



Post-operative venous thromboembolism in patients after extracranial otologic surgery: A case series

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ABSTRACT

Objective: This study aimed to report 9 venous thromboembolism (VTE) cases after extracranial otologic surgery and analyze the potential risk factors.

Study design: Case series.

Setting: Single tertiary-level academic center.

Methods: Totally, 9 cases of VTE were identified among adults who underwent extracranial otologic surgery at our hospital from January 2018 to December 2020. Caprini risk scores were calculated, and comprehensive preoperative, operative, and postoperative clinical data within 14 days were collected to assess the evidence of VTE.

Results: The median age of 9 patients was 64 years old. Among them, 7 (77.8%) patients presented with intramuscular vein thrombosis, 1 (11.1%) patient had deep vein thrombosis, and 1 (11.1%) patient experienced pulmonary embolism. Preoperatively, 8 (88.9%) patients had low or middle Caprini risk scores (≤ 4) with an average of 2.67 ± 0.47 points. The average Caprini scores for all patients were 4.44 ± 0.35 on postoperative day (POD)1 and 5.67 ± 0.64 on POD14. D-dimer levels were collected, indicating an average of 0.55 ± 0.17 mg/FEU preoperatively, 8.53 ± 3.94 mg/FEU at day 1, and 3.76 ± 0.45 mg/FEU at POD14. In postoperative period, 7 (77.8%) patients experienced vertigo/dizziness and/or head immobility/bed rest.

Conclusion: The present study highlighted that patients with low- and middle-risk of VTE undergoing otologic surgery should be also vigilant about postoperative VTE. Vertigo/dizziness and/or head immobility/bed rest in postoperative period should be considered as minor risk factors for developing VTE in patients undergoing extracranial otologic surgery. Conducting perioperative assessments, including Caprini risk score evaluation, D-dimer testing, and venous ultrasound of lower extremities, is recommended to ensure patients' safety.

1. Introduction

Venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE), is a noticeable healthcare burden that remains under-recognized (Bartholomew, 2017). Even with the use of anticoagulant therapy, the mortality rate and the risk of recurrence are still high in the early phase of VTE. It has serious long-term complications, including chronic pulmonary hypertension and post-thrombotic syndrome, both of which require substantial healthcare

resources for their management and are associated with remarkable morbidity (Wang et al., 2018).

Otologic surgery mainly refers to surgery of the middle ear related to chronic otitis media, including tympanoplasty, ossiculoplasty, mastoidectomy, and lateral skull base surgery. To date, the risk factors associated with VTE in patients undergoing otology surgery have not been thoroughly investigated.

In this study, our preliminary single-center experience on otology patients who developed post-operative VTE was reported. The clinical

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characteristics were described and the risk factors for patients who underwent otologic surgery with spontaneous development of VTE in postoperative period were analyzed. The present study aimed to provide more information on the clinical characteristics and underscore the importance of perioperative diagnosis for VTE patients undergoing extracranial otologic surgery.

2. Methods

A retrospective study was conducted using collected data from the medical records of patients who underwent extracranial otologic surgery at the Otolaryngology, Head & Neck Surgery Department of Beijing Tsinghua Changung Hospital Affiliated to Tsinghua University (Beijing, China) between January 1, 2018, and December 31, 2020.

2.1. Study population

2.1.1. Inclusion criteria

- (1) Surgical procedures encompassed all otologic surgeries, including those involving the outer ear, middle ear, inner ear, and lateral skull base area;
- (2) VTE could be automatically identified using the Tsinghua database of Venous Thromboembolism Prevention and Control in Hospital (TEACH) crisis value system. The DVT determination standard was based on the terms “thrombosis,” “embolism,” or “incompressible”, as described in the venous ultrasound report or radiology report. The PE determination standard was based on the terms “pulmonary embolism” or “multiple pulmonary embolisms”, as described in the radiology report;
- (3) The perioperative period was defined as the day of admission to 14 days after surgery.

2.1.2. Exclusion criteria

- (1) Patients aging under 18 years old;
- (2) Patients with old thrombus as reported by imaging results;
- (3) Patients diagnosed with VTE-positive before admission to the ENT department;
- (4) Patients who never underwent otologic surgery.

Any discovery of risk factors or the presence of the following signs, symptoms, and/or laboratory findings related to VTE that persisted beyond the postoperative 14 days was considered indicative of a clinical manifestation compatible with VTE. These included edema of lower extremities in the postoperative period, elevated D-dimer level, and findings described in the venous ultrasound report or radiology report.

The Caprini scores were manually gathered and calculated perioperatively in accordance with the Caprini risk score assessment table. The calculation of Caprini risk scores were conducted according to American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (Gould et al., 2012; Cronin et al., 2019) (Supplemental Table 1). A risk score of 0 point was classified as very low-risk, 1-2 points as low-risk, 3-4 points as moderate-risk, and ≥ 5 points as high-risk for the development of VTE.

Patients' characteristics (age, sex, previous medical history, chronic diseases, prior VTE occurrence), preoperative Caprini risk score, and D-dimer level, surgical details (operation time, site, and type of anesthesia), and postoperative complications (e.g., vertigo/dizziness and/or head immobility/bed rest) were collected. Additionally, postoperative Caprini risk score and D-dimer level (day 1 to day 14) were recorded.

Normally distributed quantitative variables were expressed as mean and standard error of the mean (SEM). Data were analyzed using SPSS 19.0 software. The association between perioperative Caprini risk score and D-dimer level (preoperative, postoperative day 1, and postoperative day 14) was examined using Student's t-test.

Study design and approval: The study was approved by the Institutional Review Board of Beijing Tsinghua Changung Hospital Affiliated to Tsinghua University (Approval No. 19242-4-01).

3. Results

By the end of 2020, a total of 609 patients were included, and 9 patients were diagnosed with VTE, and there were no reported mortal outcomes. The overall incidence of postoperative VTE was 1.48% in this study. Among these cases, 5 were women (55.6%) and 4 were men (44.4%), with an average age of 64.2 ± 1.8 years old. Table 1 summarizes the preoperative and operative data. The overall average age of all patients was 64.2 ± 1.8 years old. Specifically, the average age of women was 63.8 ± 2.4 years old, and it was 64.8 ± 2.6 years old for men ($P = 0.8221$).

Out of the total, 8 (88.9%) patients had a low- or middle-risk of developing VTE (≤ 4) with an average Caprini risk score of 2.67 ± 0.47 points. One (11.1%) patient had a high-risk of developing VTE, with a preoperative Caprini risk score of 6. Preoperatively, 7 (77.8%) patients underwent D-dimer analysis, with the highest score recorded at 1.64 and an average of 0.55 ± 0.17 mg/FEU (Table 2).

Regarding the type of surgery, 8 (88.9%) patients underwent middle ear surgery, which included 1 mastoidectomy, 2 tympanoplasties, 1 subtotal temporal bone resection, and 4 tympanoplasties with ossicular chain reconstruction. One (11.1%) patient had undergone canalplasty. All patients received general anesthesia, and the average operation time was 4.16 ± 0.69 h, with the longest operation time of 9.73 h (Table 2).

Out of the 9 patients, 8 were suspected to have VTE due to elevated D-dimer levels in the postoperative period, despite the absence of VTE-related symptoms. Their diagnosis was subsequently confirmed through ultrasound (US) and/or computer tomography of the pulmonary artery (CTPA). Among these 8 patients, based on the results of US and CTPA, 7 (77.8%) exhibited intramuscular thrombosis of the lower limbs and were treated with anticoagulants. One (11.1%) patient developed DVT and was referred to the department of vascular surgery for further management. Another patient (11.1%) (patient 2, Table 3) experienced sudden-onset dizziness, hypoxemia, and transient cardiopulmonary arrest on postoperative day 1 (POD1) and was diagnosed with PE through CTPA. This patient underwent cardiopulmonary resuscitation and was transferred to the intensive care unit (ICU) for intravenous thrombolysis.

In the postoperative period, all patients exhibited high Caprini risk scores, with an average of 4.44 ± 0.35 points on day 1 and an average of 5.67 ± 0.64 points on day 14 (Table 3). Paired t-test of patients' preoperative, postoperative day 1, and postoperative day 14 scores yielded the following results: preoperative vs. postoperative day 1 ($P^{**} = 0.0012$), preoperative vs. postoperative day 14 ($P^{**} = 0.0013$), postoperative day 1 vs. postoperative day 14 ($P^* = 0.0226$). Additionally, all

Table 1
Baseline characteristics.

Baseline	VTE Patients n = 9
Age (years old)	64.22 \pm 1.80
≤ 40	0
41-60	2(22.2%)
61-74	7(77.8%)
≥ 75	0
Sex	
Male	4(44.4%)
Female	5(55.6%)
BMI > 25 kg/m ²	1(11.1%)
Hypertension	3(33.3%)
Diabetes Mellitus	2(22.2%)
Stroke	0
COPD	0
Malignant tumor	1(11.1%)
VTE history	0

Table 2
Patients' characteristics and preoperative/operative factors.

No	Sex	Age	Preoperative		Operative		
			Caprini	D-Dimer/mg/FEU	Surgical site	Anesthesia	Time/hours
1	Female	71	2.00	0.2	Middle Ear	General	2.48
2	Female	55	2.00	-	Middle Ear	General	4.40
3	Female	61	4.00	0.48	Middle Ear	General	3.96
4	Female	66	2.00	0.34	Middle Ear	General	3.71
5	Male	70	6.00	0.21	Lateral Skull Base	General	9.73
6	Female	66	3.00	0.93	Middle Ear	General	3.23
7	Male	56	1.00	1.64	Inner Ear	General	2.73
8	Male	66	2.00	0.42	Middle Ear	General	3.06
9	Male	67	2.00	0.15	Middle Ear	General	4.13

Table 3
Postoperative diagnosis and complications, VTE subtypes, and treatment.

No	Caprini Score		D-dimer		Vertigo/Dizziness	Head Immobility/Bed Rest	VTE	
	day 1	day 14	day 1	day 14			subtypes	treatment
1	5.00	7.00	3.1		No	No	Intramuscular	Anticoagulants
2	4.00	6.00	40.81	4.84	No	No	PE	Thrombolysis/Anticoagulants
3	6.00	9.00	11.44	2.45	Yes	Yes	Intramuscular	Anticoagulants
4	4.00	4.00	7.61	3.45	No	Yes	DVT	Anticoagulants
5	6.00	7.00	0.72	4.29	Yes	No	Intramuscular	Anticoagulants
6	3.00	3.00	4.35		No	No	Intramuscular	Anticoagulants
7	3.00	3.00	3.91		Yes	Yes	Intramuscular	Anticoagulants
8	4.00	7.00	1.89		No	Yes	Intramuscular	Anticoagulants
9	5.00	5.00	2.97		Yes	No	Intramuscular	Anticoagulants

patients exhibited high D-dimer levels, with an average score of 8.53 ± 0.18 , and the highest score recorded was 40.81 in the patient who developed PE on postoperative day 2 (Table 3).

Paired *t*-test was conducted on patients' preoperative and postoperative day 1 data, yielding a result of $P^* = 0.0144$. Unpaired *t*-test was performed on patients' preoperative, postoperative day 1, and postoperative day 14 data with the following results: preoperative vs. postoperative day 14 ($P^{****} < 0.0001$), postoperative day 1 vs. postoperative day 14 ($P = 0.4731$). Regrettably, the preoperative D-dimer analysis result for the patient with PE was unavailable.

In the postoperative period, 4 (44.4%) patients experienced vertigo and/or dizziness, while 4 (44.4%) patients exhibited head immobility and/or bed rest. In contrast, only 2 (22.2%) patients did not demonstrate such complications postoperatively (Table 3).

4. Discussion

VTE stands as the third most prevalent ailment within the global vascular society, trailing only heart attack and stroke in frequency. Each day numerous patients are diagnosed with this condition, and health-care professionals diligently seek optimal methods for its prevention and treatment (Benjamin et al., 2018). Various factors contribute to the occurrence of VTE, with commonly recognized causes encompassing extended periods of bed rest, prolonged surgery, a familial predisposition to VTE, lower limb fractures, etc. The annual incidence ranges from 300,000 to 600,000 cases, with a mortality rate ranging from 10% to 30% (Borst et al., 2015; Moneta and Foley, 2008). VTE can affect individuals of all races, ethnicities, age groups, and genders (Moneta and Foley, 2008), presenting a significant public health concern exacerbated by increasing risk factors, such as advanced age, immobility, surgery, and obesity (Beckman et al., 2010). Advancements in professional expertise and technology have facilitated the diagnosis and prevention of VTE.

Nevertheless, numerous aspects and potential outcomes of VTE remain insufficiently explored, and one such domain is the occurrence of VTE in patients undergoing otologic surgery. To date, few studies have concentrated on VTE in the context of otology surgery. Khyati et al.

(Kitajiri et al., 2001) reported a 35-year-old female patient who developed PE and experienced a fatal outcome five days after undergoing stapedectomy. In this context, findings were presented from a study spanning 3 years, detailing 9 cases of VTE following extracranial otologic surgery, including one case that resulted in PE.

Preoperative Caprini risk scores play a crucial role in predicting postoperative VTE in patients (Yago et al., 2020; Bartlett et al., 2020). The Caprini scoring system provides a consistent, comprehensive, and effective means of risk stratification and prophylaxis selection for preventing venous thrombosis (Gould et al., 2012). Despite its recognized utility, few studies have concentrated on the application of the Caprini scoring system in otologic patients. Song et al. (2019) indicated that the Caprini risk assessment model might overestimate the risk of VTE in patients undergoing extracranial otologic surgery, reporting zero VTE cases among 1213 otology surgical patients. In contrast, our case series demonstrated that postoperative Caprini risk scores were significantly higher than those in the preoperative period. The Caprini risk factor score emerges as an effective predictive marker for VTE development in otologic patients. Notably, the present study revealed that patients, initially categorized as having low or moderate VTE risk preoperatively, may transition to a high VTE risk in the postoperative period. This underscores the importance of recalculating risk factors in the perioperative period for effective VTE prevention and ensuring patient safety.

D-dimer levels are recognized as predictive markers for postoperative VTE (Samama et al., 2005; Shi et al., 2019). As a biomarker of fibrin formation and degradation, elevated D-dimer level has been independently associated with incident VTE, recurrent VTE, and mortality (Cohen et al., 2014; Cushman et al., 2003; Eichinger et al., 2003; Knowlson et al., 2010; Halaby et al., 2015). On one hand, a negative result of D-dimer (below the threshold value) aids in excluding VTE (Di Nisio et al., 2007; Adam et al., 2009). On the other hand, a positive D-dimer result alone is insufficient for a VTE diagnosis, necessitating additional imaging studies (including ultrasound or CTPA) for confirmation (Riley et al., 2016; Bates et al., 2012). In the present study, all patients exhibited elevated postoperative D-dimer level, with an average score of 8.53 ± 0.18 and the highest score reaching 40.81 in the patient who developed PE on postoperative day 2. Furthermore, 8 patients were

suspected of having VTE due to elevated postoperative D-dimer level and were subsequently diagnosed through further ultrasound or CTPA, despite the absence of related symptoms. Thus, the elevated postoperative D-dimer level may serve as a predictive factor for VTE in patients undergoing extracranial otologic surgery. For cases with the elevated D-dimer level after otologic surgery, additional imaging tests, such as deep vein ultrasound, may be necessary to rule out suspected VTE.

In addition, 44.4% of patients experienced vertigo and/or dizziness in the postoperative period, and an equal percentage (44.4%) exhibited head immobility and/or bed rest. In contrast, only 22.2% of patients did not encounter such complications during the postoperative period. This study demonstrated, for the first time, the proposition that vertigo, dizziness, head immobility, and bed rest could serve as potential predictive markers of postoperative VTE for otology patients. Hence, if patients present any of these mentioned risk factors, a comprehensive investigation for VTE is recommended to ensure their postoperative safety. Further research is warranted to obtain a more precise understanding of these associations.

However, certain limitations should be acknowledged in the present study. Firstly, the sample size was relatively small. Nonetheless, as this study introduced potential distinctive predictive markers of postoperative VTE for otology patients, valuable knowledge could be added to the current field. Secondly, this study is a case series, and future case-control studies are necessary to validate and further elucidate the predictive markers of VTE in extracranial otologic surgery.

Statement of ethics

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Authors' contributions

Davit A. Mazmanyan and Juanjuan Gao: Authorship of the original draft, acquisition of data, approval of all drafts, and accountability for accuracy of the final version. Weiwei Wu and Haijin Yi: Shaping of aims of the project, acquisition of data, approval of all drafts, and accountability for accuracy of the final version. Rongrong Zhu and Yu Yang: Shaping of aims of the project, acquisition of data, statistical analysis, and accountability for accuracy of the final version. Jiake Zhong and Junyan Chen: Acquisition of data and statistical analysis.

Declaration of competing interest

The authors declare that there is no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.joto.2024.01.001>.

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