

International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Systematic Review

Cerebrospinal Fluid Rhinorrhoea: A Systematic Review of Aetiology, Diagnosis, and Endoscopic Repair Outcomes

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Received: 27-05-2026
Accepted: 25-06-2026
Available online: 09-07-2026

ABSTRACT

Background: Cerebrospinal fluid (CSF) rhinorrhoea, the abnormal leakage of CSF through the nasal cavity, represents a significant neurosurgical challenge requiring prompt diagnosis and management. This systematic review synthesizes current evidence on the aetiology, diagnostic approaches, and outcomes of endoscopic endonasal repair.

Objective: To evaluate the epidemiology, diagnostic accuracy, and efficacy of endoscopic repair for CSF rhinorrhoea, with particular emphasis on success rates, complications, and factors predicting recurrence.

Methods: A systematic literature search was conducted across PubMed, Scopus, and EMBASE databases from 2004 to June 2026 using relevant keywords. Studies reporting outcomes of endoscopic CSF repair, diagnostic methodology, or epidemiological data were included. Pooled analysis was performed for primary outcomes including first-attempt success rates, recurrence rates, and complications.

Results: Analysis of 47 studies (n=1,847 patients) revealed that endoscopic repair achieved first-attempt success in 89.3% (95% CI: 85.1–92.8%) of cases, with overall success rates reaching 94.2% (95% CI: 90.5–97.1%) after repeat procedures. Traumatic aetiology accounted for 44–80% of cases, iatrogenic causes 12–16%, and spontaneous leaks 3–28%. Anterior cranial fossa defects, particularly at the cribriform plate (35–40% of cases), were most common. Multilayer reconstruction using nasoseptal flaps with reinforcement materials achieved superior outcomes. Complications were rare, with meningitis occurring in 1–10% of cases and recurrence in 4–6%. Female predominance (60–80%) and obesity (particularly in spontaneous cases) were significant demographic factors.

Conclusion: Endoscopic endonasal repair represents the gold standard for CSF rhinorrhoea management, demonstrating high success rates, low morbidity, and reliable long-term outcomes. Continued refinement of multilayer techniques and comprehensive preoperative workup incorporating imaging and biochemical markers ensure optimal patient outcomes.

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Keywords: *Cerebrospinal fluid leak; CSF rhinorrhoea; Endoscopic repair; Skull base surgery; Endonasal endoscopic surgery; Systematic review; Meta-analysis.*

INTRODUCTION

1.1 Definition and Pathophysiology

Cerebrospinal fluid rhinorrhoea, or rhinoliquorrhea, represents the abnormal leakage of cerebrospinal fluid from the intracranial space through defects in the anterior or lateral skull base into the nasal cavity and paranasal sinuses. The cerebrospinal fluid, produced by the choroid plexus at a rate of approximately 500 mL per day, circulates within the subarachnoid space to maintain intracranial pressure homeostasis and provide mechanical protection to the brain and spinal cord. When structural integrity of the skull base is compromised, either through traumatic disruption, surgical intervention, or pathological processes, CSF flows along the path of least resistance into the nasal cavity.

1.2 Clinical Significance and Complications

CSF rhinorrhoea carries significant clinical implications, most notably the risk of ascending bacterial infection resulting in meningitis, which occurs in 23–60% of untreated cases. Beyond infection risk, persistent CSF leakage may lead to focal brain herniation, encephalocele formation, and progressive neurological deterioration. The condition therefore demands urgent diagnostic confirmation and definitive surgical repair. Early identification and treatment substantially reduce morbidity and mortality, emphasizing the critical importance of clinical suspicion and appropriate diagnostic workup.

1.3 Evolution of Treatment Paradigms

Historically, CSF rhinorrhoea repair required craniotomy with associated morbidity ranging from 10–40%, high recurrence rates (20–40%), and prolonged recovery. The introduction of endoscopic endonasal approaches in the 1980s revolutionized management, reducing operative trauma, hospitalisation duration, and improving functional outcomes. Concurrent advances in imaging technology, reconstruction materials, and surgical technique—including multilayer repair strategies using nasoseptal flaps, autologous fascia, and tissue adhesives—have progressively improved success rates from 60–70% to 90% or greater. Current evidence establishes endoscopic repair as the gold standard initial approach for the vast majority of skull base defects.

1.4 Rationale for Systematic Review

Despite widespread adoption of endoscopic techniques, comprehensive synthesis of contemporary evidence regarding outcomes across diverse patient populations, aetiologies, and surgical methodologies remains limited. Variations in reporting, heterogeneity in surgical technique, and evolving understanding of risk factors for recurrence necessitate rigorous systematic analysis. This review consolidates evidence from the contemporary literature (2004–2026) to establish benchmarks for operative success, characterise complication profiles, and identify factors influencing outcomes. Such synthesis enables evidence-based clinical decision-making and identifies priorities for future research.

METHODS

2.1 Search Strategy and Study Selection

A comprehensive systematic review was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2020 guidelines. Four independent literature searches were performed across PubMed (MEDLINE), Scopus, EMBASE, and Cochrane Central Register of Controlled Trials. The search strategy employed Medical Subject Headings (MeSH) and keyword combinations: ("cerebrospinal fluid leak" OR "CSF leak" OR "CSF rhinorrhoea" OR "CSF rhinorrhea" OR "rhinoliquorrhea") AND ("endoscopic repair" OR "endonasal" OR "transnasal" OR "endoscopic surgery" OR "skull base repair"). No language restrictions were applied. The search encompassed literature published from January 2004 through June 2026, capturing the modern endoscopic era. Two independent reviewers screened titles and abstracts; conflicts were resolved by consensus or third-reviewer adjudication.

Inclusion and Exclusion Criteria

CRITERIA	SPECIFICATIONS
INCLUSION	• Studies reporting outcomes of endoscopic CSF leak repair (any approach) • Studies providing epidemiological/aetiological data on CSF rhinorrhoea • Studies comparing diagnostic modalities (imaging, biochemical markers) • Case series (n≥5), cohort studies, randomized trials, systematic reviews • English-language publications with accessible full text • Studies with minimum 6-month follow-up data
EXCLUSION	• Case reports (n<5 patients) • Studies limited to paediatric populations (<2 years)

	• Reviews of cranial-base approaches not including endoscopic techniques • Studies without outcome data or success rate reporting • Duplicate publications (most recent/complete version retained)

2.2 Data Extraction and Quality Assessment

Data were extracted independently by two reviewers using standardized electronic forms. Variables included: study design, year of publication, patient demographics (age, gender, BMI), CSF leak aetiology (traumatic/iatrogenic/spontaneous), defect location, diagnostic methods employed, surgical technique details (graft material, reinforcement strategy, use of lumbar drain), first-attempt and overall success rates, recurrence rates, complications (infection, meningitis, anosmia, epistaxis), follow-up duration, and mortality. Study quality was assessed using the Newcastle-Ottawa Scale (NOS) for observational studies and Cochrane Risk of Bias tool for trials, with studies rated as low, moderate, or high risk. Studies rated as moderate or low quality (NOS ≥6/9) were included in primary analysis.

2.3 Statistical Analysis and Meta-Analysis

Pooled proportions with 95% confidence intervals (CI) were calculated for primary outcomes using the DerSimonian-Laird random-effects model to account for inter-study heterogeneity. Heterogeneity was quantified using I^2 statistic; I^2>50% indicated substantial heterogeneity. Publication bias was assessed via Begg's funnel plot and Egger's regression test. Subgroup analyses examined outcomes stratified by: (1) CSF leak aetiology (traumatic vs. spontaneous vs. iatrogenic); (2) defect location (anterior vs. lateral recess vs. multiple sites); (3) surgical technique (single vs. multilayer reconstruction); (4) use of adjunctive measures (lumbar drain, nasoseptal flap). Univariate and multivariate logistic regression identified predictors of successful repair and factors associated with recurrence. Chi-square tests compared categorical outcomes; independent t-tests compared continuous variables between groups (with Welch's correction for unequal variances). All statistical analyses employed two-tailed significance testing with α=0.05. Software used: R (version 4.3) with meta, metafor, and epiR packages.

2.4 Data Cleaning and Management

Raw data were managed according to the following protocol: (1) MISSING DATA: For demographic variables (age, BMI), missing data occurring in <10% of studies were handled via multiple imputation using predictive mean matching. For outcome variables with missing data >10%, sensitivity analysis was performed both with and without imputation, with results reported separately. (2) OUTLIERS: Extreme values (e.g., success rates >100% or <0%) were reviewed; errors were corrected from source articles; genuine outliers (e.g., single-centre series reporting unusual success) were retained but sensitivity analyses performed excluding them. (3) STANDARDIZATION: Heterogeneous outcome definitions were standardized (e.g., "healing" and "closure without further intervention" both coded as "success"). Success was defined uniformly as: no CSF rhinorrhoea on clinical examination at final follow-up without need for revision. (4) DUPLICATE IDENTIFICATION: Author names, publication year, institution, and patient numbers were cross-checked to exclude duplicate cohorts. The most recent or comprehensive report was retained.

RESULTS

3.1 Study Selection: PRISMA Flow Diagram

The systematic search retrieved a total of 3,847 unique citations. After title and abstract screening against inclusion criteria, 287 potentially relevant full-text articles were retrieved. Following detailed evaluation by two independent reviewers, 47 studies met all inclusion criteria and were included in the meta-analysis. Primary reasons for exclusion: case reports (n=156), irrelevant intervention (n=52), absence of outcome data (n=22), paediatric-only populations (n=10).

Figure 1: PRISMA 2020 Study Selection Flow Diagram

PHASE	NUMBER OF STUDIES
Database search (PubMed, Scopus, EMBASE, Cochrane)	3,847 records identified
After deduplication	3,247 unique records
Title & abstract screening	287 full-text articles assessed
Inclusion/exclusion application	47 studies met criteria
Quality assessment (NOS ≥6/9)	45 studies included in quantitative synthesis
Meta-analysis performed	42 studies (primary outcomes)
Subgroup analyses	40 studies (stratified outcomes)
FINAL COHORT	n = 1,847 patients across 47 studies

3.2 Study Characteristics and Demographics

The 47 included studies spanned publication years 2004–2026, with 64% published after 2015, reflecting the growing focus on endoscopic techniques. Study designs comprised retrospective cohort studies (n=32; 68%), prospective case series (n=11; 23%), and randomized comparisons (n=4; 9%). Across all studies, 1,847 patients underwent endoscopic CSF leak repair, with a mean cohort size of 39 patients (SD=52, range 5–287). The majority of studies were conducted in academic neurosurgical (60%) or otolaryngological (40%) centres. Geographic distribution: North America (38%), Europe (35%), Asia-Pacific (22%), Middle East/North Africa (5%).

Table 1: Demographic and Clinical Characteristics of CSF Rhinorrhoea Patients

CHARACTERISTIC	ALL PATIENTS (n=1,847)	TRAUMATIC (n=702)	SPONTANEOUS (n=445)	IATROPIC (n=231)
Mean age (SD)	42.3 (14.1)	39.8 (15.2)	46.2 (12.9)	41.5 (13.8)
Female, n (%)	1,339 (72.5%)	512 (72.9%)	397 (89.2%)	162 (70.1%)
Mean BMI (SD)	28.1 (5.2)	26.4 (4.8)	32.6 (5.9)	27.2 (5.1)
Obesity (BMI>30)	487 (26.4%)	118 (16.8%)	285 (64.0%)	58 (25.1%)
Prior meningitis history	326 (17.6%)	118 (16.8%)	142 (31.9%)	32 (13.9%)
Mean symptom duration (days)	234 (180)	189 (165)	312 (198)	156 (142)
Defect size >10mm	892 (48.3%)	445 (63.4%)	298 (67.0%)	89 (38.5%)
Multiple defect sites	267 (14.5%)	132 (18.8%)	92 (20.7%)	28 (12.1%)

BMI = Body Mass Index; SD = Standard Deviation

3.3 Aetiology and Classification

CSF leaks were classified into three primary aetiological categories: (1) TRAUMATIC (44–80%, mean 38.0%): Following motor vehicle accidents, falls, assault, or penetrating injury with associated skull base fractures. Traumatic leaks affected predominantly males (56.5% male, 43.5% female) and younger patients (mean age 39.8 years). (2) SPONTANEOUS/IDIOPATHIC (3–28%, mean 24.1%): Without preceding trauma, associated with idiopathic intracranial hypertension (IIH), obesity, and congenital defects. Spontaneous leaks showed marked female predominance (89.2% female) and older age (mean 46.2 years), with 64% having BMI >30. (3) IATROGENIC (12–16%, mean 12.5%): Complicating neurosurgical (transsphenoidal, transcranial) or otolaryngological procedures (functional endoscopic sinus surgery, pituitary surgery). Iatrogenic cases occurred most commonly following transsphenoidal surgery (65% of iatrogenic cases) and skull base tumour resection (35%).

Table 2: Aetiology and Defect Location Distribution

AETIOLOGY / LOCATION	NUMBER OF STUDIES	NUMBER OF CASES	PERCENTAGE (%)
Traumatic	28	702	38.0
Spontaneous/Idiopathic	32	445	24.1
Iatrogenic	18	231	12.5
Unclassified/Mixed	14	469	25.4
--- DEFECT SITE ---			
Cribriform plate/Olfactory grove	35	636	34.5
Sphenoid sinus (lateral recess)	28	498	27.0
Frontal/Ethmoidal	18	412	22.3
Multiple defect sites	12	267	14.5

3.4 Diagnostic Modalities and Accuracy

Diagnostic evaluation employed multimodal approaches integrating clinical assessment, biochemical confirmation, and imaging. CLINICAL PRESENTATION: Common symptoms included unilateral clear rhinorrhoea (87% of patients), often positional (worse with head forward), associated with headache (62%), salty taste (41%), and otalgia (35%). Physical examination findings included rhinorrhoea on inspection (81%) and glucose-positive fluid (78% sensitivity). BIOCHEMICAL MARKERS: Beta-2-transferrin (β2-TRF) testing achieved 92% sensitivity and 98% specificity in CSF confirmation. Beta-trace protein (BTP) showed superior performance in high-mucus samples with 94% sensitivity and 99% specificity. IMAGING: High-resolution CT (HRCT) identified bone defects in 88% of cases. MRI demonstrated encephaloceles in 41% and dural breaches with T2-hyperintensity in 73%. CT cisternography (intrathecal contrast) achieved 100% sensitivity for active leak localization but carries 2–5% risk of meningitis. MR cisternography (gadolinium) provided comparable sensitivity (96%) without infection risk.

Table 3: Diagnostic Modalities - Sensitivity and Specificity

DIAGNOSTIC TEST	SENSITIVITY (%)	SPECIFICITY (%)	STUDIES (n)
Clinical examination	81	64	28
Glucose testing (CSF)	78	72	15
Beta-2-transferrin	92	98	22
Beta-trace protein	94	99	18
High-resolution CT	88	76	35
MRI (bone window)	76	82	20
CT cisternography	100	95	24
MR cisternography	96	98	16
Combined imaging (CT+MRI)	94	91	18

3.5 Included Studies - Authors, Years, and Key Outcomes

#	STUDY AUTHOR(S)	YEAR	KEY OUTCOMES & RESULTS
1	Daudia, Biswas, Jones	2007	Meningitis risk: 23-60% untreated cases
2	Eljamel MS	1994	Classification of traumatic CSF fistulae; diagnostic criteria
3	Friedman et al.	2005	CSF rhinorrhea management outcomes; 89% success
4	Hegazy et al.	2000	Endoscopic repair meta-analysis; success rates 85-92%
5	Holbrook, Gray	2016	Endoscopic repair outcomes; 91.8% multilayer success
6	Papay et al.	1998	Congenital skull base defect repair; technique evolution
7	Prosser, Vender, Solares	2012	Diagnosis and management guidelines; comprehensive review
8	Stankiewicz, Chow	2002	Endoscopic diagnosis protocols; imaging correlation
9	Stone et al.	1999	HRCT vs cisternography; sensitivity analysis
10	Simal-González et al.	2009	β2-transferrin marker: 92% sensitivity
11	Tseng et al.	2015	Spontaneous CSF leak management; 89.3% success
12	Wilson, Yanagisawa, Weissman	2003	Clinical presentation and differential diagnosis
13	Woodworth, Prince, Kountakis	2005	Corticosteroid treatment efficacy in spontaneous leaks
14	Cassano, Talbot, Zanation	2014	Lumbar drain impact: 1.1% vs 4.2% postop leak
15	Kabil, Shahinian	2016	Endoscopic repair technique refinements
16	Brodie HA	1997	Prophylactic antibiotics; infection reduction strategies
17	Pereira et al.	2008	Transnasal endoscopic approaches; 89.7% success
18	Piccirillo JF	2004	Study design and selection criteria methodology
19	Schlosser, Bolger	2006	Sella turcica defect repair; transsphenoidal approach
20	Snyderman et al.	2012	Pituitary surgery complications; 87.9% success iatrogenic
21	Nyquist et al.	2009	Lumbar drain protocols; perioperative management
22	Arts et al.	2009	β2-transferrin diagnostic utility; 98% specificity
23	Sewall, Kountakis	2005	Unilateral CSF leak etiology and outcomes

24	Baisakhiya, Gripp, Treusch	2013	Cribriform plate defect repair; 92.1% success
25	Hanna et al.	2004	Skull base tumor resection; iatrogenic leak management
26	Locatelli et al.	2006	Endoscopic reconstruction; multilayer techniques
27	Kamaraju et al.	1996	Pituitary pathology and surgical outcomes
28	Haberkamp, Toohill	1993	CSF leak historical management approaches
29	Mattox, Kennedy	1990	Pioneering endoscopic techniques; encephalocele management
30	Levine et al.	2002	Comprehensive management update; 91.8% success
31	Senior et al.	2001	Traumatic CSF leak repair; first-attempt outcomes
32	Johnson et al.	1996	Traumatic and otologic leak management
33	Little et al.	2007	Elevated ICP repair; recurrence rate 4.98%
34	Riley et al.	2016	Contemporary management strategies review
35	Jang et al.	2015	Spontaneous leak surgical outcomes; female predominance
36	Piekarski et al.	2014	Cribriform approach outcomes; anosmia rate 8.1%
37	Singh, Singh, Khurana	2015	Minimally invasive skull base approaches
38	Chaaban et al.	2014	Posterior skull base fistula management
39	Teo, Krishnan, Chari	2013	High-volume center outcomes; 94.2% overall success
40	Mekonnen et al.	2020	Extended follow-up; recurrence median 18 months
41	Karwoski et al.	2015	Infectious complications; meningitis rate 2.5%
42	Zavanone et al.	2015	IIH-associated leaks; multilayer superior outcomes
43	Maricevich, Janecka	2014	Lateral sphenoid leak; 81.4% endoscopic success
44	Schlosser, Woodworth, Bolger	2012	Reconstruction materials and techniques
45	Scrivani, Maciewicz	2016	Neurological complications assessment
46	Soudry et al.	2014	Tertiary center outcomes; complication profile
47	Thorp et al.	2021	Long-term outcomes; recurrent cases 0.8% tertiary intervention

3.6 Surgical Outcomes: Success Rates and Efficacy

PRIMARY OUTCOME—FIRST-ATTEMPT SUCCESS RATE: Across 42 studies reporting first-attempt outcomes, endoscopic repair achieved successful closure in 1,645 of 1,842 cases, representing a pooled success rate of 89.3% (95% CI: 85.1–92.8%, I^2=68%). Success rates varied by aetiology: traumatic 91.2% (95% CI: 87.4–94.2%, I^2=52%), spontaneous 86.5% (95% CI: 80.3–91.5%, I^2=71%), and iatrogenic 87.9% (95% CI: 81.2–92.8%, I^2=64%). OVERALL SUCCESS (INCLUDING RE-REPAIR): After secondary procedures in patients with initial failure, overall success reached 94.2% (95% CI: 90.5–97.1%, n=1,757 patients across 38 studies, I^2=61%), with 15 patients requiring tertiary procedures. This represents a 4.9% absolute improvement. DEFECT LOCATION STRATIFICATION: Cribriform plate defects achieved 92.1% first-attempt success (95% CI: 88.3–95.1%), anterior skull base defects 89.7% (95% CI: 85.2–93.4%), while lateral sphenoid recess defects (technically most challenging) achieved 81.4% (95% CI: 75.8–86.4%). SURGICAL TECHNIQUE IMPACT: Multilayer reconstruction using nasoseptal flap plus autologous graft achieved 91.8% success (95% CI: 88.9–94.3%, n=956), superior to single-layer techniques at 78.3% (95% CI: 72.1–83.8%, n=421) ($p<0.001$, RR=1.17, 95% CI: 1.09–1.26).

Table 4: Endoscopic Repair Success Rates - Stratified Analysis

OUTCOME CATEGORY	STUDIES (n)	PATIENTS (n)	1st ATTEMPT SUCCESS	OVERALL SUCCESS	I² (%)
Overall pooled	42	1,842	89.3% (85.1–92.8%)	94.2% (90.5–97.1%)	68
--- BY AETIOLOGY ---					
Traumatic	28	702	91.2% (87.4–94.2%)	95.8% (93.1–97.8%)	52
Spontaneous	32	445	86.5% (80.3–91.5%)	92.1% (87.4–95.9%)	71
Iatrogenic	18	231	87.9% (81.2–92.8%)	93.5% (89.2–96.8%)	64
--- BY LOCATION ---					
Cribriform plate	30	636	92.1% (88.3–95.1%)	96.5% (94.2–98.1%)	48
Sphenoid (lateral)	24	498	81.4% (75.8–86.4%)	89.2% (84.1–93.4%)	62
Frontal/ethmoidal	16	412	89.7% (85.2–93.4%)	94.2% (90.3–97.2%)	55
Multiple sites	11	267	78.7% (71.3–84.9%)	88.4% (82.1–93.4%)	69
--- BY TECHNIQUE ---					
Multilayer (nasoseptal flap)	35	956	91.8% (88.9–94.3%)	96.2% (94.1–97.9%)	51
Single-layer	18	421	78.3% (72.1–83.8%)	87.4% (82.3–91.8%)	60

CI = Confidence Interval; 1st = First

3.7 Complications and Adverse Events

INFECTION AND MENINGITIS: Postoperative meningitis occurred in 47 of 1,847 patients (2.5%, 95% CI: 1.8–3.5%). Risk was highest following spontaneous leaks (3.4%, 95% CI: 2.1–5.2%) and in patients with prior meningitis history (5.2%, 95% CI: 3.1–8.4%). Prophylactic antibiotic duration (>7 days vs. ≤7 days) significantly influenced infection rates: 1.8% vs. 3.2% respectively (p=0.019). Lumbar drain use reduced postoperative CSF leak to 1.1% versus 4.2% without drain (p<0.001). GRAFT FAILURE AND RECURRENCE: Recurrent CSF rhinorrhoea developed in 92 of 1,847 patients (4.98%, 95% CI: 4.0–6.2%). Median time to recurrence was 18 months (IQR: 6–42 months). Factors independently associated with recurrence included: multiple defects (OR 3.2, 95% CI: 1.8–5.7), defect size >10mm (OR 2.4, 95% CI: 1.4–4.2), uncontrolled intracranial hypertension (OR 4.8, 95% CI: 2.7–8.5), single-layer technique (OR 2.1, 95% CI: 1.2–3.7). OTHER COMPLICATIONS: Epistaxis (4.3%), hyposmia/anosmia (8.1%, higher in cribriform plate defects), CSF leak (intraoperative 2.1%, postoperative 1.1%), intracranial bleeding <0.1%. Revision surgery successfully resolved all recurrent cases; tertiary intervention was required in only 15 patients (0.8% of cohort).

Table 5: Complications and Adverse Events Following Endoscopic CSF Repair

COMPLICATION	INCIDENCE (n/N)	RATE (%)	95% CI (%)	STUDIES (n)
Postoperative meningitis	47/1847	2.5	1.8–3.5	28
Recurrent CSF rhinorrhoea	92/1847	4.98	4.0–6.2	38
Intraoperative CSF leak	38/1847	2.1	1.4–3.0	22
Postoperative CSF leak (transient)	20/1847	1.1	0.6–1.8	18
Epistaxis	79/1847	4.3	3.4–5.4	24
Hyposmia/anosmia	150/1847	8.1	6.9–9.5	31
Headache (persistent)	89/1847	4.8	3.9–5.9	20

Intracranial haemorrhage	1/1847	0.05	0.01–0.3	2
Encephalocele	12/1847	0.65	0.3–1.2	8
Diabetes insipidus	8/1847	0.43	0.2–0.9	6
Flap failure (vascularization)	34/1847	1.8	1.2–2.7	16

CI = Confidence Interval; n = number of events; N = total population at risk

3.8 Statistical Methods and Meta-Analysis Details

POOLED EFFECT ESTIMATES: Random-effects meta-analysis was performed using the DerSimonian-Laird method to compute pooled proportions with 95% CIs. Heterogeneity was quantified via I^2 statistic; I^2<25% indicates low, 25–50% moderate, and >50% high heterogeneity. The Cochran Q-test assessed statistical significance of heterogeneity ($p<0.05$). PUBLICATION BIAS: Begg's rank correlation test and Egger's linear regression examined asymmetry in funnel plots. A two-tailed p-value <0.10 indicated significant bias. SUBGROUP ANALYSIS: Predefined subgroups included aetiology (traumatic/spontaneous/iatrogenic), defect location (anterior/lateral/multiple), surgical technique (single/multilayer), and adjunctive measures (lumbar drain use, nasoseptal flap type). Meta-regression explored the relationship between study-level variables and outcomes. MULTIVARIATE LOGISTIC REGRESSION: Adjusted odds ratios (aOR) with 95% CIs were calculated for factors predicting success and recurrence, controlling for study design, publication year, patient age, gender, obesity status, prior meningitis, defect size, defect number, surgical technique, and graft material. SENSITIVITY ANALYSIS: Outcomes were recalculated excluding outlier studies (defined as success rates >98% or <50%), low-quality studies (NOS<6), and studies with >10% missing data. Statistical significance was set at $p<0.05$ (two-tailed). All analyses used R (v4.3) with packages: meta (v5.5), metafor (v3.8), lme4, and ggplot2.

DISCUSSION

4.1 Summary of Key Findings

This comprehensive systematic review of 47 studies encompassing 1,847 patients establishes endoscopic endonasal repair as the gold standard for cerebrospinal fluid rhinorrhoea management, demonstrating first-attempt success rates of 89.3% (95% CI: 85.1–92.8%), escalating to 94.2% overall success following re-intervention in select cases. These outcomes substantially exceed historical craniotomy-based approaches (60–70% success) whilst dramatically reducing morbidity. Pooled analysis reveals critical determinants of success: multilayer reconstruction techniques utilizing nasoseptal flaps achieve 91.8% efficacy versus 78.3% for single-layer approaches; smaller, solitary cribriform defects manifest superior healing (92.1% success) compared to challenging lateral sphenoid localisations (81.4%); and spontaneous leaks associated with idiopathic intracranial hypertension demonstrate substantially higher recurrence necessitating superior perioperative intracranial pressure management.

4.2 Epidemiological Insights and Risk Stratification

CSF rhinorrhoea displays distinctive epidemiological patterns by aetiology. Traumatic leaks predominate in younger males (mean age 39.8 years, 56.5% male) following motor vehicle trauma and assault, manifesting robust response to surgical repair. Conversely, spontaneous leaks afflict predominantly obese, middle-aged women (89.2% female, mean BMI 32.6, 64% obesity prevalence), reflecting probable underlying intracranial hypertension. This aetiology-based phenotyping enables risk stratification and prognostication. Female gender emerges as an independent demographic characteristic across all categories (72.5% overall), potentially reflecting increased healthcare-seeking behaviour, obesity prevalence in women, and higher IIH incidence. Obesity (BMI>30) occurred in 26.4% overall but 64% of spontaneous cases, strongly implicating metabolic and pressure-related mechanisms. Recognition of these phenotypes enables targeted preventive strategies: weight management counsel in obese patients, aggressive IIH treatment pre-operatively, and trauma prevention initiatives in high-risk demographics.

4.3 Diagnostic Algorithms and Biomarkers

Modern diagnostic strategies employ integrated multimodal approaches. Beta-2-transferrin (92% sensitivity, 98% specificity) and beta-trace protein (94% sensitivity, 99% specificity) provide definitive biochemical confirmation superior to glucose testing (78% sensitivity). HRCT and MRI offer complementary advantages: HRCT precisely localises osseous defects and identifies bone erosion patterns, whilst MRI demonstrates encephalocele, dural breach, and intracranial pathology guiding perioperative planning. CT cisternography (100% sensitivity) provides absolute localisation confirmation for complex multi-site leaks but carries 2–5% infection risk and should be reserved for discordant clinical-imaging findings. MR cisternography (96% sensitivity) offers equivalent diagnostic accuracy with superior safety. The 2024 American Academy of Otolaryngology guideline recommendations endorse combining HRCT and MRI in initial workup, reserving cisternography for select complex cases. Emerging fluorescein intraoperative use (0.5% concentration, minimal toxicity risk) facilitates real-time defect identification enhancing technical precision and success rates.

4.4 Surgical Technique Evolution and Optimization

Technique-dependent outcome improvements reflect iterative refinement over two decades. Single-layer grafting (78.3% success) has been substantially superseded by multilayer reconstruction (91.8% success, RR 1.17 [95% CI 1.09–1.26]), producing 13.5 percentage-point absolute improvement. Multilayer strategies employ nasoseptal flaps as primary vascularised barrier, supplemented by underlay autologous fascia (fascia lata, rectus fascia) and overlay fat, additionally secured with fibrin glue (Tisseel, Duraseal) or synthetic matrices (Matriderm, collagen scaffold). This stratified approach maximizes neo-osteogenesis and dural reapproximation. Flap-related innovations include expanded nasoseptal flap width (accommodating larger defects), rescue manoeuvres for flap compromise (partial advancement, secondary graft materials), and emerging vascularised alternatives (pedicled mucoperichondrium, posteriorly-based nasoseptal flap) for extensive anterior-lateral defects. Lumbar drain use (48.1% of studies) reduced postoperative CSF leakage to 1.1% versus 4.2% without drain ($p<0.001$), enabling aggressive early mobilisation and discharge on postoperative day 1–2 in appropriately selected cases. Extended elevation regimen (30 degrees, 7–10 days) and activity restriction (7–14 days) further optimize graft stability.

4.5 Recurrence and Predictive Factors

Recurrent CSF rhinorrhoea, while uncommon (4.98%), represents the most frequent unsatisfactory outcome requiring intervention. Univariate predictors included: multiple defect sites (19% vs. 4%, $p<0.001$), large defects (>10mm: 11% vs. 3%, $p<0.001$), spontaneous aetiology (6.3% vs. 4.1%, $p=0.04$), and single-layer technique (8.9% vs. 3.2%, $p<0.001$). Multivariate analysis retained independent predictors: uncontrolled intracranial hypertension (aOR 4.8, 95% CI 2.7–8.5), multiple defect sites (aOR 3.2, 95% CI 1.8–5.7), single-layer reconstruction (aOR 2.1, 95% CI 1.2–3.7), and defect size >10mm (aOR 2.4, 95% CI 1.4–4.2). Clinical implications include: preoperative IIH management (furosemide, acetazolamide, weight optimisation), selective application of lumbar drain for high-risk cases, mandatory multilayer reconstruction for defects >5mm, and lower thresholds for cisternography when high-risk features present. Median recurrence interval of 18 months (IQR 6–42) suggests that both early graft complications and late resorption contribute; longer follow-up (>2 years) is essential in recurrent-risk populations.

4.6 Complications and Safety Profile

Endoscopic repair demonstrates an exceptionally favourable complication profile, substantially safer than historical open approaches. Postoperative meningitis (2.5%, 95% CI 1.8–3.5%) was dramatically lower than the 23–60% infection risk with untreated leaks. Prophylactic antibiotic therapy duration (>7 days) reduced postoperative infection to 1.8% versus 3.2% with shorter courses ($p=0.019$), supporting extended coverage protocols. Recurrence (4.98%) and graft-related complications (flap failure 1.8%, encephalocele 0.65%) were managed by revision endoscopic procedures with 97–100% success rates, avoiding craniotomy need. Olfactory dysfunction (8.1% hyposmia/anosmia) remains the most common adverse effect, predominantly associated with cribriform approach (11.3%) versus sphenoid approach (2.1%, $p<0.001$), warranting patient counselling regarding this expected outcome. Serious complications (intracranial haemorrhage 0.05%, pituitary dysfunction 0.43%, permanent neurological injury <0.1%) occur rarely. Modern extended lumbar drain protocols, protective nasopharyngeal packing, and intensive postoperative monitoring reduce adverse events further. Rare catastrophic complications (carotid artery injury, major venous injury) occurred in <0.05% and reflected surgeon inexperience or atypical anatomy; contemporary endoscopic training with high-fidelity simulation substantially mitigates such risk.

4.7 Comparison to Alternative Approaches

Endoscopic endonasal repair has displaced alternative surgical approaches given superior safety-efficacy profiles. Open transcranial craniotomy approaches carry 10–40% morbidity, 20–40% recurrence rates, and prolonged recovery requiring 6–8 weeks convalescence. Transcranial subtemporal approaches for lateral sphenoid leaks achieve 50% success in zone III defects versus 81.4% with modern endoscopic TONES (transorbital neuroendoscopic surgery), which represents an emerging evolution improving access to challenging recess locations. Conservative management (non-operative) achieves only 15–30% spontaneous closure in traumatic leaks and higher recurrence in spontaneous cases; this approach should be reserved for immediate post-traumatic presentation with small defects (<2mm) and low-pressure leaks. Contemporary evidence strongly supports early definitive surgical intervention for persistent leaks (>1–2 weeks post-trauma), spontaneous leaks (universally), and recurrent leaks. Hybrid endoscopic-microscopic techniques combining endoscopic visualization with operating microscope for added magnification represent an alternative in challenging lateral recess cases but do not substantially improve outcomes versus pure endoscopic techniques in most centres.

4.8 Implications for Clinical Practice and Future Directions

This systematic review synthesis endorses endoscopic endonasal repair as first-line treatment for 95%+ of CSF rhinorrhoea cases, with restricted open approach indications. Clinical practice recommendations include: (1) Prompt diagnostic confirmation via β2-transferrin and imaging (HRCT ± MRI) in suspected cases; (2) Multimodal preoperative assessment including IIH screening, obesity stratification, and extended imaging for complex/multiple defects; (3) Mandatory multilayer reconstruction technique utilising nasoseptal flap ± reinforcement materials for defects >5mm; (4) Prophylactic antibiotic therapy exceeding 7 days post-operatively; (5) Selective lumbar drain use in high-risk cases (multiple defects,

IIH, defect >10mm); (6) Postoperative protocols emphasizing early detection of recurrence via serial clinical examination (particularly first 6 months), extended follow-up ≥2 years for spontaneous cases; (7) Emerging techniques (intraoperative fluorescein, TONES, scaffold materials) warrant further investigation in prospective trials. Future research priorities include: prospective trials comparing lumbar drain algorithms, randomized evaluation of novel scaffold materials, definition of optimal prophylactic antibiotic regimens, long-term outcome tracking >5 years in large registries, and investigation of minimally invasive office-based approaches for uncomplicated defects.

4.9 Limitations of the Evidence Base

This systematic review acknowledges several limitations. First, heterogeneous reporting across studies necessitated multiple imputations and sensitivity analyses; however, core outcome definitions (success, recurrence, major complications) demonstrated sufficient consistency. Second, predominance of retrospective cohort designs (68%) versus prospective randomized trials introduces potential selection and recall bias; publication bias toward positive outcomes cannot be entirely excluded, though funnel plot analysis revealed minimal asymmetry. Third, wide variations in follow-up duration (6 months to 10 years) impact recurrence estimates; time-dependent analyses were not possible, and late recurrences (>5 years) may be underestimated. Fourth, limited data on long-term functional outcomes (olfactory, nasal quality of life) and patient-reported outcomes restrict comprehensive impact assessment. Fifth, sparse reporting of osseo-integration dynamics, graft revascularisation patterns, and mechanistic predictors of failure limits understanding of biological determinants. Sixth, geographic and institutional heterogeneity and surgeon experience variability introduce unmeasured confounding. These limitations support the imperative for prospective multicenter registry studies employing standardised outcome definitions and extended follow-up protocols.

CONCLUSION

Cerebrospinal fluid rhinorrhoea, a rare but clinically significant neurosurgical condition, has undergone paradigm transformation from open-operative approaches to endoscopic endonasal repair, substantially improving functional and anatomical outcomes whilst minimizing morbidity. This systematic review and meta-analysis of 47 contemporary studies involving 1,847 patients establishes endoscopic repair as the gold-standard first-line approach, achieving first-attempt success in 89.3% (95% CI 85.1–92.8%) and cumulative success of 94.2% (95% CI 90.5–97.1%) following re-intervention when needed. Multilayer reconstruction techniques employing nasoseptal flaps with reinforcement materials reproducibly outperform single-layer approaches. Patient demographics and aetiology substantially influence outcomes: traumatic leaks in younger patients demonstrate superior healing versus spontaneous leaks in older, obese patients with underlying intracranial hypertension requiring enhanced perioperative management. Rigorous preoperative diagnostic workup integrating biochemical confirmation (β2-transferrin, β-trace protein), high-resolution imaging (HRCT, MRI), and selective cisternography in complex cases optimizes intraoperative precision and success. Postoperative complications remain uncommon, with meningitis (2.5%), recurrence (4.98%), and permanent morbidity (<1%) rates substantially favourable compared to natural history. Emerging refinements—including transorbital neuroendoscopic approaches for challenging lateral recess defects, advanced scaffold materials, and intraoperative adjuncts (fluorescein, neuromonitoring)—represent ongoing evolution enhancing applicability and outcomes across diverse anatomic presentations. Continued investment in prospective multicenter trials, mechanistic investigations of graft biology and osseo-integration, and comprehensive patient-reported outcome measurement will further optimize perioperative management and long-term functional restoration in this increasingly treatable neurosurgical entity.

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