

Rates and Risk Factors for Venous Thromboembolism and Bleeding in Endonasal Skull Base Surgery: A Systematic Review and Meta-Analysis



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Abstract

Background: Endonasal skull base surgery (ESBS) reduces morbidity compared to open approaches but carries risks of venous thromboembolism (VTE) and bleeding.

Objective: To estimate rates of VTE, deep vein thrombosis (DVT), pulmonary embolism (PE), and bleeding after ESBS and assess variability across approaches and subgroups.

Methods: Systematic review and meta-analysis of English-language cohort and case-control studies per PRISMA guidelines. Outcomes pooled using random-effects models.

Results: Pooled rates: VTE 1.4% (95% CI 1.1–1.7%), DVT 1.0%, PE 1.1%, bleeding 2.2%. Higher VTE risk in Cushing's disease (3.8%) and malignancy (4.5%). Expanded approaches showed increased complications (VTE 3.1% vs 1.5%; bleeding 4.3% vs 2.0%).

Conclusions: VTE and bleeding are uncommon but clinically significant after ESBS. Risk stratification and individualized prophylaxis are essential.

Introduction

Endonasal skull base surgery (ESBS) represents a major advancement in the management of anterior skull base lesions, providing a minimally invasive alternative to traditional open craniofacial approaches. This technique reduces surgical morbidity, shortens recovery time, and improves cosmetic outcomes. Despite these benefits, ESBS is not without risk. Postoperative complications such as cerebrospinal fluid leaks, meningitis, and diabetes insipidus are well recognized, but venous thromboembolism (VTE) and bleeding events remain underreported and poorly understood.

VTE, including deep vein thrombosis (DVT) and pulmonary embolism (PE), can lead to significant morbidity and mortality, while bleeding complications such as epistaxis and hematoma pose challenges for perioperative management. Understanding the incidence and risk factors for these complications is essential for optimizing patient safety and guiding prophylactic strategies.

This study aims to address these gaps by systematically reviewing the literature and performing a meta-analysis to estimate pooled complication rates and identify risk factors for VTE and bleeding in ESBS.

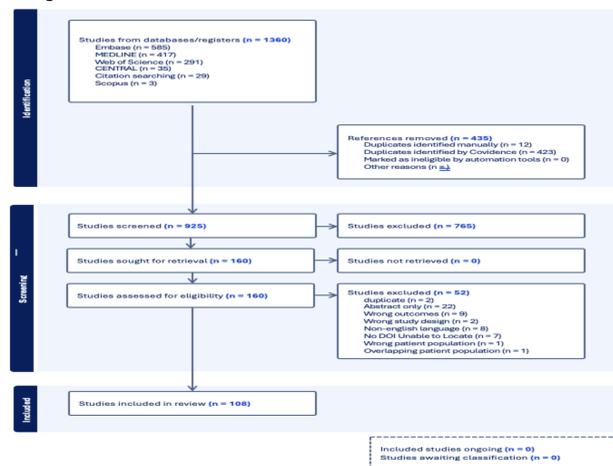
Objective

To quantify VTE, DVT, PE, and bleeding complications after endonasal skull base surgery and explore variability across studies and surgical approaches.

Methods and Materials

Systematic review registered on PROSPERO and conducted per PRISMA guidelines. Databases searched: Medline, Embase, Web of Science, Scopus, and CENTRAL. Inclusion: English-language cohort or case-control studies reporting VTE or comprehensive postoperative complications in anterior skull base surgery. Exclusion: reviews, meta-analyses, registry-only studies, pediatric-only studies, and non-English publications. Data extracted included study characteristics, surgical approach (standard vs expanded), and event counts for VTE and bleeding. Outcomes pooled using random-effects meta-analysis with prediction intervals.

Figure 1. PRISMA Diagram



Results

Study Characteristics:

- 108 studies, 25,462 patients; majority retrospective (91.7%).
- Mean age: 47.9 years; 53.2% female.
- Most cases were pituitary (84.1%), with subsets of Cushing's (12.1%) and malignancy (4.5%).

Complication Rates:

- **VTE:** 1.4% (95% CI: 1.1–1.7%; PI: 0.3–6.2%)
- **DVT:** 1.0% (95% CI: 0.8–1.2%; PI: 0.4–2.8%)
- **PE:** 1.1% (95% CI: 0.8–1.3%; PI: 0.3–3.6%)
- **Bleeding (overall):** 2.2% (95% CI: 1.8–2.7%; PI: 0.5–9.5%)
 - Epistaxis: 1.6% (95% CI: 1.3–2.0%; PI: 0.3–8.9%)
 - Hematoma: 1.0% (95% CI: 0.8–1.3%; PI: 0.3–3.4%)

Risk Factors:

- **Cushing's disease:** VTE 3.8% (95% CI 3.0–4.8%)
- **Malignancy:** VTE 4.5% (95% CI 2.9–7.1%)
- **Surgical approach:** Expanded vs Standard — VTE 3.1% (95% CI 2.1–4.8%) vs 1.5% (95% CI 1.2–1.9%).

Chart 1. Overall Rates of Venous Thromboembolism and Bleeding Complications

Outcome	Total Studies (k)	Total (N)	Total events	Zero-event studies (k)	Zero-event studies (%)	Aggregate rate (events/N)	Median of study rates	IQR	Minimum Rate	Maximum Rate	Pooled Random Effects Rate	95% CI	Prediction Interval	tau ²
VTE	108	25462	193	67	62.0	0.8%	0.0	0.0-0.0	0.0	0.2	1.4%	0.0107-0.0171	0.0028-0.0620	0.6
DVT	105	23024	86	81	77.1	0.4%	0.0	0.0-0.0	0.0	0.1	1.0%	0.0079-0.0124	0.0035-0.0279	0.3
PE	105	23024	102	71	67.6	0.4%	0.0	0.0-0.0	0.0	0.1	1.1%	0.0084-0.0133	0.0030-0.0363	0.4
Bleeding (overall)	105	25130	473	45	42.9	1.9%	0.0	0.0-0.0	0.0	0.1	2.2%	0.0176-0.0266	0.0047-0.0947	0.6
Epistaxis	105	25130	325	58	55.2	1.3%	0.0	0.0-0.0	0.0	0.1	1.6%	0.0125-0.0204	0.0027-0.0886	0.8
Hematoma	105	25130	137	73	69.5	0.6%	0.0	0.0-0.0	0.0	0.1	1.0%	0.0083-0.0128	0.0031-0.0355	0.4

Chart 2. Evaluation of Risk Factors for Venous Thromboembolism

Group	Outcome	Total Studies (k)	Total events	Total N	Pooled Random Effects Rate (%)	95% CI (%)	Prediction interval (%)	I ² (%)	tau ² (logit)
All Pituitary	VTE	80	141	18591	1.3	1.0-1.7	0.3-5.3	50.8	0.5
All Pituitary	DVT	76	56	15450	1.1	0.9-1.3	0.6-1.9	12.3	0.1
All Pituitary	PE	76	59	15450	1.1	0.8-1.4	0.5-2.2	19.8	0.1
All Non-Pituitary	VTE	22	19	1282	3.8	2.2-6.5	1.0-13.8	32.5	0.4
All Non-Pituitary	DVT	21	2	863	2.6	1.4-4.6	1.4-4.6	0.0	0.0
All Non-Pituitary	PE	21	6	863	3.7	2.1-6.5	1.2-11.0	17.6	0.2
Cushing's Disease	VTE	37	55	2431	3.8	3.0-4.8	3.0-4.8	0.0	0.0
Cushing's Disease	DVT	36	27	2143	2.7	2.0-3.6	2.0-3.6	0.0	0.0
Cushing's Disease	PE	36	25	2143	2.4	1.8-3.3	1.8-3.3	0.0	0.0
Malignancy	VTE	24	8	787	4.5	2.9-7.1	2.9-7.1	0.0	0.0
Malignancy	DVT	24	1	787	2.9	1.6-5.1	1.6-5.1	0.0	0.0
Malignancy	PE	24	7	787	4.3	2.7-6.8	2.7-6.8	0.0	0.0
TSA	VTE	71	143	13632	1.5	1.2-1.9	0.5-4.5	42.5	0.3
TSA	DVT	67	59	11558	1.1	0.9-1.4	0.8-1.7	3.7	0.0
TSA	PE	68	59	11644	1.2	1.0-1.5	1.0-1.5	0.0	0.0
EEA	VTE	34	21	1999	3.1	2.1-4.8	1.0-9.5	22.7	0.3
EEA	DVT	33	2	1580	2.1	1.4-3.4	1.4-3.4	0.0	0.0
EEA	PE	34	9	1604	3.2	2.1-4.8	1.4-7.1	9.2	0.1

Discussion

VTE and bleeding are uncommon but clinically significant. Wide prediction intervals indicate variability across settings. Higher VTE risk in Cushing's disease and malignancy supports targeted prophylaxis and expanded approaches may confer higher complication rates. Individualized strategies balancing thrombotic and hemorrhagic risks are essential.

Conclusions

Endonasal skull base surgery has low overall complication rates, but risk stratification is critical for high-risk subgroups. Standardized reporting and prospective studies are needed to refine prophylaxis strategies.

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