

Assessing the need for bed rest after anterior skull base reconstruction: insights from a multicentre retrospective observational study

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Dear Editor:

Skull base reconstruction is a critical component of endoscopic endonasal skull base surgery (EESBS). Bed rest remains an indispensable element of post-operative care, which should be carefully considered for reducing the risk of cerebrospinal fluid (CSF) leaks and enhancing surgical outcomes ^(1,2). However, the necessity of bed rest continues to be controversial as indicated by the expert consensus on perioperative management of skull base reconstruction, due to a lack of high-quality evidence to support its effectiveness ⁽¹⁻⁴⁾. This study focuses exclusively on anterior skull base reconstruction, which is frequently employed in EESBS but has not been sufficiently investigated. In this study, we retrospectively collected patient data from three skull base centres to analyse the impact of bed rest on the occurrence of post-operative CSF leakage.

A total of 119 patients in the no bed rest group and 149 patients in the bed rest group were enrolled (full methods are outlined in supplementary materials). Table S1 provides the overall and subgroup characteristics of the patients. The incidence of post-operative CSF leakage was 4.2% in the no bed rest group and 3.4% in the bed rest group. After adjusting for confounding factors, no statistically significant difference in the post-operative CSF leakage outcomes was observed between the two groups ($p=0.598$, $OR=0.66$, 95% CI 0.14-3.12) (Table 1). This non-significant association persisted after propensity score matching, with comparable CSF leakage incidence observed between the two cohorts (Table S2, S3).

The size of the skull base defect is a key focus in clinical practice. A moderate correlation was observed between defect size and bed rest duration (Kendall's $\tau=0.38$, $p<0.001$), as well as between defect size and reconstruction method (Cramer's $V=0.43$, $p<0.001$) (Figure S1). Small defects (low-flow CSF leaks) and large defects (high-flow) groups were categorized based

on the threshold of 1 cm ⁽¹⁾. Stratified analyses corroborated the absence of a statistically significant differences in postoperative CSF leakage rates between the no bed rest and bed rest groups (Table S4). However, it was observed that the incidence of CSF leakage in patients with large defects was comparatively higher in the no bed rest group than in the bed rest group (9.1% vs 4.9%). Further large-scale studies are required to validate these findings.

The potential rationale for these findings is that, in patients with small defects, the post-operative activity-induced fluctuations in intracranial pressure (ICP) exert minimal pressure on the defect site. For high-flow leaks, multi-layer (with or without pedicled flaps) repair methods are frequently in clinical practice owing to their ability to provide optimal resistance to ICP fluctuations. Moreover, post-operative iodine gauze packing is often applied to support the repair material, abrogating the ICP pressure during the first 1-2 weeks post-surgery as the risk of immediate postoperative CSF leakage can generally be excluded ⁽¹⁾. Being a retrospective cohort study, the level of evidence obtained in this study is relatively low. Some of the limitations of this investigation include potential unaccounted confounders (e.g. bed rest duration), adoption of a relatively crude classification (e.g. disease type, reconstruction method) as well as inter-centre variations in institutional protocols and counselling approaches. In future, large sample prospective cohort studies or randomized controlled trials involving multiple centres are needed to validate the current conclusions.

In summary, the present multicentre retrospective observational study has demonstrated that post-operative bed rest may not affect the incidence of CSF leaks in patients undergoing anterior skull base reconstruction in EESBS, particularly in cases with small defects. These findings provide preliminary insights for

Table 1. Logistic regression analysis of the impact of bed rest on post-operative CSF leakage incidence after adjusting for various confounding factors.

Group	Model 1		Model 2		Model 3		Model 4	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
No bed rest	Reference		Reference		Reference		Reference	
Bed rest	0.79 (0.22-2.91)	0.717	0.82 (0.21-3.17)	0.767	0.76 (0.17-3.25)	0.701	0.66 (0.14-3.12)	0.598

Abbreviations: OR, Odds Ratio; CI, Confidence Interval. Model 1: Unadjusted; Model 2: Adjusted: Age, Gender, BMI, History of diabetes, Hypertension history (Systemic factors); Model 3: Adjusted: Surgical history, Radiotherapy history, Disease types, Defect size, Reconstruction methods (Local factors); Model 4: Adjusted: Age, Gender, BMI, History of diabetes, Hypertension history, Surgical history, Radiotherapy history, Disease types, Defect size, Reconstruction methods (Systemic & Local factors).

post-operative management of anterior skull base reconstruction.

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Authorship contribution

XDY, LW and JQL: conceptualization, methodology, data curation, analysis, writing-original draft, visualization, editing, QL and HKZ: data curation, formal analysis, writing, review, WW: data curation, methodology, writing, editing, LGY and WPL: conceptualization, co-supervision, writing, review, HMY, ZLW

and YJ: conceptualization, methodology, resources, supervision, project administration, funding acquisition, review and editing. All authors approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflict of interest

The authors declare no conflicts of interest.

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This manuscript contains online supplementary material

SUPPLEMENTARY MATERIAL

Materials and methods

Study population

Retrospective data on patients underwent anterior skull base reconstruction were collected between January 1, 2021 and July 1, 2024 from three academic rhinology centres (The Affiliated Hospital of Qingdao University, Qingdao University, Qingdao, Shandong, China; Xuanwu Hospital, Capital Medical University, Beijing, China; Eye & ENT Hospital, Fudan University, Shanghai, China). The inclusion criteria were as follows: 1) Patients who underwent surgery for anterior skull base (ranges from the posterior wall of the frontal sinus to the planum sphenoidale, and laterally to the lamina papyracea) lesions via an endoscopic endonasal approach. 2) Those who had skull base defects with visible CSF leakage during surgery. 3) Those who developed anterior skull base defects and underwent reconstruction. The secondary reconstruction due to failure of the initial skull base reconstruction during the same hospitalization was excluded. All reconstruction procedures were performed by experienced senior doctors. The institutional protocols for reconstructive approaches and perioperative management were consistent. None of the included patients underwent lumbar cistern drainage.

Study variables

Based on clinical experience and a review of the literature^(3,8-10), relevant data regarding post-operative CSF leakage were collected, including age, gender, body mass index (BMI), diabetes history, hypertension history, surgical history, radiotherapy history, disease type, defect classification, reconstruction method, postoperative bed rest status, duration of bed rest (if carried out), and presence of postoperative CSF leakage. Surgical history was defined as any prior surgery performed at the same skull base site, regardless of surgical approach. Radiotherapy history was defined as the previous inclusion of the skull base site within the radiation therapy field.

Disease types were divided into three categories: 1) non-tumour lesions (e.g., spontaneous, traumatic, iatrogenic CSF rhinorrhoea, meningoencephalocele, etc.); 2) benign tumours (e.g., inverted papilloma, osteoma, etc.); and 3) malignant tumours (e.g., olfactory neuroblastoma, squamous cell carcinoma, etc.).

Defect classification was defined as follows: 1) Grade 1: no obvious dural defect, with minimal CSF leakage; 2) Grade 2: visible dural defect (maximum diameter <1 cm), with CSF leakage; and 3) Grade 3: large dural defect (maximum diameter ≥1 cm), with CSF leakage. In subsequent stratified analysis, a threshold of 1 cm was applied, categorizing cases into small defects (low-flow CSF leaks), which means concluding Grade 1 & 2 defects, and large defects (high-flow) groups.

The processes for anterior skull base reconstruction were standardized. Following resection of the lesion involving the

anterior skull base, the bone defect and, when visible, the dura were exposed. Reconstruction methods were classified into four categories: 1) single-layer free graft; 2) single-layer pedicled flap; 3) multilayer free grafts (including at least two of artificial dura mater, fascia lata, or free mucosal graft); 4) multilayer pedicled flaps (including at least one of artificial dura mater, fascia lata, added to pedicled mucosal flap). For single-layer reconstructions, the repair material was utilized to cover the defect extracranially. For multilayer reconstructions, the materials were applied in the following order from intracranial to extracranial: artificial materials, followed by autologous materials (with pedicled flap placed last). Artificial materials that are frequently utilized for reconstruction include collagen and acellular dermal matrix, while autologous fascia, particularly from the thigh, is commonly employed. The selection of the repair method is typically determined by the size of the defect, with larger defects often requiring multilayered repair. Lodoform gauze is used to support the reconstruction material, which was removed 1-2 weeks postoperatively.

Patients were divided into two groups: the no bed rest group and the bed rest group. The no bed rest group referred to patients who did not require absolute bed rest and were allowed to engage in simple activities; however, actions that were likely to increase intracranial pressure (ICP), including Valsalva manoeuvre, forceful actions, sneezing, etc., were avoided, and activities such as driving, running, swimming, flying, and exercising were restricted. The bed rest group referred to patients who were strictly confined to bed post-operatively, including bathroom privileges, as well as the aforementioned actions and activities. Fowler's position (head elevated at 20°-30°) was maintained as much as possible. In the bed rest group, the duration of bed rest (2-14 days) was recorded, usually depending on the size of the defect (analysed in the results section).

Post-operative CSF leakage was defined as CSF leakage occurring in the skull base reconstruction area from the completion of surgery to a short period after all nasal packing materials were removed.

Statistical analysis

Statistical analysis was performed using R software version 4.3.1. Skewed continuous variables (age, duration of bed rest) were presented as the median and interquartile range, whereas normally distributed data (BMI) were expressed as mean ± standard deviation. Categorical variables were presented as frequency (percentage). The correlation between defect size and duration of bed rest was analysed using Kendall's Tau-b. Dunn's test was used to compare groups with different defect sizes. Cramer's V coefficient was employed to quantify the strength of the correlation between defect size and reconstruction method. For

comparisons between continuous variables, the rank sum test or t-test was applied, while the chi-square test or Fisher's exact test was used for categorical variables. Logistic regression was employed to adjust for confounding factors and evaluate the effect of post-operative bed rest on the occurrence of CSF leaks. Propensity score matching was performed between the no bed and bed rest groups using nearest-neighbour matching with a calliper of width equal to 0.1 of the standard deviation of the logit. The incidence of post-operative CSF leakage was compared between the two matched groups. The impact of bed rest on post-operative CSF leakage occurrence was compared between the two groups after defect size stratification. All statistical tests were two-tailed, and a significance level was set at $\alpha=0.05$.

Results

Propensity score matching and sensitivity analysis

Patient characteristics overall and by subgroup are presented in Table S1. After propensity score matching, the number of cases in both the no bed and bed rest group was 69. The incidence of post-operative CSF leakage demonstrated no statistically significant difference ($p=1.000$) between the two groups (Table S2). After adjusting for age, gender, BMI, history of diabetes, hypertension history, surgical history, radiotherapy history, disease type, defect classification, and reconstruction method, no statistically significant difference in the post-operative CSF leakage outcomes was found between the two groups ($p=0.556$, OR=0.44, 95% CI 0.02-6.25) (Table S3).

Stratified analysis based on defect size

In the bed rest group, the median duration of bed rest was 8.00 days (interquartile range [IQR] 6.00, 10.00). No significant difference in bed rest duration was found between Grade 1 and 2 defects ($p=0.31$). However, significant differences were observed between Grade 1 and 3 defects ($p<0.001$), as well as between Grade 2 and 3 defects ($p<0.001$) (Figure S1A). Larger defects were more likely to be repaired in multiple layers (Figure S1B). Small defects, defined as a dural defect with a maximum diameter of <1 cm, including cases with defect classifications of Grades 1 and 2 (no bed rest group: 97 cases, bed rest group: 88 cases). Large defects, defined as a dural defect with a maximum diameter of ≥ 1 cm, corresponding to defect classification Grade 3 (no bed rest group: 22 cases, bed rest group: 61 cases). For small defects, the incidence of post-operative CSF leakage was 3.1% in the no bed rest group and 2.3% in the bed rest group. After adjusting for age, gender, BMI, history of diabetes, hypertension history, surgical history, radiotherapy history, disease type, defect classification, and reconstruction method, no statistically significant difference in the incidence of post-operative CSF leakage was found between the two groups ($p=0.571$, OR=2.23, 95%CI 0.14-44.18). For large defects, the incidence of post-operative CSF leakage was 9.1% in the no bed rest group and 4.9% in the bed rest group. After adjusting for confounding factors, no statistically significant difference in the incidence of post-operative CSF leakage was found between the two groups ($p=0.357$, OR=0.29, 95%CI 0.01-3.98) (Table S4).

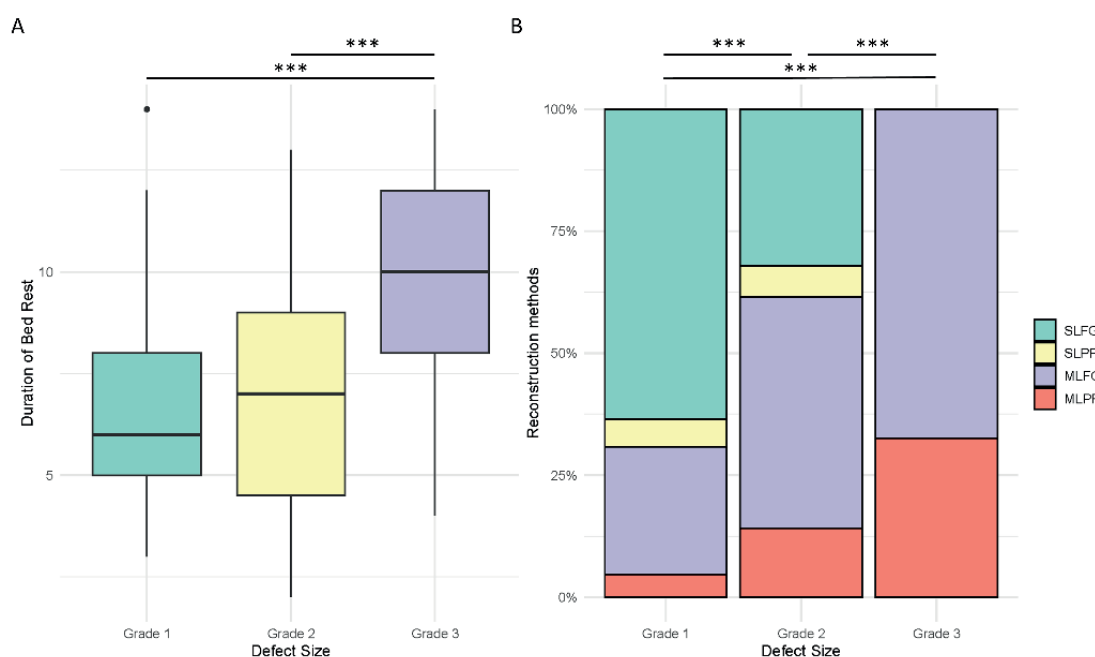


Figure S1. A) Moderate correlation between defect size and bed rest duration (Kendall's $\tau=0.38$, $p<0.001$), B) Moderate correlation between defect size and reconstruction method (Cramer's $V=0.43$, $p<0.001$). ***, $p<0.001$. SLFG, single-layer free graft; SLPF, single-layer pedicled flap; MLFG, multilayer free grafts; MLPF, multilayer pedicled flaps.

Table S1. Comparison of patient characteristics between no bed and bed rest groups after anterior skull base reconstruction.

Variables	Level	Total 268	No bed rest 119	Bed rest 149	p-value
Age (year)		51.00 (24.25)	51.00 (23.50)	52.00 (26.00)	0.126
Gender	Female	114 (42.5)	62 (52.1)	52 (34.9)	0.007
	Male	154 (57.5)	57 (47.9)	97 (65.1)	
BMI (kg/m ²)		24.07 (3.91)	24.00 (4.22)	24.13 (3.65)	0.785
Diabetes	No	250 (93.3)	114 (95.8)	136 (91.3)	0.221
	Yes	18 (6.7)	5 (4.2)	13 (8.7)	
Hypertension	No	210 (78.4)	96 (80.7)	114 (76.5)	0.501
	Yes	58 (21.6)	23 (19.3)	35 (23.5)	
Surgical history	No	202 (75.4)	92 (77.3)	110 (73.8)	0.606
	Yes	66 (24.6)	27 (22.7)	39 (26.2)	
Radiotherapy history	No	222 (82.8)	95 (79.8)	127 (85.2)	0.316
	Yes	46 (17.2)	24 (20.2)	22 (14.8)	
Disease types	Non-tumour lesions	75 (28.0)	34 (28.6)	41 (27.5)	0.981
	Benign tumours	52 (19.4)	23 (19.3)	29 (19.5)	
	Malignant tumours	141 (52.6)	62 (52.1)	79 (53.0)	
Defect size	Grade 1	107 (39.9)	62 (52.1)	45 (30.2)	<0.001
	Grade 2	78 (29.1)	35 (29.4)	43 (28.9)	
	Grade 3	83 (31.0)	22 (18.5)	61 (40.9)	
Reconstruction methods	SLFG	93 (34.7)	35 (29.4)	58 (38.9)	0.001
	SLPF	11 (4.1)	3 (2.5)	8 (5.4)	
	MLFG	121 (45.1)	69 (58.0)	52 (34.9)	
	MLPF	43 (16.0)	12 (10.1)	31 (20.8)	
Postoperative CSF leakage	No	258 (96.3)	114 (95.8)	144 (96.6)	0.969
	Yes	10 (3.7)	5 (4.2)	5 (3.4)	

Abbreviations: BMI, body mass index; CSF, cerebrospinal fluid; SLFG, single-layer free graft; SLPF, single-layer pedicled flap; MLFG, multilayer free grafts; MLPF, multilayer pedicled flaps; Grade 1: no obvious dural defect, with minimal CSF leakage; Grade 2: visible dural defect (maximum diameter <1 cm), with CSF leakage; Grade 3: large dural defect (maximum diameter ≥1 cm), with CSF leakage.

Table S2. Comparison of patient characteristics between the no bed and bed rest groups after propensity score matching.

Variables	Level	No bed rest 69	Bed rest 69	p-value
Age (year)		50.00 (25.00)	48.00 (27.00)	0.767
Gender	Female	36 (52.2)	31 (44.9)	0.496
	Male	33 (47.8)	38 (55.1)	
BMI (kg/m ²)		24.19 (4.59)	24.12 (3.67)	0.924
Diabetes	No	65 (94.2)	66 (95.7)	1.000
	Yes	4 (5.8)	3 (4.3)	
Hypertension	No	55 (79.7)	58 (84.1)	0.658
	Yes	14 (20.3)	11 (15.9)	
Surgical history	No	52 (75.4)	54 (78.3)	0.84
	Yes	17 (24.6)	15 (21.7)	
Radiotherapy history	No	57 (82.6)	58 (84.1)	1.000
	Yes	12 (17.4)	11 (15.9)	
Disease types	Non-tumour lesions	22 (31.9)	18 (26.1)	0.512
	Benign tumours	11 (15.9)	16 (23.2)	
	Malignant tumours	36 (52.2)	35 (50.7)	
Defect size	Grade 1	29 (42.0)	26 (37.7)	0.870
	Grade 2	18 (26.1)	19 (27.5)	
	Grade 3	22 (31.9)	24 (34.8)	
Reconstruction methods	SLFG	27 (39.1)	22 (31.9)	0.778
	SLPF	3 (4.3)	4 (5.8)	
	MLFG	30 (43.5)	35 (50.7)	
	MLPF	9 (13.0)	8 (11.6)	
Postoperative CSF leakage	No	67 (97.1)	68 (98.6)	1.000
	Yes	2 (2.9)	1 (1.4)	

Abbreviations: BMI, body mass index; CSF, cerebrospinal fluid; SLFG, single-layer free graft; SLPF, single-layer pedicled flap; MLFG, multilayer free grafts; MLPF, multilayer pedicled flaps; Grade 1: no obvious dural defect, with minimal CSF leakage; Grade 2: visible dural defect (maximum diameter <1 cm), with CSF leakage; Grade 3: large dural defect (maximum diameter ≥1 cm), with CSF leakage.

Table S3. Sensitivity analysis of the impact of bed rest on post-operative cerebrospinal fluid (CSF) leakage incidence after propensity score matching.

Group	Model 1		Model 2		Model 3		Model 4	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
No bed rest	Reference		Reference		Reference		Reference	
Bed rest	0.49 (0.02-5.26)	0.567	0.38 (0.02-4.45)	0.458	0.72 (0.03-9.06)	0.798	0.44 (0.02-6.25)	0.556

Abbreviations: OR: Odds Ratio, CI: Confidence Interval. Model 1: Unadjusted; Model 2: Adjusted: Age, Gender, BMI, Diabetes, Hypertension (Systemic factors); Model 3: Adjusted: Surgical history, Radiotherapy history, Disease types, Defect size, Reconstruction methods (Local factors); Model 4: Adjusted: Age, Gender, BMI, Diabetes, Hypertension, Surgical history, Radiotherapy history, Disease types, Defect size, Reconstruction methods (Systemic & Local factors).

Table S4. Logistic regression analysis of the impact of bed rest on post-operative CSF leakage incidence after adjusting for confounding factors, stratified by defect size.

Group	Small defect*		Large defect**	
	OR (95% CI)	p-value	OR (95% CI)	p-value
No bed rest	Reference		Reference	
Bed rest	2.23 (0.14-44.18)	0.571	0.29 (0.02-3.98)	0.357

Abbreviations: OR, Odds Ratio; CI, Confidence Interval; *, dural defect with a maximum diameter of <1 cm; **, diameter of ≥1 cm. Adjusted: Age, Gender, BMI, Diabetes, Hypertension, Surgical history, Radiotherapy history, Disease types, Defect size, Reconstruction methods.