

Aetiology of cerebrospinal fluid rhinorrhoea in a Dutch retrospective cohort from two tertiary referral centres*

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Abstract

Background: Cerebrospinal fluid (CSF) rhinorrhoea has different aetiologies, with spontaneous leaks related to female gender and obesity. Limited data is available on patient characteristics and surgical outcomes across different aetiologies of CSF leaks in relatively non-obese populations.

Methods: Retrospective cohort study from two tertiary referral centres including adult patients that underwent surgical closure of a CSF leak, divided into four aetiologies: traumatic, iatrogenic, secondary to structural intracranial pathology (SIP), and spontaneous. Data included patient characteristics, presenting symptoms, preoperative radiologic findings, intracranial pressure (ICP) and surgical outcomes.

Results: 72 patients were included: 9 traumatic, 15 iatrogenic, 4 SIP and 44 spontaneous leaks. Primary surgical success was 79%, rising to 93% with reinterventions. Spontaneous leak cases displayed highest female proportion and BMI. A meningo(-encephalo)cele was present in 33 patients and was associated with surgical failure and previous meningitis. No significant differences were observed between different aetiologies regarding patient characteristics, presenting symptoms, or surgical success rates.

Conclusions: Even in a relatively non-obese population, the majority of CSF leaks is spontaneous and associated with female gender and obesity. Otherwise, no differences exist across aetiologies regarding patient characteristics, presenting symptoms or surgical success.

Key words: cerebrospinal fluid rhinorrhea, aetiology, idiopathic intracranial hypertension, obesity, retrospective study

Introduction

Cerebrospinal fluid (CSF) leaks arising from defects in the anterior and middle cranial fossa usually present with clear watery rhinorrhoea, and occur in approximately 0.5-2 individuals per 100.000 annually ⁽¹⁾. Associated complications include bacterial meningitis and brain abscess ⁽²⁻⁴⁾.

CSF rhinorrhoea can be classified according to its underlying aetiology ⁽⁵⁾, subdivided into traumatic (including iatrogenic) ⁽⁶⁾ and non-traumatic leaks. The latter includes congenital leaks, leaks secondary to increased intracranial pressure ⁽⁷⁾, and spontaneous (in absence of any apparent cause) ⁽⁵⁾. A systematic review of 55 studies containing 1685 leaks demonstrated that traumatic and

non-traumatic aetiologies were evenly distributed with both ~50% of all cases ⁽⁸⁾. The largest group consisted of spontaneous leaks (41.1%), followed by iatrogenic leaks (30.1%). Treatment of CSF leaks usually involves endoscopic repair, which has been shown to be a successful approach with surgical success rates over 90% ⁽⁸⁻¹⁰⁾.

Non-traumatic leaks are associated with increased intracranial pressure, which in turn might be idiopathic or secondary to structural intracranial causes ⁽¹¹⁾. Pre-existent idiopathic intracranial hypertension (IIH) has been implicated to play a major role in spontaneous CSF rhinorrhoea ⁽¹²⁾. Characteristic complaints of IIH are headaches and visual impairment, but it often

remains asymptomatic^(13,14). Radiographic findings suggestive of IIH include empty sella, meningo(-encephalo)cele, increased CSF volume surrounding the optic nerves, and arachnoid protrusions⁽¹⁵⁻¹⁷⁾. Female gender and obesity are important risk factors for IIH. In parallel, these factors are also associated with spontaneous leaks. In a systematic review on the management of elevated intracranial pressure in spontaneous leaks including 56 studies on 679 patients, there was indeed a high prevalence of female gender (77%) and a high body mass index (BMI; mean 35.8 kg/m²)⁽¹⁸⁾. As obesity numbers vary between countries, so does the incidence of spontaneous CSF leaks, with a reported incidence varying between 0.9 and 323 per 100,000 individuals annually⁽¹⁹⁾. Consequently, the rise of patients with obesity over the past decades may also result in an increase in spontaneous CSF leaks⁽²⁰⁾.

There is scarce literature on CSF rhinorrhoea from Northern European countries. In this study we therefore investigated and compared CSF rhinorrhoea of different aetiologies in a Dutch population. This is characterized by a relatively low obesity rate (12.6%), which is two- to threefold higher in other Western countries^(21,22). Our main goal was to determine whether the distribution of CSF rhinorrhoea aetiologies was comparable to other populations and whether this may influence surgical success rate. Our secondary objective was to compare patient characteristics, presenting symptoms, and complication rates between aetiologies of CSF rhinorrhoea.

Methods

Patients

A retrospective chart review was conducted on eligible patients from two Dutch tertiary referral centres, the Amsterdam University Medical Center (AUMC), location AMC, and Erasmus Medical Center Rotterdam (EMC). All patients with CSF rhinorrhoea that underwent surgical endoscopic closure between January 2003 and December 2021 were retrieved using the procedural surgical coding system of the Otorhinolaryngology and Neurosurgery departments' databases. Patients below eighteen years of age and those with a CSF leak as a (direct) complication of skull base procedures were not included (e.g. surgery of the pituitary gland, meningioma of the anterior fossa). CSF rhinorrhoea was based on patient history, imaging, surgical findings, and - whenever possible - confirmed through beta-trace and beta-2-transferrin tests. Beta-trace test results were regarded positive when above 1.69 mg/L. Additional beta-2-transferrin testing was carried out when results were between 1.31 mg/L and 1.69 mg/L.

Aetiology and definitions

The total study population was divided into four different groups based on aetiology: (I) traumatic, (II) iatrogenic, (III) non-traumatic and secondary to structural intracranial pathology

(SIP), and (IV) spontaneous i.e., non-traumatic without apparent other cause.

Traumatic leaks were defined as CSF leaks directly inflicted by high-energetic accidental head trauma with corresponding radiographic imaging and perioperative findings. CSF leaks were regarded iatrogenic when occurring within two years after endoscopic sinus surgery (ESS) with a leakage site corresponding to the original surgery performed. If the time interval between trauma or ESS and the first event of CSF leakage exceeded two years, the aetiology was decided in a group discussion between the authors, based on medical history, presenting symptoms, radiographic images and intraoperative findings. Patients were allocated to SIP in case of intracranial pathology elevating the intracranial pressure (ICP), e.g., intracranial tumours, sinus thrombosis or disruption of normal CSF circulation. A diagnosis of spontaneous CSF rhinorrhoea was made when: 1) no prior surgical procedures at/near skull base level were performed, or prior surgery was carried out more than two years before CSF rhinorrhoea, or prior surgery did not correspond with anatomical CSF leaking site; 2) no recent traumatic event, or traumatic event happened more than two years before CSF rhinorrhoea; 3) no structural intracranial disease was observed.

Idiopathic intracranial hypertension (IIH) was deemed present if: 1) signs suggestive of intracranial hypertension were confirmed radiographically (see below); 2) symptoms suggestive of intracranial hypertension were present (chronic headache, visual impairment, nausea), and/or when ICP values transcended 25 cmH₂O and when no alternative explanation for symptoms and radiologic findings was available (such as structural intracranial pathology).

Baseline characteristics and radiology

From the patient records, gender at birth, age at time of first surgery, BMI at the time of surgery, prior endoscopic sinus surgeries, prior meningitis, and presenting symptoms were recorded. A preoperative CT and/or MRI was performed in all patients. From the imaging reports, any radiologic signs suggestive of intracranial pathology and/or hypertension, such as increased CSF surrounding the optic nerves, partial or complete empty sella, and arachnoid protrusions were retrieved, as well as the presence of a meningo(-encephalo)cele.

Skull base defect characteristics

The location of the skull base defect was radiographically established by experienced neuro-radiologists. Based on radiological and intra-operative findings five different anatomical sites were distinguished: (I) the sphenoid roof; (II) the lateral recess of the sphenoid; (III) the ethmoid roof; (IV) the cribriform plate; (V) the

Table 1. Patient characteristics.

	Aetiology of CSF leak				Total population	p-value***
	Traumatic	Iatrogenic	SIP**	Spontaneous		
Study subjects	9	15	4	44	72	
Female gender (%)*	3 (33)	3 (20)	2 (50)	30 (68)	38 (53)	0.002^
Age, mean and SD	32 ± 16.3	49.8 ± 15.6	27 - 52	46.7 ± 11.4	44.9 ± 13.8	0.018\$
Median BMI (kg/m ²) (IQR)	22.6 (20.5-25.0)	26.6 (25.0-30.0)	19.1 - 25.2	29.5 (25.6-35.9)	26.9 (25.0-32.9)	< 0.001§
Obese (BMI > 30) (%)*	0	4 (27)	0	22 (50)	26 (36)	0.017^
Extreme obese (BMI > 35) (%)*	0	1 (7)	0	12 (27)	13 (18)	0.037^
Prior ESS (%)*	0	15 (100)	2 (50)	6 (14)	23 (32)	< 0.001^
Preoperative meningitis*	6 (67)	7 (47)	2 (50)	11 (25)	26 (36)	0.033^
≥ 2 episodes	5 (56)	3 (20)	1 (25)	6 (14)	15 (21)	

* Percentage of subgroup total. ** for SIP, ranges are given as there are only 4 subjects. *** values when excluding SIP group from analysis. ^ Fisher's exact; \$ One-way ANOVA; § Kruskal-Wallis. SIP = structural intracranial pathology; BMI = body mass index; ESS = endoscopic sinus surgery; IQR = interquartile range; SD = standard deviation.

posterior wall of the frontal sinus.

To establish the extent of the skull base defects, the maximum diameter in any direction was measured on CT and/or MRI and noted in millimetres. To categorize the size of the defects, three groups were defined: (I) small, when the defect was not measurable or below 4 mm; (II) intermediate, when the maximum diameter of the defect measured 4-10 mm; (III) large, when the maximum diameter of the defect measured 10 mm or more.

Intracranial pressure

If present, values of ICP were retrieved. These were obtained either through lumbar puncture or measured via an external lumbar drain (ELD) and are displayed in cmH₂O. Measurements were performed perioperatively or at the out-patient clinic by a trained neurologist or neurosurgeon. ICP measurements obtained during an active episode of meningitis were discarded. In case of multiple ICP values, the most recent preoperative value was used.

Surgical success and postoperative care

From the patient records, postoperative measures were retrieved, such as

- Surgical technique of defect closure
- Surgical success or failure
- Reinterventions for failed primary surgery
- Complications of surgery
- Duration of follow-up
- Use of ELD placement or permanent CSF shunts (e.g., lumbar-peritoneal shunt (LPS) or ventricular-peritoneal shunt (VPS))
- Use and dosage of acetazolamide

Statistical analysis

Data were collected using a predefined electronic case report form (Castor EDC, Amsterdam, the Netherlands). Normally distributed data are presented as means with standard deviations (SD), whereas non-normally distributed data are presented as medians with (interquartile) ranges. Continuous data were compared using the Kruskal-Wallis test and Mann-Whitney U test (non-normally distributed), or a one-way ANOVA (normally distributed) with post-hoc t-tests. Nominal and dichotomous variables were compared between groups using Pearson's chi square test and Fisher's exact test. Threshold for statistical significance was set at $p < 0.05$; in case of multiple testing a Bonferroni correction was applied. For subgroup comparisons, group III (CSF leak secondary to structural intracranial pathology) was excluded because of its low sample size ($n=4$).

All statistical analyses were performed using IBM SPSS Statistics version 28.0 (IBM, Armonk, NY, USA).

Results

In total, 72 patients underwent surgical treatment following biochemically confirmed CSF rhinorrhoea. 49 patients were treated in Amsterdam UMC, 23 patients were treated in EMC. Both populations were comparable concerning age, BMI, gender or aetiology (not shown).

Prevalence of aetiologies, patient characteristics and surgical success

Traumatic leaks were seen in 9 cases (12.5%), iatrogenic leaks in 15 (20.8%), non-traumatic and secondary to structural intracranial pathology in 4 (5.6%), and non-traumatic spontaneous cases in 44 (61.1%). Baseline characteristics of these groups are

Table 2. Postoperative outcomes.

	Aetiology of CSF leak				Total population
	Traumatic	Iatrogenic	SIP	Spontaneous	
Study subjects	9	15	4	44	72
Recurrence of CSF rhinorrhoea (%)*	3 (33)	2 (13)	0	10 (23)	15 (21)
Recurrence < 2 weeks	0	1	0	3	4
Recurrence 3-6 weeks	0	1	0	3	4
Recurrence > 6 weeks	3	0	0	4	7
Revision surgery (%)**	3 (100)	2 (100)	0	8 (80)	13 (87)
CSF rhinorrhoea after revision surgery (%)*	1 (11)	0	n/a	4 (9)	5 (7)
Headache (%)	1 (11)	4 (27)	2 (50)	14 (33)	21 (29)
Anosmia (%)	0	1 (7)	0	7 (16)	8 (11)

* Percentage of subgroup total. ** Percentage of subgroup recurrence. CSF = cerebrospinal fluid; SIP = structural intracranial pathology.

Table 3. Perioperative characteristics.

	Aetiology of CSF leak				Total population
	Traumatic	Iatrogenic	SIP	Spontaneous	
Study subjects	9	15	4	44	72
Meningo(-encephalo)cele at diagnosis (%)*	5 (56)	7 (47)	2 (50)	19 (43)	33 (46)
Radiographic signs of IH (%)*	0	0	4 (100)	12 (27)	16 (22)
Perioperative acetazolamide (%)*	0	1 (7)	3 (75)	12 (27)	16 (22)
Postoperative shunting (%)*	0	2 (13)	1 (25)	16 (37)	19 (27)
ICP pre-operative (n)	n/a	3	2	12	17
Median (range)	n/a	21 (12 – 22)	21 / 28	22 (18 – 48)	21 (12 – 48)
ICP post-operative (n)	1	1	n/a	9	11
Median (range)	21 (n/a)	23 (n/a)	n/a	30 (20 – 36)	28 (20 – 36)
Postoperative ICP >25 cmH ₂ O (n)	n/a	0	n/a	7	7

* Percentage of subgroup total. ELD = external lumbar drain, ICP = intracranial pressure, IH = intracranial hypertension; SIP = structural intracranial pathology.

shown in Table 1, showing higher prevalence of female gender in the non-traumatic spontaneous group (68%), as well as higher prevalence of obesity compared to the traumatic and iatrogenic groups (50%, 0%, and 26.7%, respectively; $p = 0.018$). The traumatic group was younger than the iatrogenic and the non-traumatic spontaneous groups ($p < 0.05$ for each). The overall surgical success was 79% after primary surgery, and 93% after revision surgery over a mean follow-up time of 438 days (range 7–2495). The success rate was comparable between the different aetiologies (Table 2).

The subgroup of cases with IIH (signs and symptoms, and/or elevated ICP without structural abnormalities upon imaging) consisted of 15 patients, all with spontaneous CSF rhinorrhoea. Their mean age (48.0 ± 9.8 years) was comparable to the full

group of non-traumatic spontaneous leaks. Female proportion (86.7%; $p = 0.002$) and BMI (33.0 ± 6.2 kg/m²; $p = 0.009$) were significantly higher in the subgroup of IIH.

The initial surgical success rate in this group was 67%, with four out of five recurrences occurring within 6 weeks of surgery. After reintervention (3 cases), medical therapy (acetazolamide), and in 1 case permanent shunting, success had risen to 93%; 1 case is still awaiting the placement of a VPS.

Presenting symptoms

Clear rhinorrhoea was present in all patients, with 10 cases (15.4%) showing bilateral rhinorrhoea. Twenty-nine patients (40.3%) suffered from chronic headaches preoperatively, of whom nineteen patients had a spontaneous CSF leak (45.5% of spontaneous subgroup). Twenty-six patients (36.1%) were

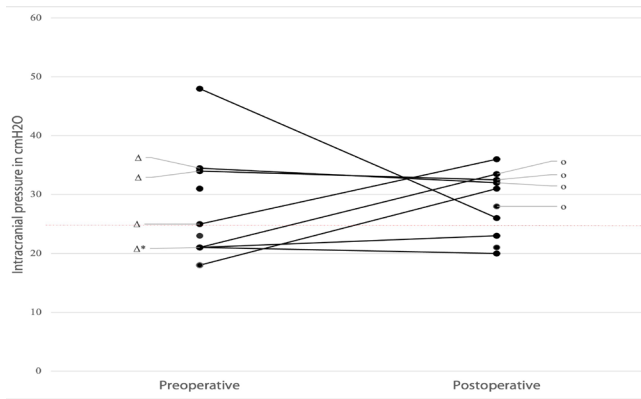


Figure 1. Intracranial pressure (ICP) in spontaneous leaks. Eight lines connecting preoperative and postoperative values indicate both preoperative and postoperative ICP measurements were obtained.

Δ = radiographic signs of intracranial hypertension; o = acetazolamide use during measurement. Δ* is the value raising to 23 cmH₂O postoperatively.

treated for bacterial meningitis before surgical repair. In eight patients the reported headaches were due to an episode of meningitis. The presence of preoperative meningitis was significantly different between the groups of aetiology, with the traumatic group having the highest numbers of multiple episodes (Table 1).

Radiological findings

A meningo(-encephalo)cele was present in 33 (45.8%) patients, and the distribution was not different between aetiology groups (Table 3). They were predominantly found in the intermediate sized defect group (74%, $p < 0.001$). The presence of meningo(-encephalo)celes was significantly associated with episodes of bacterial meningitis ($p = 0.046$). In addition, meningo(-encephalo)celes were associated with failure of primary surgery: eleven out of fifteen primary failures had a meningo(-encephalo)cele preoperatively ($p = 0.002$).

Intracranial pressure

Preoperative ICP measurements were available in a subset of patients ($n = 17$), all with an active CSF leak during measurement, with a median of 21.0 cmH₂O (range 12 - 48) (Table 3). Six patients showed ICP of 25 cmH₂O or above preoperatively, all from non-traumatic aetiologies.

Figure 1 shows ICP values of patients with a non-traumatic spontaneous leak. Seven (70%) postoperative ICP values exceeded 25 cmH₂O, proving intracranial hypertension. Five of these patients had a higher ICP after primary surgery in comparison to preoperative measurements. In five patients postoperative ICP was measured when acetazolamide therapy had already commenced. Two patients using acetazolamide still showed elevated ICP compared to preoperative measures.

Skull base defect characteristics

The location of the skull base defects (Table 4) differed significantly between all aetiologies ($p < 0.001$). All leaks originating in the lateral recess of the sphenoid sinus, and 88% of leaks originating in the cribriform plate, were of spontaneous aetiology. 87% of iatrogenic leaks were found in the ethmoid roof.

Postoperative care and complications

Sixteen (22.2%) patients were treated perioperatively with acetazolamide, of which three SIP cases, one iatrogenic and twelve of the spontaneous cases (Table 3). Dosage ranged from once daily 125mg, to twice daily 500mg. In three patients, acetazolamide had already been administered prior to primary surgical intervention.

A total of nineteen (26.4%) patients received additional shunting. Seventeen (23.6%) patients received an ELD. Of these, one patient later received a permanent LPS. Two patients received a VPS; one SIP and one spontaneous case.

Common complications and outcomes included headache and anosmia. Three patients developed meningitis postoperatively after closure: one traumatic, one SIP and one spontaneous CSF leak. Three patients suffered shunt related complications: one VPS was dislocated into subcutaneous tissue, one patient suffered radiculopathy and one patient suffered back pains with progressive loss of strength in the ipsilateral leg. Two patients needed an additional intervention due to postoperative bleeding, two patients had a defect of the lamina papyracea and two patients suffered vidian nerve dysfunction. Donor site infection of a fascia lata graft was reported in one patient, and one patient suffered a brain abscess. Occurrence of surgical complications was equal among different aetiological groups ($p > 0.05$).

Discussion

We set out to retrospectively analyse all CSF rhinorrhoea patients and to investigate the underlying aetiology in a cohort from two tertiary referral centres. Strikingly, the proportion of spontaneous leaks was relatively high (60.6%) compared to the literature (41.1%)⁽⁸⁾. Given our relatively non-obese population, the opposite was to be expected. Possibly, the increased knowledge of and technical advances within the field of endoscopic sinus surgery over the past decades have reduced the proportion of iatrogenic leaks (21.1% in our study versus 30.1% in literature)⁽⁸⁾. The same might be true for traumatic leaks with increasing traffic safety (12.7% in our study versus 23.2% in literature)⁽⁸⁾. This finding might also be (partly) a result of selection bias, as we have excluded all patients below 18 years of age, which excludes most congenital causes (3% in literature) and might skew the traumatic group. Nonetheless, the proportion of spontaneous CSF leaks in our cohort is high.

Table 4, Perioperative and skull base defect characteristics.

		Aetiology of CSF leak				Total population	p-value***
		Traumatic	Iatrogenic	SIP**	Spontaneous		
Study subjects		9	15	4	44	72	
Diagnostic beta-trace or beta-2-transferrin*	Unknown	3 (33%)	3 (20%)	1 (25%)	6 (14%)	13 (18%)	p = 0.075^
	Negative	1 (11%)	1 (7%)	0	0	2 (3%)	
	Positive	5 (56%)	11 (73%)	3 (75%)	38 (86%)	57 (79%)	
Anatomical site of defect (%)*	Sphenoid roof	1 (11%)	0	0	3 (7%)	4 (6%)	p < 0.001^
	Sphenoid lateral recess	0	0	0	8 (18%)	8 (11%)	
	Ethmoid roof	5 (56%)	13 (87%)	2 (50%)	9 (20%)	29 (40%)	
	Cribiform plate	0	2 (13%)	1 (25%)	24 (55%)	27 (38%)	
	Frontal sinus posterior wall	1 (11%)	0	1 (25%)	0	2 (3%)	
	Multiple	2 (22%)	0	0	0	2 (3%)	
Size of skull base defect*	Small < 4 mm	2 (22%)	5 (33%)	2 (50%)	23 (52%)	32 (44%)	p = 0.115^
	Intermediate 4-10 mm	7 (78%)	7 (47%)	2 (50%)	19 (43%)	35 (49%)	
	Large > 10mm	0	3 (20%)	0	2 (5%)	5 (7%)	
Use of fluorescein intraoperatively		7 (78%)	9 (60%)	4 (100%)	36 (82%)	56 (78%)	p = 0.277^
Closure technique***	Free flap	0	5 (33%)	2 (50%)	29 (66%)	36 (50%)	p < 0.001^
	Free flap with extra material (fascia, fat, bone, etc.)	3 (33%)	9 (60%)	2 (50%)	12 (27%)	26 (36%)	
	Pedicled flap	3 (33%)	0	0	1 (2%)	4 (6%)	
	Pedicled flap with extra	1 (11%)	0	0	1 (2%)	2 (3%)	
Postoperative drain/shunt (n)*		0 (0%)	2 (13%)	1 (25%)	16 (36%)	19 (26%)	p = 0.037^
Primary surgical success %*		67%	87%	100%	77%	79%	p = 0.564^

* Percentage of subgroup total. ** 2 recurrences were not surgically treated. *** 4 patient records did not report surgical technique. **** values when excluding SIP group from analysis. ^ Fisher's exact test; § Kruskal-Wallis. IQR = interquartile range; SIP = structural intracranial pathology

Although the primary surgical success rates were similar across the different aetiologies, the group of spontaneous CSF leaks represents a distinct clinical entity where more than just surgical measures seem necessary to achieve optimal results, especially in those with suggested IIH⁽¹⁸⁾. Even in our relatively non-obese population, there is a clear association between female gender, higher BMI and spontaneous CSF leaks. This is especially true when signs, symptoms and/or ICP measurements point towards IIH. In these patients, attention should be given to ICP and weight management. Multiple studies have already indicated that weight loss after bariatric surgery could resolve complaints of elevated ICP like headache and papilledema^(23,24) and even lower ICP after diet alteration⁽²⁵⁾. Yet little proof on the effect of

weight loss on spontaneous CSF leaks exists.

Our surgical success rates are in line with literature. The presence of a meningo(-encephalo)cele preoperatively was significantly related to surgical failure. This might be due to a larger skull base defect with associated higher chances of failure, and/or due to underlying elevated ICP which could hamper proper operative closure. Given the fact that meningo(-encephalo)celes were also associated with meningitis preoperatively, its presence should be actively looked for in patients with CSF rhinorrhoea. In our population, the number of meningo(-encephalo)celes is relatively high and their distribution quite even between the aetiologies. We do not have a clear explanation for this finding.

Hypothesizing that complaints of chronic headache are especially seen as a result of elevated ICP, a higher prevalence of preoperative headache in spontaneous and SIP cases was to be expected. However, no differences between aetiologies were calculated. A possible explanation is the hypothetical valve function of the skull base defect, releasing elevated ICP and resolving headache complaints. On the contrary, liquor hypotension syndrome could lead to headache complaints in all aetiologies (26). Additionally, it's reported that intracranial hypertension can exist asymptotically^(13, 14).

Although almost one third of spontaneous leaks (and all the leaks caused by SIP) showed radiographic signs of intracranial hypertension, the majority of the spontaneous leaks did not show any aberrant features on CT or MRI.

Physiological compensation of intracranial hypertension is a process potentially preventing or reversing the characteristics of IIH⁽²⁷⁾. This could subsequently lower the total amount of patients showing radiographically confirmed IIH. Pivotal hypothetical features of this compensation mechanism are the speed with which ICP values rise, peak values, period of pathological values and frequency of occurrence.

Strengths and limitations

Patients included were all treated in two tertiary referral centres by a small number of specialized surgeons. This restricts inter-individual differences in performing the skull base repair procedure and brings performance bias to a minimum. Different ethnicities (Dutch Caucasian, Indonesian, Asian, Surinamese, Eastern-European, Northern-African) were represented. Both benefit the generalisability of this recent study.

The retrospective design is an obvious limitation, although missing data was still uncommon. Due to the small population

size, CSF leaks elicited by SIP are mainly disregarded in statistical analyses. Furthermore, preoperative and postoperative ICP measurements were available in only a small portion of our population and were prone to selection bias, i.e. those measurements were more likely to be performed in cases where high ICP was suspected clinically. Limited data about ICP may introduce both over-diagnosis and under-diagnosis of IIH. On the other hand, pre- and postoperative ICP measurements in all CSF leak patients might constitute a large burden to the individual patient and is not deemed appropriate as standard procedure.

Conclusion

Even in a relatively non-obese population, most CSF leaks have a spontaneous origin. They are predominantly located in the cribriform plate, small-sized and associated with female gender, high body weight, and a suspicion of IIH. The latter presents as the most challenging group.

Otherwise, no differences exist across aetiologies regarding patient characteristics, presenting symptoms, surgical success, and complications.

Authorship contribution

The study was conceived by SR and GA. Data were collected and analysed by one author (WdJ) by review of medical records and verified by a second, third and fourth author (SR, JH, and PN). WdJ wrote the initial manuscript, and all other authors helped in finalizing it. SR acted as corresponding author.

Conflict of interest

There are no conflicts of interest.

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References

- Markey K, Mollan S, Jensen R, Sinclair A. Understanding idiopathic intracranial hypertension: mechanisms, management, and future directions. *Lancet Neurol* 2016; 15(1); 78-91.
- Daudia A, Biswas D, Jones N. Risk of meningitis with cerebrospinal fluid rhinorrhea. *Ann Otol Rhinol Laryngol* 2007; 116(12); 902-905.
- Harvey R, Smith J, Wise S, Patel S, Frankel B, Schlosser R. Intracranial complications before and after endoscopic skull base reconstruction. *Am J Rhinol* 2008; 22(5); 516-521.
- Bernal-Sprekelsen, M, Bleda-Vázquez C, Carrau R. Ascending meningitis secondary to traumatic cerebrospinal fluid leaks. *Am J Rhinol* 2000; 14(4); 257-260.
- Har-El, G. What is spontaneous cerebrospinal fluid rhinorrhea? Classification of cerebrospinal fluid leaks. *Ann Otol Rhinol Laryngol* 1999; 108(4); 323-326.
- Ziu M, Savage J, Jimenez D. Diagnosis and treatment of cerebrospinal fluid rhinorrhea following accidental traumatic anterior skull base fractures. *Neurosurg Focus* 2012; 32(6); E3.
- Ommaya A, Di Chiro G, Baldwin M, Pennybacker J. Non-traumatic cerebrospinal fluid rhinorrhea. *J Neurol Neurosurg Psychiatry Res* 1968; 31(3); 214-25.
- Psaltis A, Schlosser R, Banks C, Yawn J, Soler Z. A systematic review of the endoscopic repair of cerebrospinal fluid leaks. *Otolaryngol Head Neck Surg* 2012; 147(2); 196-203.
- Song X, Wang D, Sun X, et al. Endoscopic repairs of sinonasal cerebrospinal leaks: outcome and prognostic factors. *J Craniofac Surg* 2018; 29(1); 182-187.
- Banks C, Palmer J, Chiu A, O'Malley B, Woodworth B, Kennedy D. Endoscopic closure of CSF rhinorrhea: 193 cases over 21 years. *Otolaryngol Head Neck Surg* 2009; 140(6); 826-833.
- Degnan A, Levy L. Pseudotumor cerebri: brief review of clinical syndrome and imaging findings. *Am J Neuroradiol* 2011; 32(11); 1986-1993.
- Yang Z, Wang B, Wang C, Liu P. Primary spontaneous cerebrospinal fluid rhinorrhea: a symptom of idiopathic intracranial hypertension? *J Neurosurg* 2011; 115(1); 165-170.
- Corbett J. Problems in the diagnosis and treatment of pseudotumor cerebri. *Can J Neurol Sci* 1983; 10: 221-229.
- Gondi K, Chen K, Gratton S. Asymptomatic versus symptomatic idiopathic intracranial hypertension in children. *J Child Neurol* 2019; 34(12); 751-756.
- Aaron G, Doyle J, Vaphiades M, Riley K, Woodworth B. Increased intracranial pres-

- sure in spontaneous CSF leak patients is not associated with papilledema. *Otolaryngol Head Neck Surg* 2014; 151(6): 1061-1066.
16. Silver R, Moonis G, Schlosser R, Bolger W, Loevner L. Radiographic signs of elevated intracranial pressure in idiopathic cerebrospinal fluid leaks: a possible presentation of idiopathic intracranial hypertension. *Am J Rhinol* 2007; 21(3): 257-261.
 17. Schlosser R, Bolger W. Spontaneous nasal cerebrospinal fluid leaks and empty sella syndrome: a clinical association. *Am J Rhinol* 2003; 17(2): 91-6.
 18. Teachey W, Grayson J, Cho D, Riley K, Woodworth B. Intervention for elevated intracranial pressure improves success rate after repair of spontaneous cerebrospinal fluid leaks. *Laryngoscope* 2017; 127(9): 2011-2016.
 19. Friedman D, Liu G, Digre K. The pseudotumor cerebri syndrome. *Neurol Clin* 2014; 32(2): 363-396.
 20. Hamdallah I, Shamseddeen H, Getty J, Smith W, Ali M. Greater than expected prevalence of pseudotumor cerebri: a prospective study. *Surg Obes Relat Dis* 2013; 9(1): 77-82.
 21. <https://statline.cbs.nl>, accessed March 28, 2023
 22. <https://stats.oecd.org>, accessed March 28, 2023
 23. Sugerman H, Felton W, Salvant J, Sismanis A, Kellum J. Effects of surgically induced weight loss on idiopathic intracranial hypertension in morbid obesity. *Neurology* 1995; 45(9): 1655-1659.
 24. Sugerman H, Felton W, Salvant J, Sismanis A, Kellum J, DeMaria E, Sugerman E. Gastric surgery for pseudotumor cerebri associated with severe obesity. *Ann Surg* 1999; 229(5): 634.
 25. Sinclair A, Burdon M, Nightingale P, et al. Low energy diet and intracranial pressure in women with idiopathic intracranial hypertension: prospective cohort study. *BMJ* 2010; 341; c2701.
 26. Mokri B. Spontaneous cerebrospinal fluid leaks: from intracranial hypotension to cerebrospinal fluid hypovolemia—evolution of a concept. *Mayo Clin Proc* 1999; 74(11): 1113-1123.
 27. Iencean S, Ciurea A. Intracranial hypertension: classification and patterns of evolution. *J Med Life* 2008; 1(2): 101-107.

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