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Factors impacting postoperative haemorrhage after transnasal endoscopic surgery*

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Abstract

Background: Transnasal endoscopic surgery (TES) is an established procedure for the treatment of chronic rhinosinusitis, septal deviation, and paranasal benign tumours. Postoperative haemorrhage (POH) is a common complication following TES. Various studies have addressed the risk factors for intraoperative bleeding and the methods to improve the operative field by reducing bleeding. However, the factors affecting POH following TES have not been fully elucidated. Therefore, we aimed investigate the risk factors for POH following TES.

Methodology: We studied 807 patients who underwent TES. The variables between cases with and without POH were compared using univariate and multivariate models. We also examined the site and timing of bleeding.

Results: POH was observed in 21 cases (2.6%). Seven cases required treatment in the operation room (0.9%). The most common sites of bleeding were around sphenopalatine foramen, and the median time to POH was the 7th day after surgery. Multivariate analysis showed that anti-thrombotic medication, low platelet count, and surgical indication for sinonasal tumour were independent risk factors for POH.

Conclusions: POH after TES is a relatively common complication. Careful intraoperative haemostatic procedures may be required in these cases.

Key words: endoscopic sinus surgery, postoperative haemorrhage, anti-thrombotic medication, sinonasal tumour, low platelet count

Introduction

Transnasal endoscopic surgery (TES) is an established procedure for the treatment of chronic rhinosinusitis, septal deviation, paranasal cysts, allergic rhinitis, benign tumours, and more [1–6]. Postoperative haemorrhage (POH) is a common complication that can occur after any surgery, including TES. Stankiewicz et al. indicated that POH after endoscopic sinus surgery (ESS) was the most frequent complication [7]. Dalziel et al. showed that the median rate of POH after nasal polyp surgery was 2.5% (0.2–21.1%) in a systematic review [8]. Regarding septoplasty, the rate of POH has been reported to be 0.8–3.0% [9–11]. These results suggest that POH is a common complication following TES. In recent years, the indication for ESS has expanded beyond chronic sinusitis to include lacrimal and orbital diseases, cranial base diseases, and some malignancies. Therefore, the risk of POH may be increased.

Intraoperative bleeding interferes with the surgical view, and this may lead to complications. Several solutions have been reported [12–14]. However, attention to the subject of POH following TES has been lacking.

POH negatively affects quality of life, and readmission or longer hospital stays may be required following POH. In addition, prolongation of postoperative treatment increases healthcare costs. However, the factors impacting POH following TES have

not been fully elucidated. Identification of the risk factors for POH enables better surgical planning and aids in providing an appropriate explanation to patients.
The study aimed to retrospectively investigate POH in our institute and identify the risk factors for POH.

Materials and methods

Patients

This retrospective study was approved by the institutional review board of Osaka University Hospital (#16329). We included patients who underwent ESS between 2014 and 2018 at the Department of Otorhinolaryngology Head and Neck Surgery, Osaka University Hospital. All patients were followed up for six months. The exclusion criteria included surgery for malignant tumours, skull base surgeries, laser surgery for the treatment of allergic rhinitis, sphenopalatine artery ligation for severe epistaxis, and laser surgery or coblation for hereditary haemorrhagic telangiectasia.
POH was defined as a haemorrhage requiring haemostatic procedures or surgery, such as gauze packing, mucosal cauterization, or clipping of blood vessels by physicians, within 30 days following surgery. Minor POH was defined as bleeding that could be stopped in the treatment room or outpatient setting and did not require surgery; major POH was defined as bleeding that required surgery under local or general anaesthesia.

Site and timing of postoperative haemorrhage

The bleeding sites were classified as the sphenopalatine foramen areas, middle turbinate, inferior turbinate, nasal septal mucosa, anterior face of sphenoid sinus, ethmoid sinus, and others. The timing of bleeding was divided into 1–3 days, 4–6 days, 7–10 days, 11–14 days, and ≥15 days after surgery.

Data collection

The following preoperative information was collected about the patients: sex, age, body mass index (BMI), blood pressure on admission, haemoglobin A1c (HbA1c), activated partial thromboplastin time (APTT), prothrombin time/international normalized ratio (PT-INR), platelet count, and anti-thrombotic medications (anti-coagulant or anti-platelet medications). Surgical indication and surgical factors (operation time, type of anaesthesia, and operating procedure) were also extracted. Given that there was an issue with missing data, we analysed HbA1c in 457 patients.

Statistical analyses

All statistical analyses were performed using JMP Pro. 14 Software (SAS Institute Inc., Cary, NC, USA). The chi-square test was used to perform univariate analyses. Predictors that were found to be related to POH ($p \leq 0.20$) were then entered into a multivariate logistic regression model, using stepwise forward and backward selection. $P<0.05$ was considered statistically significant.

Results

Demographics of the cases

We included 807 patients in this study, and their clinical data are presented in Table 1. There were 60.6% male and 37.4% female patients, with a median age of 57 years. Forty-four patients (5.5%) were on internal antithrombotic medication before the surgery. The surgical indications were sinusitis in 51.7% of patients, nasal septal deviation in 10.9%, benign tumour in 9.9%, paranasal cyst in 9.5%, allergic rhinitis in 5.6%, fungus ball in 3.8%, and other sinus diseases in 8.6%. In addition, 80.7%, 49.6%, and 36.8% of patients had ESS, septoplasty, and submucosal resection of the inferior turbinectomy, respectively. Among the various diseases, patients with chronic rhinosinusitis had the highest number of cases of postoperative bleeding at 2.2%, while patients with benign tumours had the highest frequency of postoperative bleeding at 6.3% (Table 2).

The major bleeding commonly occurred after the 7th postoperative day

POH was observed in 21 of 806 patients (2.6%; Table 1). The percentage of patients requiring treatment for POH in the operating room (major bleeding) was 0.9%. The 21 cases of POH included 9 cases of chronic rhinosinusitis, 5 cases of paranasal benign tumour, 4 cases of paranasal cyst, and 2 cases of allergic rhinitis. There were 7 cases of major bleeding and 14 cases of minor bleeding according to the degree of bleeding. POH was detected at the sphenopalatine foramen area in 7 cases, the middle turbinate area in 5 cases, the anterior face of sphenoid sinus in 2 cases, the nasal septum in 2 cases, and other areas in 5 cases (Figure 1a). Four cases with bleeding from the sphenopalatine foramen area and 3 cases from anterior face of sphenoid sinus required revision surgery. Bleeding occurred most commonly 7–10 days after surgery (median time, 7 days); except for one patient, all major bleeding occurred after the 7th postoperative day (Figure 1b).

Surgery for benign tumours, low platelet count, and anti-thrombotic medication were all independent risk factors for postoperative haemorrhage

We performed univariate analyses of factors affecting POH by using the chi-square test (Table 2). Sex, BMI, HbA1c, PT, age, blood pressure, operation time, type of anaesthesia, and operating procedure showed no significant association with the incidence of POH. Furthermore, operative procedures for ESS, septoplasty, or submucosal resection of the inferior turbinectomy did not affect the rate of POH.
Factors associated with POH included delayed APTT (14.3% vs. 2.3%, $p<0.01$), low platelet count (30.0% vs. 2.3%, $p<0.01$), anti-thrombotic medication use (13.6% vs. 2.0%, $p<0.01$), and a surgical indication for benign tumours (6.3% vs. 2.2%, $p=0.03$). Based on these results, we further performed a multivariate

Table 1. Demographics of the cases.

Characteristics		Median (range)	N	%
Sex	Male		499	60.6%
	Female		308	37.4%
Age (median)	(years old)	57 (6 - 95)		
BMI (median)	(kg/m^2)	23.2 (14 - 41.3)		
Blood pressure on admission	Diastolic	122 (76 - 210)		
	Systolic	74 (43 - 143)		
APTT (median)	(sec)	29 (23 - 127)		
PT-INR (median)		1.01(0.89 - 2.78)		
Platelet count (median)	(×10^3/μl)	233 (22 - 522)		
ESS			651	80.7%
Septoplasty			400	49.6%
Submucosal resction of inferior turbinate			297	36.8%
Draf type 3			46	5.7%
Medication of antithrombotic drugs			44	5.5%
Type of anaesthesia	Local		290	35.9%
	General		517	64.1%
Operation time (median)	(min)	115 (19 - 440)		
Surgical indication	Tumour		80	9.9%
	Other than tumour		727	90.1%
Postoperative haemorrhage	Minor bleeding		14	1.7%
	Major bleeding		7	0.9%

APTT = activated partial thromboplastin time; BMI = body mass index; ESS = endoscopic sinus surgery; HbA1c = haemoglobin A1c; PT-INR = prothrombin time-international normalized ratio; OR = odds ratio. Due to incomplete data, we analysed only 457 cases for HbA1c.

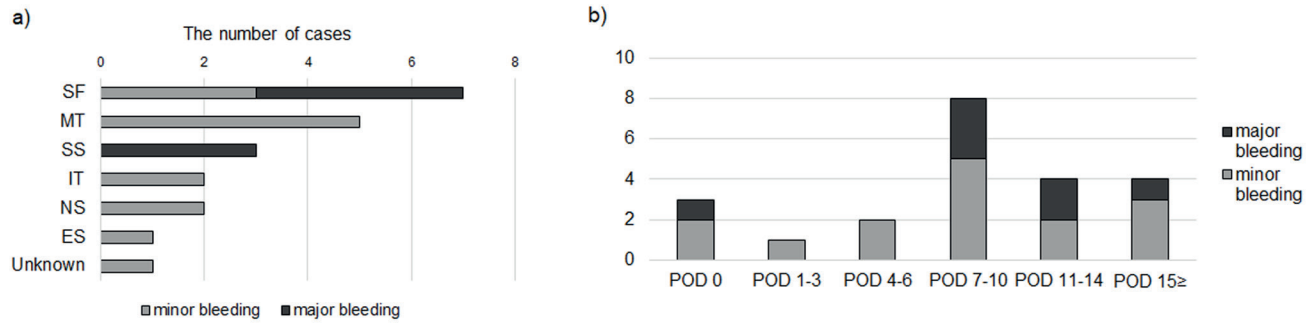

Figure 1. The site and timing of postoperative hemorrhage. a) The site of bleeding. b) The timing of postoperative haemorrhage. SF = sphenopalatine foramen; MT = middle turbinate; SS = anterior face of sphenoid sinus; IT = inferior turbinate; NS = nasal septum; ES = ethmoid sinus; POD = postoperative day.

analysis by logistic analysis. This analysis showed that surgery for benign tumour (odds ratio [OR], 3.11; 95% CI, 1.04–9.27), low platelet counts (OR, 16.64; 95% CI, 2.53–109.41), and anti-thrombotic medication (OR, 5.48; 95% CI 1.64–18.32) were all independent risk factors for POH (Table 3).

Discussion

TES is a standard procedure for nasal and sinus disease without malignancy. POH is one of the most common complications following TES. Previous studies have focused on POH as a complication, but few reports have studied its risk factors. This is the first study to analyse risk factors for POH after not only ESS, but also endoscopic nasal surgeries in general. A previous systematic review showed a median POH rate of 2.5% (0.2–21.1%)[8]. Asaka et al. reported that severe intraoperative bleeding (more than 100 ml) was seen in 2.5% of cases, and POH was seen in

Table 2. Univariate analysis of association between factors enrolled and postoperative haemorrhage.

Variables	Categories	Postoperative haemorrhage			Odds ratio	P value
		Yes	No	%		
Sex	male	17	482	3.4%	2.68	0.07
	female	4	304	1.3%		
Age	≥75	3	74	3.9%	1.60	0.45
	<75	18	712	2.5%		
BMI	≥25	5	241	2.0%	0.71	0.50
	<25	16	545	2.9%		
HbA1c	≥6.5%	3	61	4.7%	1.88	0.34
	<6.5%	10	383	2.5%		
PT-INR	>1.2	1	12	7.7%	3.23	0.25
	≤1.2	20	774	2.5%		
APTT	≥39	3	18	14.3%	7.11	<0.01
	<39	18	768	2.3%		
Platelet count	≤100	3	7	30.0%	18.55	<0.01
(×103/µl)	<100	18	779	2.3%		
BP (systolic)	≥140	4	123	3.1%	1.27	0.67
	<140	17	663	2.5%		
BP (diastolic)	>90	3	96	3.0%	1.20	0.78
	<90	18	690	2.5%		
Antithrombotic medication use	yes	6	38	13.6%	7.87	<0.01
	no	15	748	2.0%		
Type of anaesthesia	local	14	503	2.7%	1.13	0.80
	general	7	283	2.4%		
Operation time	≥180	6	151	3.8%	1.68	0.28
(min)	<180	15	635	2.3%		
Surgical indication	tumour	5	75	6.3%	2.96	0.03
	ex-tumour	16	711	2.2%		
ESS	yes	16	635	2.5%	0.76	0.81
	no	5	151	3.2%		
Septoplasty	yes	8	392	2.0%	0.62	0.40
	no	13	394	3.2%		
Submucosal resection of inferior turbinate	yes	8	289	2.7%	1.06	0.92
	no	13	497	2.6%		
Draf type 3	yes	1	47	2.1%	0.79	0.82
	no	20	739	2.6%		

APTT = activated partial thromboplastin time; BMI = body mass index; BP = blood pressure; ESS = endoscopic sinus surgery; HbA1c = haemoglobin A1c; PT-INR = prothrombin time-international normalized ratio

0.7% of cases[15]. Among the 3,128 patients undergoing ESS for chronic rhinosinusitis or nasal polyposis, excessive perioperative bleeding was observed in 5.0%, and POH requiring treatment was observed in 0.8% of the cases, and half of them required a return to the operating room for haemostasis[16]. Suzuki et al. analysed a nationwide Japanese inpatient database and reported postoperative complications of hematoma (0.09%), blood transfusion (0.1%), and POH (0.18%) in 50,734 Japanese patients undergoing ESS for chronic rhinosinusitis treatment[17]. Our results showed a higher frequency of POH than those from this Japanese database, but this could be because our institution is a tertiary care institution and we may have had more

Table 3. Multivariate analysis of factors associated with postoperative haemorrhage.

Variables	Odds ratio	95% CI lower	95% CI upper	P value
Surgical indication, tumour vs. non-tumour	3.11	1.04	9.27	0.04
Platelet count ($\times 10^3$/μl), ≥100 vs <100	16.64	2.53	109.41	<0.01
Anti-thrombotic drugs, yes vs no	5.48	1.64	18.32	<0.01

CI = confidence interval

severe cases. Ramakrishnan et al. showed that the percentage of patients with haemorrhage requiring transfusion was 0.76%[18]. In previous reports, the frequency of POH had varied, possibly because of differences in the operative procedure, surgical indications, and definition of POH. In this study, we included all the patients who underwent any kind of treatment after the end of the surgery. In a previous systematic review, 2.2% (1.2–4.6%) of cases required gauze packing or hospitalization, which was comparable to our results[8].

There have been few previous reports of POH following nasal surgery. The rate of POH associated with septoplasty was reported to be approximately the same as that of ESS, ranging from 0.8–3.0%[9–11], and this figure was similar in our study.

Common areas of postoperative nasal bleeding were related to the sphenopalatine artery region. At least 10 cases (47.1%) with POH at the sphenopalatine foramen and anterior face of the sphenoid sinus were considered to have bleeding originating from the sphenopalatine artery. All cases requiring haemostasis surgery was related to the sphenopalatine artery. In cases posterior bleeding, it is difficult to identify the source of bleeding; in such cases, it is preferable to perform the procedure in the operating room using an endoscope[19,20].

The second most common POH occurred in the middle turbinate, and that may have been caused by partial resection of the middle turbinate during ESS. Reduction of the middle turbinate was performed with the aim of improving ventilation to the middle meatus and olfactory cleft[21]. While middle turbinate resection did not increase the risk of major POH, minor bleeding has been reported to be significantly increased, particularly if the patient was on anticoagulants[22]. The frequency of bleeding from the middle turbinate was high; however, none of the cases in our study required revision surgery. These results suggest that the bleeding from the middle turbinate was easy to stop. To prevent POH, cauterizing the edge of the mucosa and avoiding turbinate bone exposure are important.

The median time of POH occurrence was 7 days after surgery. Most of the major bleeding cases occurred after the 7th postoperative day. Usually, patients are discharged by the 7th postoperative day. Therefore, it is necessary to inform the patient in advance that there is a risk of bleeding after discharge. The delayed postoperative haemorrhage may be explained by the process of wound healing, which is divided into three phases: the inflammation phase, proliferation (new tissue formation) phase, and remodelling phase[23,24]. The inflammation phase lasts up to 48 hours after injury and has a hypoxic or ischemic environment in which fibrin masses are formed. The proliferation stage lasts 48 hours to 10 days. During this period, a crust is formed, and neovascularization appears. Increased blood flow through capillaries along with fibroblasts and macrophages replaces the fibrin matrix with granulation tissue.

In our study, the three cases of bleeding on the day of surgery were thought to be caused by inadequate haemostasis during the operation. In contrast, late onset haemorrhage was thought to occur in the proliferation phase of wound healing. Experiments involving tonsillectomy in mice have shown that the crust was removed followed by exposure of neovascularization during the proliferation phase[25]. The reason for the high frequency of POH in the proliferation phase after TES could be active neovascularization and the loss of crusting by nasal washing. There were eight cases with POH after 11 days postoperatively, and this complication seemed to occur due to delayed wound healing by infection. Several reports reported asthma, presence of nasal polyps, symptom severity, health-related quality of life, the polyp score, and the Lund-Mackay score as risk factors for major complications in ESS[16]. Many reports have examined intraoperative bleeding in ESS, but none have examined the risk factors for POH in detail. Siedek et al. examined the correlation between the experience of surgeons and both intraoperative and POH[26]. Interestingly, the POH rates encountered by surgeons with 5–6 years of experience were significantly greater than those of surgeons with 0–4 years of experience or surgeons with >6 years of experience.

In the present study, multivariate analysis revealed that antithrombotic medication, low platelet counts, and benign tumour surgery were all independent risk factors for POH. Antithrombotic medication and low platelet counts directly impact haemostatic function. The number of patients taking anticoagulant medication worldwide is increasing, and several guidelines have been developed for their management[27]. However, the perioperative use of antithrombotic agents for ESS has not been well studied. A retrospective case control study indicated that ESS is a safe procedure when performed in patients receiving anticoagulation or antiplatelet therapy and suggests that ESS could be classified as a type of surgery with moderate bleeding risk[28]. It is difficult to weigh the risk of thromboembolism due to the withdrawal of medication during the perioperative period as well as the risk of haemorrhage due to continued use. It is now strongly recommended to develop original guidelines and policies for handling of anti-thrombotic drugs during surgical

procedures in all facilities[29,30].

Regarding platelet count, only 10 patients had a low platelet count (<100,000/μl), but three had POH. Therefore, low platelet count was considered to be a risk factor for POH. The Cochrane library notes that low platelet counts increase the risk of bleeding, but there is insufficient evidence that platelet transfusions reduce POH or all-cause mortality[31]. At present, one should consider platelet transfusion using judgement based on individual clinical experience and expertise. In our institution, all patients were treated with NSAIDs without opioids after surgery. NSAIDs impair platelet function and may make bleeding more likely. However, Moeller et al. conducted a randomised trial of ketorolac and compared it to fentanyl, evaluating the analgesic effect and postoperative bleeding[32]. The study found no difference in analgesia or postoperative bleeding between the two groups and concluded that ketorolac is a safe analgesic that can be used after TES. A state of the art review indicated that the clinical impact on perioperative bleeding is low[33]. In this study, the use of NSAIDs could not be considered a risk factor for postoperative bleeding because NSAIDs were used in all patients.

The significantly higher risk of POH in patients with benign tumours could be attributed to two reasons. First, the range of bone exposure during surgery for the tumour is more extensive compared to normal sinusitis surgery. Second, the feeding artery of the tumour may not be properly cauterized. If the artery originates in the bone, it may be difficult to cauterize sufficiently. In recent years, the indications for ESS have expanded for a variety of paranasal tumours; for example, inverted papillomas[4] and almost all benign tumours in our institution are operated on endoscopically. Careful cauterization or ligation of feeding arteries is thought to reduce POH.

This study had several limitations. First, it was a single-centre retrospective study. Second, anti-thrombotic drugs were discontinued preoperatively in most cases, but the timing of resumption after surgery varied. We did not separate anticoagulants and antiplatelet agents for the purposes of analysis. Third, the treatment for POH was not well established and varied between physicians. The physician could have chosen the treatment in the operating room, even if it was not necessary. Therefore, all cases of POH, whether treated in the operating room or not, were analysed. A shorter duration of treatment can be achieved in patients with initial cauterisation for epistaxis compared with other treatments[34]. However, it is necessary to identify the bleeding site for the cauterisation and it is difficult to find a haemostatic point in the situation of severe bleeding. Systematic endoscopic assessment (SEA) has been proposed as an observation method to make it easy to find the bleeding site(35). In SEA, active bleeding is stopped with gauze packing, followed by observation with a rigid scope under general anaesthesia in a defined order to identify bleeding sites. In our institution, observation and haemostasis methods for postoperative bleeding were not unified, so in some cases, gauze packing was chosen without identifying the bleeding point. It is necessary to devise a routine observation method for postoperative bleeding based on the data of the bleeding point of this study. In addition, it was considered necessary to aim for a short treatment period by cauterisation treatment when the bleeding point was identified.

Conclusions

Postoperative haemorrhage following endoscopic nasal sinus surgery occurred in 2.7% of patients. Treatment in the operating room for POH was required in 0.9% of the cases. The majority of haemorrhages occurred after the 7th postoperative day. The independent risk factors for POH were surgery for the tumour, low platelet counts, and antithrombotic medication use. In patients with these factors, extra care is needed with haemostasis.

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Authorship contribution

HI and MH supervised the project. KA, HA, TT, YM, and MH analysed the data and wrote the manuscript. KA, MH, HA, TT, KT, and YM recruited and clinically characterized patients. KA, MH, HA, AN, SO, YM, and KT provided advice on project planning and data interpretation. All authors participated in discussion of the results and critically polished and approved the final draft.

Conflict of interest

The authors declare that there is no conflict of interest.

Ethics approval

This report was approved by the Institutional Review Board of Osaka University Hospital.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Abbreviations

TES: transnasal endoscopic surgery; POH: post-operative hemorrhage; ESS: endoscopic sinus surgery; BMI: body mass index; HbA1c: haemoglobin A1c; APTT: activated partial thromboplastin time; PT-INR: prothrombin time/international normalized ratio; OR: odds ratio.

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