measurement findings in obese and non-obese patients, as detailed above, but until recently no studies had examined these variables in those

with sleep apnea. A recent study helped fill this gap in the literature by investigating calvarial and skull base findings in OSA, non-OSA, and sCSF leak patients [14**].

The study first identified over 1000 non-spontaneous CSF leak patients who had obtained high resolution CT scans and level 1 PSG studies at a large academic institution in the past decade [14**]. Non-OSA patients (AHI<5) and moderate-severe OSA patients (AHI>25) were then matched for age, BMI, and hemoglobin A1c [14**]. Skull calverium, skull base, and zygoma thickness were measured in a consistent and reproducible manner (**Figure 3A&B**). Patients with OSA were found to have thinner mean (SD) calvaria and thinner skull bases than non-OSA patients (**Figure 3C**) [14**]. OSA and non-OSA patients in this same cohort were compared to previously identified spontaneous CSF leak patients. Spontaneous CSF leak patients had significantly thinner calvaria than non-OSA patients, with a 17.9% difference in thickness; while calvarial thickness was not significantly different between OSA patients and sCSF leak patients (**Figure 3C**). The extracranial zygoma thickness was not different between the three groups (**Figure 3D**)**.** The tegmen mastoideum was dehiscent in nearly twice as many patients with OSA as those without (37% vs 20%).

Overall, this study showed that, in a cohort of obese non-sCSF leak patients, those with moderate-severe OSA have thinning of the squamous portion of the temporal bone and skull base when compared with non-OSA patients, a relationship independent of age, BMI, gender, and multiple co-morbidities [14**].

Though there is an association of OSA with thinning of the calvarium and skull base, the potential mechanism of this remains under study. We hypothesize that OSA, when left untreated in the long term, plays a role in a progressive thinning of intracranial bones through its transient effects on ICP during apneic episodes. When patients are apneic overnight, they have transient hypercarbia, resultant cerebral vasodilation and impairment of venous drainage, and this can lead to spikes in ICP [43*, 44]. Over time, this progressive thinning can lead to sCSF leak, especially in inherently thin areas of the skull base such as the tegmen and cribriform plate, where erosion of bone to a magnitude of 1 mm can lead to CSF otorrhea and/or rhinorrhea [7*].

CONCLUSION

The pathophysiology of sCSF leak has been extensively studied in recent years, and the current literature suggests that a multifactorial process involving obesity and its related factors is responsible for the development of sCSF leak. The sCSF leak patient is typically obese, middle-aged, and more often female than male. The interplay between obesity, ICP, and OSA over time is likely what leads to tegmen dehiscence and resultant sCSF leak. There are inherent limitations to studying ICP in these patients, but the current literature strongly suggests that transient and chronic elevations of ICP play a role in skull base dehiscence and ultimately sCSF leaks.

KEY POINTS:

- Patients with sCSF leaks have been found to have overall thinner calvariums than age and BMI matched cohorts.
- Increased ICP has been shown to positively correlate with obesity and contribute to skull thinning.
- The prevalence of OSA in sCSF leak patients has been found to be over 80% in a recent prospective observational study.
- OSA contributes to thinning of the skull calvarium and skull base and likely plays a role in the pathophysiology and mechanism of sCSF leaks.
- Though sCSF leak patients tend to be obese, obesity alone does not independently affect skull thickness, suggesting that obesity-related factors such as OSA and elevated ICP are more likely responsible.

ACKNOWLEDGEMENTS

None.

Financial support and sponsorship

This work was supported by the Department of Otolaryngology – Head and Neck Surgery, Indiana University, Indianapolis, IN, USA.

Conflicts of interest

None.

Figure legends:

Figure 1

Heading: Calvarial Thinning in sCSF Leak Patients

Legend: Axial temporal bone CT scan images of a normal cochlear implant patient and a spontaneous CSF leak patient centered at the level of the optic canal. Note the difference in the thickness of the calvarium between the patients.

Source Previously Published: Nelson RF, Hansen KR, Gantz BJ, Hansen MR. Calvarium thinning in patients with spontaneous cerebrospinal fluid leak. *Otol Neurotol*. 2015;36(3):481-5. [2*]

Figure 2

Heading: Effect of Opening Pressure and Age on Calvarium Thickness

Legend: General linear model univariate regression analysis of the relationship between opening pressure, calvarium thickness and age. Prediction of calvarial thickness with advancing age in patients with low OP (grey circles) and high OP (black squares). OP = opening pressure; mm = millimeter; cm = centimeter; y = years

Source Pending Publication: Rabbani C, Patel JM, Nag AK, Schueth EA, Saltagi MZ, Kao R, et al. Association of Intracranial Hypertension with Calvarial and Skull Base Thinning. *Otol Neurotol*. 2019;Accepted Manuscript, in Press. [42**]

Figure 3

Heading: Calvarial and Zygoma Measurements in Non-OSA, OSA, and spontaneous CSF leak Patient.

Legend: (**A**) Measurements were taken in the coronal plane of a 15 mm (height) segment of the thinnest portion of the squamous temporal bone. Segments were highlighted bilaterally, starting at the level of the foramen rotundum anteriorly and extending posteriorly to the level of the upper extent of the superior semicircular canal. Volume was calculated using 3D Slicer's Volumetric Analysis tool (version 4.6.2, http://www.slicer.org). (**B**) A 3D reconstruction illustrating the highlighted calvarial segment. (**C**) OSA patients and spontaneous CSF leak patients had statistically significant thinner skulls than Non-OSA patients. Skull thickness was not statistically-significantly different between OSA and spontaneous CSF leak patients. (**D**) There were no statistically-significant differences in zygoma thickness between Non-OSA, OSA,

and spontaneous CSF leak patients. Dashed line indicates that spontaneous CSF leak patients were not part of the original database search.

Abbreviations: NS = non-significant (clinically and statistically), n = number of measurements; OSA = OSA; sCSF = spontaneous cerebrospinal fluid leak, mm = millimeters, *d* = Cohen's *d*.

Source Previously Published: Rabbani C, Saltagi MZ, Ye MJ, Patel JM, Manchanda S, Nelson RF. Association of Obstructive Sleep Apnea With Calvarial and Skull Base Thinning. *JAMA Otolaryngol Head Neck Surg.* 2018;144(6):513-8. [14**]

References and recommended reading:

• of special interest

•• of outstanding interest

[1] Reddy M, Baugnon K. Imaging of Cerebrospinal Fluid Rhinorrhea and Otorrhea. Radiologic clinics of North America 2017; 55:167-187.

[2] Nelson RF, Hansen KR, Gantz BJ, Hansen MR. Calvarium thinning in patients with spontaneous cerebrospinal fluid leak. Otol Neurotol 2015; 36:481-485.

*This paper demonstrates that sCSF leak patients have 22% thinner calvarium compared to controls. This thinning is isolated only to the skull and not extracranial bones (i.e. zygoma) and is independent of obesity. This suggests an intracranial process leads to the development of sCSF leaks.

[3] Lobo BC, Baumanis MM, Nelson RF. Surgical repair of spontaneous cerebrospinal fluid (CSF) leaks: A systematic review. Laryngoscope Investig Otolaryngol 2017; 2:215-224.

[4] Vivas EX, McCall A, Raz Y *et al.* ICP, BMI, Surgical Repair, and CSF Diversion in Patients Presenting With Spontaneous CSF Otorrhea. Otol Neurotol 2014; 35:344-347.

[5] Allen KP, Perez CL, Kutz JW *et al.* Elevated intracranial pressure in patients with spontaneous cerebrospinal fluid otorrhea. The Laryngoscope 2014; 124:251-254.

*This study performed lumbar puncture on sCSF leaks patients and found the incidence of elevated ICP in sCSF leak patients is 35% (8 of 22 patients).

[6] Fleischman GM, Ambrose EC, Rawal RB *et al.* Obstructive sleep apnea in patients undergoing endoscopic surgical repair of cerebrospinal fluid rhinorrhea. The Laryngoscope 2014; 124:2645-2650.

[7] Nelson RF, Gantz BJ, Hansen MR. The rising incidence of spontaneous cerebrospinal fluid leaks in the United States and the association with obesity and obstructive sleep apnea. Otol Neurotol 2015; 36:476-480.

*Using a national database of 81 academic health centers in the United States, the repair of sCSF leaks doubled from 2002 to 2012. This rise is consistent with the rise in obesity rates in the United States.

[8] Stucken EZ, Selesnick SH, Brown KD. The role of obesity in spontaneous temporal bone encephaloceles and CSF leak. Otol Neurotol 2012; 33:1412-1417.

[9] Wang EW, Vandergrift WA, 3rd, Schlosser RJ. Spontaneous CSF Leaks. Otolaryngologic clinics of North America 2011; 44:845-856, vii.

[10] LeVay AJ, Kveton JF. Relationship between obesity, obstructive sleep apnea, and spontaneous cerebrospinal fluid otorrhea. The Laryngoscope 2008; 118:275-278.

[11] Brainard L, Chen DA, Aziz KM, Hillman TA. Association of benign intracranial hypertension and spontaneous encephalocele with cerebrospinal fluid leak. Otol Neurotol 2012; 33:1621-1624.

*This study performed lumbar puncture on sCSF leaks patients and found the incidence of elevated ICP in sCSF leak patients is 66% (6 out of 9 patients).

[12] Flegal KM, Kruszon-Moran D, Carroll MD *et al.* Trends in Obesity Among Adults in the United States, 2005 to 2014. Jama 2016; 315:2284-2291.

[13] Cheng E, Grande D, Leonetti J. Management of spontaneous temporal bone cerebrospinal fluid leak: A 30-year experience. American journal of otolaryngology 2019; 40:97-100.

[14] Rabbani C, Saltagi MZ, Ye MJ *et al.* Association of Obstructive Sleep Apnea With Calvarial and Skull Base Thinning. JAMA otolaryngology-- head & neck surgery 2018; 144:513-518.

**This study demonstrated that moderate-severe OSA patients have significantly thinner calvarium and skull bases compared to match controls. This is the first demonstration that OSA independently thins the skull and skull base.

[15] Rabbani CC, Saltagi MZ, Manchanda SK *et al.* Prevalence of Obstructive Sleep Apnea (OSA) in Spontaneous Cerebrospinal Fluid (CSF) Leaks: A Prospective Cohort Study. Otol Neurotol 2018; 39:e475-e480.

**The first prospective study demonstrating the prevalence of OSA in sCSF leak patients to be 83%.

[16] Berdahl JP, Fleischman D, Zaydlarova J *et al.* Body mass index has a linear relationship with cerebrospinal fluid pressure. Investigative ophthalmology & visual science 2012; 53:1422-1427.

[17] Kutz JW, Jr., Johnson AK, Wick CC. Surgical management of spontaneous cerebrospinal fistulas and encephaloceles of the temporal bone. The Laryngoscope 2018; 128:2170-2177.

[18] Quatre R, Attye A, Righini CA *et al.* Spontaneous Cerebrospinal Fluid Rhinorrhea: Association with Body Weight and Imaging Data. Journal of neurological surgery. Part B, Skull base 2017; 78:419-424.

[19] Son HJ, Karkas A, Buchanan P *et al.* Spontaneous cerebrospinal fluid effusion of the temporal bone: repair, audiological outcomes, and obesity. The Laryngoscope 2014; 124:1204-1208.

[20] Stevens SM, Lambert PR, Rizk H *et al.* Novel radiographic measurement algorithm demonstrating a link between obesity and lateral skull base attenuation. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery 2015; 152:172-179.

[21] Hatch JL, Schopper H, Boersma IM *et al.* The Bone Mineral Density of the Lateral Skull Base and its Relation to Obesity and Spontaneous Cerebrospinal Fluid Leaks. Otol Neurotol 2018; 39:e831-e836.

*This paper measured bone mineral density of the lateral skull base in obese, non-obese, and sCSF-L patients and found no significant differences among the three groups.

[22] Rizk HG, Hatch JL, Stevens SM *et al.* Lateral Skull Base Attenuation in Superior Semicircular Canal Dehiscence and Spontaneous Cerebrospinal Fluid Otorrhea. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery 2016; 155:641-648.

*This study compared SSCD patients with sCSF-L patients and 3 control groups with varying BMIs, showing that SSCD and sCSF-L patients had significant association of their skull base compared with all BMI control groups.

[23] Stevens SM, Rizk HG, Golnik K *et al.* Idiopathic intracranial hypertension: Contemporary review and implications for the otolaryngologist. The Laryngoscope 2018; 128:248-256.

[24] Schlosser RJ, Woodworth BA, Wilensky EM *et al.* Spontaneous cerebrospinal fluid leaks: a variant of benign intracranial hypertension. The Annals of otology, rhinology, and laryngology 2006; 115:495-500.

[25] Subramaniam S, Fletcher WA. Obesity and Weight Loss in Idiopathic Intracranial Hypertension: A Narrative Review. Journal of neuro-ophthalmology : the official journal of the North American Neuro-Ophthalmology Society 2017; 37:197-205.

[26] Schlosser RJ, Wilensky EM, Grady MS, Bolger WE. Elevated intracranial pressures in spontaneous cerebrospinal fluid leaks. American journal of rhinology 2003; 17:191-195.

*10 of 16 patients with sCSF leaks found to have empty sella on imaging

[27] Bidot S, Levy JM, Saindane AM *et al.* Do Most Patients With a Spontaneous Cerebrospinal Fluid Leak Have Idiopathic Intracranial Hypertension? Journal of neuro-ophthalmology : the official journal of the North American Neuro-Ophthalmology Society 2019.

[28] Martinez-Capoccioni G, Serramito-Garcia R, Martin-Bailon M *et al.* Spontaneous cerebrospinal fluid leaks in the anterior skull base secondary to idiopathic intracranial hypertension. Eur Arch Otorhinolaryngol 2017; 274:2175-2181.

[29] Perez MA, Bialer OY, Bruce BB *et al.* Primary spontaneous cerebrospinal fluid leaks and idiopathic intracranial hypertension. Journal of neuro-ophthalmology : the official journal of the North American Neuro-Ophthalmology Society 2013; 33:330-337.

[30] Rosenfeld E, Dotan G, Kimchi TJ, Kesler A. Spontaneous cerebrospinal fluid otorrhea and rhinorrhea in idiopathic intracranial hypertension patients. Journal of neuro-ophthalmology : the official journal of the North American Neuro-Ophthalmology Society 2013; 33:113-116.

[31] Sugerman HJ, Felton WL, Salvant JB *et al.* Effects of surgically induced weight loss on idiopathic intracranial hypertension in morbid obesity. Neurology 1995; 45:1655-1659.

[32] Teachey W, Grayson J, Cho DY *et al.* Intervention for elevated intracranial pressure improves success rate after repair of spontaneous cerebrospinal fluid leaks. The Laryngoscope 2017; 127:2011-2016.

*This was a prospective case series and literature review evaluating if intervention to decrease ICP lowers recurrence rates of CSF leak following repair.

[33] Fridley J, Foroozan R, Sherman V *et al.* Bariatric surgery for the treatment of idiopathic intracranial hypertension. Journal of neurosurgery 2011; 114:34-39.

[34] Handley JD, Baruah BP, Williams DM *et al.* Bariatric surgery as a treatment for idiopathic intracranial hypertension: a systematic review. Surgery for obesity and related diseases : official journal of the American Society for Bariatric Surgery 2015; 11:1396-1403.

[35] Manfield JH, Yu KK, Efthimiou E *et al.* Bariatric Surgery or Non-surgical Weight Loss for Idiopathic Intracranial Hypertension? A Systematic Review and Comparison of Meta-analyses. Obesity surgery 2017; 27:513-521.

[36] Ottridge R, Mollan SP, Botfield H *et al.* Randomised controlled trial of bariatric surgery versus a community weight loss programme for the sustained treatment of idiopathic intracranial hypertension: the Idiopathic Intracranial Hypertension Weight Trial (IIH:WT) protocol. BMJ open 2017; 7:e017426.

*This is an ongoing prospective randomized control trial to assess whether bariatric surgery is an effective long-term treatment for patients with IIH with a BMI over 35.

[37] Perez-Sanchez JR, Arnoriaga Rodriguez M, Diaz-Otero F, Breton Lesmes I. Treatment of idiopathic intracranial hypertension with bariatric surgery. Neurologia (Barcelona, Spain) 2016.

[38] Nelson RF, Roche JP, Gantz BJ, Hansen MR. Middle Cranial Fossa (MCF) Approach Without the Use of Lumbar Drain for the Management of Spontaneous Cerebral Spinal Fluid (CSF) Leaks. Otol Neurotol 2016; 37:1625-1629.

[39] Kim L, Wisely CE, Dodson EE. Transmastoid approach to spontaneous temporal bone cerebrospinal fluid leaks: hearing improvement and success of repair. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery 2014; 150:472-478.

[40] Shetty PG, Shroff MM, Fatterpekar GM *et al.* A retrospective analysis of spontaneous sphenoid sinus fistula: MR and CT findings. AJNR. American journal of neuroradiology 2000; 21:337-342.

[41] Schlosser RJ, Bolger WE. Spontaneous nasal cerebrospinal fluid leaks and empty sella syndrome: a clinical association. American journal of rhinology 2003; 17:91-96.

[42] Rabbani C, Patel JM, Nag AK *et al.* Association of Intracranial Hypertension with Calvarial and Skull Base Thinning. Otol Neurotol 2019; Accepted Manuscript, in Press.

**This paper demonstrates that IIH is independently associated with calvarial and skull base thinning and thinning worsens with age.

[43] Jennum P, Borgesen SE. Intracranial pressure and obstructive sleep apnea. Chest 1989; 95:279-283.

*Demonstrates spikes in intracranial pressure during apnea episodes

[44] Sugita Y, Iijima S, Teshima Y *et al.* Marked episodic elevation of cerebrospinal fluid pressure during nocturnal sleep in patients with sleep apnea hypersomnia syndrome. Electroencephalography and clinical neurophysiology 1985; 60:214-219.

[45] Lee W, Nagubadi S, Kryger MH, Mokhlesi B. Epidemiology of Obstructive Sleep Apnea: a Population-based Perspective. Expert review of respiratory medicine 2008; 2:349-364.

[46] Li C, Ford ES, Zhao G *et al.* Prevalence of self-reported clinically diagnosed sleep apnea according to obesity status in men and women: National Health and Nutrition Examination Survey, 2005-2006. Preventive medicine 2010; 51:18-23.

[47] Bakhsheshian J, Hwang MS, Friedman M. Association Between Obstructive Sleep Apnea and Spontaneous Cerebrospinal Fluid Leaks: A Systematic Review and Meta-analysis. JAMA otolaryngology-- head & neck surgery 2015; 141:733-738.

[48] Thurtell MJ, Trotti LM, Bixler EO *et al.* Obstructive sleep apnea in idiopathic intracranial hypertension: comparison with matched population data. J Neurol 2013; 260:1748-1751.