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WILEY
When Should Therapeutic Anticoagulation Be Restarted Following Major Head and Neck Surgery?

Ashok R. Jethwa, MD; Samir S. Khariwala, MD, MS

BACKGROUND

Each year in the United States, approximately 250,000 patients are faced with a challenging situation regarding the periprocedural management of their anticoagulation and antiplatelet medications.1 The most common of these medications include aspirin, warfarin, and clopidogrel. However, several new oral anticoagulants including rivaroxaban, apixaban, and dabigatran, among others, have emerged. Head and neck cancer surgeries are considered high-risk bleeding procedures, and thus, the decision to resume these medications following surgery must be made thoughtfully.1,2 Several studies have demonstrated an increased risk of venous and arterial thromboembolism during lapses in these medications.1 Conversely, earlier resumption of these medications can increase the risk of postoperative hemorrhage and hematoma. The development of these complications in a patient who has undergone major head and neck surgery can be a significant setback and may result in prolonged hospitalization, airway distress, wound complications, and need for transfusions. Currently, clarity is lacking among head and neck surgeons regarding the optimal timing of restarting anticoagulation following head and neck surgery. Thus, we sought to review the existing literature addressing periprocedural resumption of anticoagulant/antiplatelet medications.

LITERATURE REVIEW

Anticoagulant Agents

Long-term anticoagulation is typically performed using the oral vitamin K antagonist, warfarin.3 Warfarin acts by inhibiting the enzyme vitamin K epoxide reductase. This interferes with the development of the vitamin K dependent coagulation factors II, VII, IX, X, and protein C and S. The full antithrombotic effect of warfarin is not achieved for several days. There is limited literature within head and neck surgery regarding the optimal time to resume warfarin postoperatively. However, the American College of Chest Physicians has released guidelines on this topic based on a systematic review. In their most recent edition, it is recommended that warfarin be resumed 12 to 24 hours after surgery and when there is adequate hemostasis.3 Douketis et al. investigated the rates of complications in a prospective cohort of 650 patients with atrial fibrillation, mechanical heart valve, or embolic stroke who required cessation of warfarin before surgery. One hundred eight patients underwent high risk bleeding procedures (including a small proportion undergoing head/neck surgery) and were routinely restarted on warfarin on the evening of surgery as long as there was adequate hemostasis.2 The authors suggested restarting of warfarin on the day of surgery without bridging via low-molecular-weight heparin following high bleeding-risk surgery.

Newer oral anticoagulants include rivaroxaban, apixaban, and dabigatran. Dabigatran is a direct factor II inhibitor, whereas rivaroxaban and apixaban are direct factor X inhibitors. These medications have a short onset of action (1–3 hours). In patients undergoing high-risk bleeding surgery, rivaroxaban, apixaban, and dabigatran should be resumed 2 to 3 days postoperatively.1 Schulman et al. investigated a group of 541 patients who required interruption of dabigatran for surgery and looked at perioperative complications. Forty percent of these patients underwent high-risk bleeding procedures such as abdominal surgery, orthopedic surgery, neurosurgery, pacemaker insertion, urologic surgery, or neck surgery.4 Their protocol was to resume dabigatran after 48 to 72 hours in those patients undergoing high-risk bleeding procedures. In their study, 10 (1.8%) patients had major bleeding complications.5 In patients at high risk of thromboembolism, resumption of these medications at a reduced dose on the evening after surgery is a reasonable consideration. A study that
investigated patients undergoing orthopedic surgery demonstrated that there was no increased risk of postoperative bleeding in those receiving reduced-dose dabigatran on the evening after surgery compared to enoxaparin for thromboembolism prophylaxis.\(^1\)

**Antiplatelet Agents**

Oral antiplatelet drugs are commonly initiated after coronary angioplasty and stenting. In Western countries, more than 2 million patients per year undergo coronary artery dilation, and 90% of them require stenting.\(^5\) Dual antiplatelet therapy is indicated in the high-risk period after stent insertion to reduce the risk of stent occlusion and restenosis.\(^5\) The high-risk period can be up to, or even longer than, 12 months.\(^5\) Aspirin and Plavix are the most common antiplatelet agents used.\(^5\) Aspirin permanently inactivates cyclooxygenase, and thus the antiplatelet effect lasts the entire life span of the platelet, approximately 8 to 10 days.\(^5\) Clopidogrel irreversibly inhibits the P2Y\(_{12}\) platelet receptor, which disrupts platelet aggregation. Aspirin is rapidly absorbed, and its antiplatelet effects are evident 1 hour after ingestion.\(^5\) Maximum platelet inhibition after clopidogrel administration occurs in 12 to 15 hours.\(^3,5\) In situations in which aspirin and/or clopidogrel have been held, it is recommended that they are restarted 24 hours after surgery.\(^3,5\) In the Douketis et al. study described above, those patients on antiplatelet medications, including aspirin and clopidogrel, resumed their antiplatelet medication on postoperative day 1.\(^2\) Other studies have reported a similar protocol for resumption of antiplatelet medications.\(^3\)

Given that much of head and neck surgery is performed on cancer patients who are inherently hypercoagulable, it is worthwhile to determine the impact, if any, of a cancer diagnosis and hypercoagulable state on decisions regarding restarting anticoagulation. The data cited above include a subset of patients with cancer diagnoses. Although there is no specific literature examining the importance of cancer-related hypercoagulability in anticoagulation-related decision making, the guidelines described below (Table I) can be expected to result in fewer bleeding complications in cancer patients as a result of the hypercoagulable state.

**BEST PRACTICE**

Head and neck surgeries are considered high-risk bleeding procedures. It is recommended that warfarin be resumed 12 to 24 hours after surgery; rivaroxaban, apixaban, and dabigatran can be resumed 2 to 3 days postoperatively; aspirin and clopidogrel can be resumed 24 hours after surgery.

**LEVEL OF EVIDENCE**

The appropriate time to resume therapeutic anticoagulation in major head and neck surgery is based on level 2 to 4 evidence.

**BIBLIOGRAPHY**


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**TABLE I.**

Postoperative Resumption of Antiplatelet and Anticoagulant Medications.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Recommended Time to Resume</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin</td>
<td>Resume 12 to 24 hours after surgery*</td>
</tr>
<tr>
<td>Rivaroxaban, apixaban, and dabigatran</td>
<td>Resume 2 to 3 days after surgery</td>
</tr>
<tr>
<td>Aspirin</td>
<td>Resume 24 hours after surgery</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>Resume 24 hours after surgery</td>
</tr>
</tbody>
</table>

*Can consider starting a reduced dose immediately after surgery in patients at high risk of thromboembolism.*