Antithrombotic Therapy for Venous Thromboembolism and Prevention of Thrombosis in Otolaryngology–Head and Neck Surgery: State of the Art Review

John D. Cramer, MD¹, Andrew G. Shuman, MD², and Michael J. Brenner, MD²

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

Abstract

Objective. The aim of this report is to present a cohesive evidence-based approach to reducing venous thromboembolism (VTE) in otolaryngology–head and neck surgery. VTE prevention includes deep venous thrombosis and pulmonary embolism. Despite national efforts in VTE prevention, guidelines do not exist for otolaryngology–head and neck surgery in the United States.

Data Sources. PubMed/MEDLINE.

Review Methods. A comprehensive review of literature pertaining to VTE in otolaryngology–head and neck surgery was performed, identifying data on incidence of thrombotic complications and the outcomes of regimens for thromboprophylaxis. Data were then synthesized and compared with other surgical specialties.

Conclusions. We identified 29 articles: 1 prospective cohort study and 28 retrospective studies. The overall prevalence of VTE in otolaryngology appears lower than that of most other surgical specialties. The Caprini system allows effective individualized risk stratification for VTE prevention in otolaryngology. Mechanical and chemoprophylaxis (“dual thromboprophylaxis”) is recommended for patients with a Caprini score ≥7 or patients with a Caprini score of 5 or 6 who undergo major head and neck surgery, when prolonged hospital stay is anticipated or mobility is limited. For patients with a Caprini score of 5 or 6, we recommend dual thromboprophylaxis or mechanical prophylaxis alone. Patients with a Caprini score ≤4 should receive mechanical prophylaxis alone.

Implications for Practice. Otolaryngologists should consider an individualized and risk-stratified plan for perioperative thromboprophylaxis in every patient. The risk of bleeding must be weighed against the risk of VTE when deciding on chemoprophylaxis.

Keywords

deep vein thrombosis, pulmonary embolus, DVT, PE, VTE, thromboprophylaxis, chemoprophylaxis, otolaryngology, patient safety, quality improvement, anticoagulation, enoxaparin, heparin, head and neck cancer, guidelines, complications

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Venous thromboembolism (VTE) includes deep venous thrombosis (DVT) and pulmonary embolism (PE). VTE is the number one cause of preventable death among perioperative patients.¹ VTE causes approximately 150,000 to 200,000 deaths each year in the United States.² Approximately one-third of these deaths occur after surgery.² Ten percent of patients who suffer a PE will die within the first hour of onset.³ If untreated, up to 30% will die of acute PE, whereas the death rate of treated PE is 8%.³ VTE causes significant morbidity in addition to mortality. Among patients with PE, 5% will develop cardiac dysfunction in the form of right heart strain that may progress to right heart failure.⁴ Postthrombotic syndrome will develop in the lower extremities of 20% to 50% of patients with DVT.⁵ Prevention, early recognition, and treatment of VTE can minimize associated morbidity and mortality.

VTE can be prevented for many hospitalized patients through mechanical and/or chemoprophylaxis with low-dose enoxaparin or heparin.⁶ VTE is coming under increasing scrutiny from multiple stakeholders. The Agency for

¹Department of Otolaryngology–Head and Neck Surgery, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, USA
²Department of Otolaryngology–Head and Neck Surgery, School of Medicine, University of Michigan, Ann Arbor, Michigan, USA

Corresponding Author:
Michael J. Brenner, MD, Department of Otolaryngology–Head and Neck Surgery, School of Medicine, University of Michigan, 1500 East Medical Center Drive, SPC 5312, 1904 Taubman Center, Ann Arbor, MI 48109-5312, USA.
Email: mbren@med.umich.edu
Healthcare Research and Quality identified VTE prevention as the number one strategy to improve patient safety in the hospital. Major VTE prevention initiatives are underway by the Joint Commission on Accreditation of Health Care Organizations, the US Surgeon General, the National Quality Forum, and the Center for Medicare and Medicaid Services, the last of which now considers it to be a pay-for-performance measure.

To provide evidence-based recommendations, the American College of Chest Physicians (ACCP) published guidelines for the prevention of VTE in surgical patients. These guidelines tailor recommendations to individual surgical specialties; however, these guidelines do not include recommendations for otolaryngology–head and neck surgery (OHNS). Data suggest that the risks and benefits of VTE prevention in OHNS may differ from other surgical fields. Similar to the ACCP guidelines, the ENT.UK guidelines recommend risk assessment and consideration of dual mechanical and chemoprophylaxis for patients at high risk. However, there is little evidence in the literature supporting the ENT.UK risk assessment methodology, and it has been criticized for failing to reflect practice, making the guidelines poor candidates for more widespread adoption. However, there are limited high-level data comparing the risk and benefits of different VTE prevention strategies in OHNS.

While many institutions have broad policies for perioperative risk stratification and prevention of VTE, otolaryngologists retain discretion on their implementation, especially given the dearth of specialty-specific recommendations. In a survey of otolaryngologists, 88% believed that guidelines for the prevention of VTE would be useful. Compliance with protocols that rely on risk stratification is challenging and requires buy-in from a number of stakeholders. In an OHNS department that used a risk stratification approach, 69% of patients were compliant with recommendations. Integration of computerized clinical decision support systems into the

### Table 1. Guidelines for VTE Prevention.\(^a\)

<table>
<thead>
<tr>
<th>Risk factors for VTE</th>
<th>Mobility reduced for ( \geq 3 ) d</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Total anesthetic time ( \geq 90 ) min</td>
</tr>
<tr>
<td></td>
<td>Active cancer</td>
</tr>
<tr>
<td></td>
<td>Age ( \geq 60 ) y</td>
</tr>
<tr>
<td></td>
<td>Critical care admission</td>
</tr>
<tr>
<td></td>
<td>Dehydration</td>
</tr>
<tr>
<td></td>
<td>Known thrombophilia</td>
</tr>
<tr>
<td></td>
<td>Obesity (BMI ( \geq 30 ))</td>
</tr>
<tr>
<td></td>
<td>( \geq 1 ) medical comorbidities (eg, heart disease; metabolic, endocrine, or respiratory pathology; acute infectious disease; inflammatory condition)</td>
</tr>
<tr>
<td></td>
<td>History of first-degree relative with VTE</td>
</tr>
<tr>
<td></td>
<td>Use of hormone replacement therapy</td>
</tr>
<tr>
<td></td>
<td>Use of estrogen-containing contraception</td>
</tr>
<tr>
<td></td>
<td>Varicose veins with phlebitis</td>
</tr>
<tr>
<td>If no risk factors</td>
<td>No VTE prophylaxis required</td>
</tr>
<tr>
<td>If risk factors for VTE</td>
<td>Encourage early mobilization</td>
</tr>
<tr>
<td></td>
<td>Offer patient graduated compression stockings</td>
</tr>
<tr>
<td></td>
<td>Consider intermittent pneumatic compression device when immobile</td>
</tr>
<tr>
<td></td>
<td>Assess for bleeding risk factors</td>
</tr>
</tbody>
</table>

**Assess patient for bleeding risk factors**

<table>
<thead>
<tr>
<th>Risk factors for bleeding</th>
<th>Active bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Acquired bleeding disorder (eg, acute liver failure)</td>
</tr>
<tr>
<td></td>
<td>Anticoagulation</td>
</tr>
<tr>
<td></td>
<td>Lumbar puncture, epidural, or spinal anesthesia expected within next 12 h</td>
</tr>
<tr>
<td></td>
<td>Acute stroke</td>
</tr>
<tr>
<td></td>
<td>Thrombocytopenic (platelets ( &lt;75,000 ))</td>
</tr>
<tr>
<td></td>
<td>Uncontrolled hypertension (BP ( \geq 230/120 ))</td>
</tr>
<tr>
<td></td>
<td>Untreated inherited bleeding disorder (eg, hemophilia, von Willebrand's disease)</td>
</tr>
<tr>
<td>If no risk of bleeding</td>
<td>Offer patient chemoprophylaxis for VTE</td>
</tr>
<tr>
<td>If bleeding risk factors</td>
<td>Do not give chemoprophylaxis</td>
</tr>
<tr>
<td></td>
<td>Review if bleeding risk has changed in 24 h</td>
</tr>
</tbody>
</table>

**Abbreviations:** BMI, body mass index; BP, blood pressure; VTE, venous thromboembolism.

\(^a\)Adapted from ENT.UK (http://www.entuk.org).
The high-quality metric (Figure 1, Table 2). Appendix Table S1 (available in the online version of the article) summarizes the results from the 29 studies. Many studies on VTE in OHNS were limited by small sample size, retrospective designs, short time horizons (<30 days), without information on VTE that occurred after hospital discharge, and had missing or incomplete information about the type of prophylaxis received.

Discussion

Incidence of VTE in OHNS

The interpretation of the incidence of VTE in individual studies is challenging, as VTE depends on a number of patient-, procedure-, and study-related factors. All VTE incidence studies in OHNS have inherent limitations that influence the assessment of actual risk. Studies in OHNS reported widely varying rates of VTE, from 0% to 26%. When synthesized, the extant literature suggests that the overall rate of VTE is low (<1%). A systematic review and meta-analysis of 23 studies of VTE in OHNS identified an incidence of 0.4%, consistent with a very-low-risk population. However, this study was criticized for including outpatient and inpatient surgery and specific populations in OHNS that may not reliably represent the broader population. Since the analysis did not examine patients with a risk stratification system, it necessarily underestimates and oversimplifies the incidence of VTE. The focus of intervention is in the inpatient arena, as VTE occurs at a 150-fold-greater rate for hospitalized patients. Among perioperative OHNS inpatients, incidence of VTE may be higher.

Two studies used universal DVT screening to estimate the rates of VTE in OHNS. In the only prospective study of VTE in OHNS, Clayburgh et al performed universal lower extremity duplex ultrasound screening of 100 patients undergoing major head and neck surgery who were at high risk of VTE (Caprini score >5). The authors identified a 13% rate of VTE (8% rate of symptomatic VTE, including 7% DVT and 1% PE). The incidence of VTE observed was significantly higher than in other series, but there are several contributing factors to consider. All patients were at high risk (Caprini score >5) and underwent long and complex procedures (80% underwent free tissue transfer), and there was scant use of chemoprophylaxis. In a similar study, Kakei et al examined 133 patients undergoing free or regional flap reconstruction of the oral cavity with universal lower extremity duplex ultrasound on postoperative day 2. The authors identified a 26% rate of VTE, and the majority of these were superficial DVTs. The rate of symptomatic VTE was not reported. In the absence of chemoprophylaxis, the rate of asymptomatic DVT ranges from 10% to 80% in different groups. Thus, even those the rates in this study are higher than those observed in studies in OHNS, the rates remain on the lower end of the spectrum, and the clinical impact remains uncertain.

We identified 5 high-quality studies in OHNS, 4 of which focused on head and neck surgery. The overall rate

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of symptomatic VTE in these studies was 1.5% (95% CI, 1.1%-1.8%; Table 2). While this remains consistent with a low-risk field, this is 3-fold higher than what was reported in the aforementioned meta-analysis.¹⁰

**VTE Risk Factors**

Patient risk factors and procedural characteristics interact to create a risk for VTE. The UK Million Women Study demonstrated that relative risk of VTE was 110-fold above baseline after inpatient surgery and 10-fold above baseline after outpatient surgery.²² After outpatient surgery, there is a 19-fold variation in the rate of VTE in different groups, with some having up to a 1.2% risk of VTE.²³ While these data suggest that a population of outpatient surgical patients might benefit from additional prevention strategies, the role in OHNS remains unknown, and it is difficult to power a study, given the low incidence.

Patient risk factors include age, cancer, prior VTE, family history of VTE, prothrombotic predisposition, Charlson comorbidity score, lung disease, recent stroke, central venous access, sepsis, pregnancy, and inpatient hospital stay >2 days.²⁴-²⁶ Cancer is an established risk factor for VTE, but the level of risk depends on the type of cancer. Cramer et al identified that patients with cancers of the upper aerodigestive tract had an 11-fold greater rate of VTE than patients with thyroid malignancy.²⁷ In this study, patients with thyroid and salivary gland malignancy experienced a lower incidence of VTE; those with cancers of the skin had intermediate rates; and those with cancers of the upper aerodigestive tract demonstrated high rates.²⁷ There is no validated risk stratification system that distinguishes type of malignancy. Furthermore, it remains speculative whether this risk is driven by cancer biology, underlying differences in patient characteristics, procedure type, or associated risk factors (eg, immobility).

Procedure-specific risk factors are linked to length of hospital stay and ability to ambulate. One challenge in creating VTE prevention recommendations for OHNS is the tremendous variety of procedures within the field. Several studies identified free tissue transfer as being associated with higher rates of VTE.²⁷,²⁸ Regional tissue transfer appears to have similar rates of VTE as free tissue transfer.²⁹ Analysis of data from 31,896 patients in the National Surgical Quality Improvement Program identified a 10-fold variation in the rate of VTE based on the type of procedure.²⁷ This study identified a subgroup at high risk of VTE based on procedure type, including major head and neck surgery (free or regional tissue transfer, laryngectomy, oral cavity composite resection), skull base surgery, and incision and drainage of an abscess.²⁷ These operations resulted in a prolonged hospital stay after surgery (mean length of stay, 9 days). Therefore, postoperative OHNS patients with a prolonged hospital stay may resemble patients from higher-risk surgical fields, where more aggressive prevention strategies for VTE have proven efficacious.⁸

### Table 2. Incidence of VTE in High-Quality Studies in Otolaryngology–Head and Neck Surgery²

<table>
<thead>
<tr>
<th>First Author (Year)</th>
<th>Study Type</th>
<th>Size, n</th>
<th>Population</th>
<th>Prophylaxis, %</th>
<th>Symptomatic VTE, % (95% CI)</th>
<th>Capiri Risk-Adjusted VTE, % (95% CI)</th>
<th>Capiri Bleeding Complication, %</th>
<th>Bleeding Complication, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bahl (2010)²⁴</td>
<td>Retrospective cohort study</td>
<td>3498 Inpatient, all OHNS</td>
<td>100, mechanical; 42, chemoppx</td>
<td>1.3 (1.0-1.7)</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td></td>
</tr>
<tr>
<td>Clayburgh (2013)¹⁶</td>
<td>Prospective single-center study</td>
<td>100 Inpatient, major head and neck</td>
<td>100, mechanical; 14, chemoppx</td>
<td>8 (4.1-15.0)</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td></td>
</tr>
<tr>
<td>Thai (2013)⁴¹</td>
<td>Single-center case series with chart review</td>
<td>134 Inpatient, free flaps</td>
<td>80%, free flaps</td>
<td>15 (0.3-9.9)</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td></td>
</tr>
<tr>
<td>Sinha (2017)²⁹</td>
<td>Single-center case series with chart review</td>
<td>517 Inpatient, free or regional flaps</td>
<td>517, mechanical; 100, chemoppx</td>
<td>1.7 (0.9-3.3)</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td></td>
</tr>
<tr>
<td>Lodders (2015)⁴²</td>
<td>Single-center case series with chart review</td>
<td>233 Inpatient, oral cavity cancer</td>
<td>233, mechanical; 100, chemoppx</td>
<td>100, mechanical; 100, chemoppx</td>
<td>1 (0.1-2.4)</td>
<td>Not reported</td>
<td>Not reported</td>
<td></td>
</tr>
<tr>
<td>Overall rate</td>
<td>Mixed</td>
<td>4615 Mixed</td>
<td>Mixed</td>
<td>100, mechanical; 100, chemoppx</td>
<td>1 (0.1-1.1)</td>
<td>1 (0.1-1.1)</td>
<td>1 (0.1-1.1)</td>
<td></td>
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</tbody>
</table>

Abbreviations: ASA, aspirin; chemoppx, chemoprophylaxis; OHNS, otolaryngology–head and neck surgery; SQH, subcutaneous heparin; VTE, venous thromboembolism.

Observation period per study: 30 days.
VTE Risk Stratification

An appreciation for the interaction of patient and procedural risk factors led to the development of risk stratification systems that reliably predict for patients at high risk of VTE. Risk stratification is crucial for VTE prevention. The ACCP guidelines support personalized VTE risk stratification based on individual characteristics. The 2 major risk scoring systems to select patients at high risk for VTE are the Caprini and Rogers systems. The Caprini scoring system is more widely used and user-friendly. The Rogers scoring system is not discussed here, as it has not been evaluated in OHNS.

The Caprini risk assessment model uses 40 preoperative patient characteristics to create an overall risk score (Table 3). Caprini scores can be used to guide management on the type of prophylaxis for VTE. The ACCP recommends different thresholds for initiating chemoprophylaxis based on the procedural risk factors for individual surgical specialties. OHNS is not included in these recommendations.

The Caprini risk scoring has been validated in 5 studies in the OHNS population (Table 4). In these studies, the Caprini scoring system reliably predicts patients at high risk for VTE. OHNS patients with a Caprini score ≥8 had a 10% to 33% incidence of VTE without chemoprophylaxis versus 0% to 0.5% for those with a Caprini score <6. These rates are lower than those for patients with similar Caprini scores in other surgical specialties but indicate that Caprini scores can be successfully used to identify patients at risk for VTE. One study compared the rate of VTE in OHNS with that in general surgery and plastic surgery. It indicated that the rate of VTE in OHNS is significantly lower than both general surgery and plastic surgery.

The Caprini risk assessment model has several limitations when applied to OHNS. For example, open surgery is simply classified as <45 minutes or >45 minutes in duration and there is no further risk stratification for procedures that may take >8 hours that can be common in major head and neck surgery. Increased operative time is clearly associated with risk of VTE. Harvesting of tissue for reconstruction from extremities that are immobilized postoperatively may also increase the risk of VTE.

Risks and Benefits of VTE Prevention

The need for a comprehensive and thoughtful VTE prevention strategy is clear. In OHNS, VTE is associated with a 14-fold-higher 30-day mortality (5.1% with VTE vs 0.4% without), and this risk is modifiable. Figure 2 outlines our recommended approach for VTE prevention in OHNS.

Preoperative Evaluation and Risk Modification

Preoperative evaluation begins with a complete assessment, including risk stratification. Many preoperative clinics routinely calculate Caprini scores to help with risk stratification and perioperative decision making. Examination of the Caprini risk score reveals that many of the 40 risk factors are potentially modifiable. Obesity, oral contraceptive use,
and central venous lines (eg, chemotherapy ports) are all risk factors that may be optimized prior to elective surgery. General anesthesia, specifically with paralysis, further predisposes to venous stasis and VTE. Adopting alternatives to general anesthesia and avoidance of paralytics should be considered when possible. Finally, the duration of surgery should be minimized, as prolonged anesthesia correlates with VTE. Very-high-risk patients may benefit from preoperative hematology consultation, such as those with prior VTE and those with suspected heritable coagulopathy or known prothrombotic mutations.

**Mechanical Prophylaxis**

Two main forms of mechanical prophylaxis exist: elastic stockings and sequential compression devices (SCDs). A meta-analysis examined the benefit of SCDs and found that they reduce the risk of proximal DVT by 50%. Elastic stockings are also effective at preventing VTE. However, guidelines prefer SCDs to elastic stockings for 2 reasons. First, the incidence of skin complications associated with elastic stockings is significant (5.3% with stockings vs 1.3% without). Second, SCDs appear superior to elastic stockings in prevention of VTE. However, adherence to and compliance with SCDs throughout the hospital stay are often limited.

No studies have specifically examined the risk reduction of VTE with mechanical prophylaxis in OHNS. However, data from other fields appear compelling to inform recommendations, particularly in light of the small consequences and risks thereof, with the exception of cost.

**VTE Chemoprophylaxis in OHNS**

Numerous randomized controlled trials in heterogeneous general, urologic, and orthopedic surgical populations proved the effectiveness of chemoprophylaxis. Low-dose unfractionated heparin reduced the odds of fatal PE by 47% and the odds of death by 18%. Similarly, low-dose low-molecular-weight heparin reduced the risk of PE by 70%.

There are no prospective studies examining the effectiveness of chemoprophylaxis in OHNS. A retrospective single-center cohort study revealed the misleading conclusions that can arise from failing to stratify risk in OHNS. When considering all OHNS patients, the authors found no difference in the rate of VTE between those with chemoprophylaxis (1.2%) and those without (1.3%). However, for patients with a Caprini score >7, those given prophylaxis were less likely to have VTE (5.3% vs 10.4%). Similarly, after free tissue transfer regardless of Caprini score, chemoprophylaxis was associated with a decreased risk of VTE (2.1% vs 7.7%).

No studies have directly compared the timing of chemoprophylaxis initiation in OHNS. Plastic surgical recommendations suggest initiating chemoprophylaxis at 6 to 8 hours after surgery and continuing until discharge from the hospital. When chemoprophylaxis is given, there is no evidence that pre- or intraoperative initiation of chemoprophylaxis is
superior to postoperative prophylaxis in a similar-risk surgical population. In very-high-risk surgical fields, such as hip fracture and joint replacement, patients are considered for extended-duration chemoprophylaxis that is continued after discharge from the hospital. We identified no studies that examined extended-duration chemoprophylaxis in OHNS. Further research may help to determine if very-high-risk or otherwise selected patients might benefit from continuation of chemoprophylaxis after discharge.

No studies have directly compared different forms of chemoprophylaxis in OHNS. In the absence of such studies, we recommend basing decisions on the ACCP guidelines, which recommend either low-dose low-molecular-weight heparin or low-dose unfractionated heparin.

### Risks of VTE Chemoprophylaxis

There is controversy regarding the risk of bleeding complications associated with perioperative chemoprophylaxis. A meta-analysis reported that unfractionated heparin is associated with a 57% increase in the rate of nonfatal bleeding. In the OHNS population, several studies similarly identified that use of chemoprophylaxis is associated with an increased risk of bleeding. Bahl et al found that bleeding complication risk was 3.5% for patients given chemoprophylaxis versus 1.2% for those not given it. The same study reported that chemoprophylaxis increased the risk of a bleeding complication after free tissue transfer (11.9% with vs 4.5% without).

Achieving an appropriate balance between bleeding risk and VTE is problematic. Proportionality of harm is a critical consideration. Thromboprophylaxis may result in hematoma that may necessitate reoperation, but it is rarely fatal; flap viability or airway concerns are certainly necessary to consider for selected patients. However, VTE that progresses to PE may be fatal for 30% of patients if untreated and is thus a similarly dire albeit rare situation.

### Rationale for Final Recommendations

Table 5 summarizes our recommendations for VTE prophylaxis in OHNS. These emphasize adapting current ACCP clinical practice guidelines from other surgical specialties to the unique aspects of OHNS. While the overall body of evidence in otolaryngology is limited, studies comparing the incidence of VTE between plastic surgery and OHNS indicate similar risk of VTE. The mortality risk associated with VTE exceeds that from bleeding complication, thus informing our choice of a Caprini score as a threshold for dual prophylaxis.

In keeping with our strategy to adapt ACCP guidelines to OHNS, we also recommended consideration of

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**Figure 2. Pathway for venous thromboembolism (VTE) prevention. OHNS, otolaryngology–head and neck surgery.**

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chemoprophylaxis or mechanical prophylaxis alone for patients with an intermediate risk of VTE (Caprini score, 5 or 6). This gray zone gives patients and surgeons some flexibility in weighing the risks of VTE versus bleeding based on the type of surgery. Future research efforts on this intermediate risk will also be helpful to guide refinements in recommendations.

**Special Considerations**

Patients undergoing skull base surgery have an elevated risk of VTE but may also be at risk for complications from intracranial bleeding. Many such patients are jointly managed with neurosurgery, and VTE prevention guidelines for neurosurgery as summarized by the ACCP will often take precedence. Patients undergoing skull base surgery have a risk profile for VTE similar to that of patients undergoing major head and neck surgery, complicating decisions on VTE prophylaxis.\(^5\) ACCP guidelines for neurosurgery recommend mechanical prophylaxis when there is a high risk of major complication from bleeding, with chemoprophylaxis to be initiated once the risk of bleeding diminishes.\(^6\) If a patient having neurosurgery is at low risk of major bleeding-related complications, however, the ACCP guidelines recommend dual mechanical and chemoprophylaxis for a Caprini score \(\geq 5\) (and consideration of chemoprophylaxis for patients with a Caprini score of 3 or 4).\(^6\) There is limited guidance on how to determine when the risk of bleeding has sufficiently diminished such that chemoprophylaxis can be safely started. Decisions about whether and when to start chemoprophylaxis must be individualized after discussion among members of the skull base team.

**Implications for Practice**

Patients undergoing OHNS will benefit from a cohesive specialty-specific approach for prevention of VTE. Risk stratification based on the Caprini model allows surgeons to identify those patients who are most likely to benefit from chemoprophylaxis. The difficulty in adapting current guidelines to OHNS belies a dearth of data and the diversity of the specialty. Nonetheless, data from studies within otolaryngology provide a rational basis for identifying patients most likely to benefit from dual thromboprophylaxis. The approach presented herein is informed by these specialty-specific data and by the experience of other surgical fields.

**Author Contributions**

**John D. Cramer**, conception and design, drafting, analysis, interpretation of data, revising critically, final approval; agree to be accountable; **Andrew G. Shuman**, interpretation of data, revising work critically, final approval; agree to be accountable; **Michael J. Brenner**, conception and design, analysis, interpretation of data, revising work critically, final approval; agree to be accountable.

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**Supplemental Material**

Additional supporting information is available in the online version of the article.

**References**


*Note that studies based on references 43-61 are detailed in the online appendix.*