Analysis of Postoperative Bleeding and Risk Factors in Transoral Surgery of the Oropharynx

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IMPORTANCE With an increasing incidence of oropharyngeal carcinoma and prevalence of transoral surgical techniques, postoperative bleeding, with its associated risk factors, deserves evaluation.

OBJECTIVE To classify and review postoropharyngectomy hemorrhage rates and associated risk factors.

DESIGN, SETTING, AND PARTICIPANTS Single-institution, multicenter retrospective medical chart review analyzing surgical procedures in 906 patients treated with transoral surgery for oropharyngeal carcinoma at a tertiary care, academic referral center from 1994 to 2012. Tumor stage, previous treatment, resection method, and transcervical external carotid branch ligation were analyzed in relationship to postoperative hemorrhage rate, and severity. A novel classification system was created, grading bleeding episodes as minor, intermediate, major, or severe based on management method and related sequelae.

RESULTS Postoperative bleeding occurred in 5.4% of patients (49 of 906) with 67.3% of these (33 of 49) requiring operative intervention. Severe bleeding episodes were very rare (1.1% of patients). Transcervical external carotid system vessel ligation was performed with the primary resection in 15.6% of patients with no overall difference in bleeding rate or severity of bleeding in patients who underwent ligation vs those who did not (P = .21 and P = .66, respectively). Vessel ligation was performed more frequently in patients with a higher T stage (P = .002). In previously treated patients, severity of bleeding was decreased if vessels were ligated (P > .05). Higher T-stage tumors had a higher bleeding rate (P = .02). Bleeding rates were similar between those treated with laser (5.6%) and robotic (5.9%) oropharyngectomy (P = .80); however, patients with significantly higher T-stage tumors were treated with laser vs robot techniques (P < .001).

CONCLUSIONS AND RELEVANCE Transoral resection of oropharyngeal carcinoma is safe, and severe life-threatening hemorrhage is rare. Although transcervical vessel ligation did not result in an overall decrease in bleeding rate, there is a trend toward reduced postoropharyngectomy bleeding severity with ligation. We recommend ligation for higher T-stage tumors, primary tonsil tumors, and patients undergoing revision surgery.
Head and neck squamous cell carcinoma (SCC) represents the sixth most common cancer diagnosed worldwide. While the incidence of cancer in all non-oropharyngeal subsites has been steadily decreasing, over the past few decades, incidence of oropharyngeal squamous cell carcinoma (OPSCC) has been increasing. This has resulted in the identification of a causative relationship between human papillomavirus and OPSCC. Human papillomavirus-associated OPSCC presents in younger patients with less correlation to tobacco use, responds more effectively to current treatment modalities, and has high disease-specific and overall survival rates.

Transoral surgery (TOS) has been well established as a safe, effective treatment modality for cancer of the upper aerodigestive tract, yielding excellent functional and oncologic outcomes. Additional advantages of TOS techniques include shorter length of hospitalization, decreased patient morbidity, and lower surgical complication rates. Initial descriptions utilizing electrocautery and diathermy were further expanded as laser dissection methods or transoral laser microsurgery (TLM) was recognized. More recently, transoral robotic surgery (TORS) has been popularized. The use of both TLM and TORS to treat the increasing numbers of palatine tonsil and tongue base SCC has been well documented.

Surgical complications, including bleeding, trismus, dysphagia, aspiration, taste disturbance, and infection, can occur as a result of both the traditional open approach and transoral oropharyngectomy. Post–transoral surgery hemorrhage is unpredictable and potentially catastrophic, with published rates for all head and neck subsite malignant neoplasms of 1.4% to 9%. Bleeding rates following transoral oropharyngectomy of 3% to 10% have been documented, which correlate with published postoperative tonsilllectomy bleeding rates of 0.5% to 10%. A direct correlation between previous cancer treatment (surgery or radiation therapy) and all head and neck subsite bleeding rates has been shown. Whether external carotid artery branch ligation at the time of TOS (typically performed with concurrent neck dissection) has any effect on surgical outcomes is still under investigation.

### Methods

Institutional review board approval from the Mayo Clinic Arizona was obtained, and a secure database was created that included 906 patients with oropharyngeal cancer treated from May 12, 1994, to May 31, 2012. Patients undergoing transoral oropharyngectomy (TLM, TORS, or handheld electrocautery) with or without previous cancer treatment at Mayo Clinic sites in Phoenix, Arizona; Rochester, Minnesota; and Jacksonville, Florida; were included. Patients were excluded if they underwent an open cancer resection, the defect required reconstruction, or they lacked follow-up data. Standard, informed written consent was received at the time of surgery. Data collection included patient demographics, tumor pathologic findings, location and T stage, surgical technique, external carotid branch vessel ligation, and presence of postoperative bleeding with its associated severity and management.

Postoperative hemorrhage was graded, using a newly created classification system, as minor, intermediate, major, or severe. This was based on quantity of blood loss, type of surgical management required, and development of life-threatening complications or need for emergent life-saving intervention (Table 1).

### Results

All 906 patients met inclusion criteria, with 4 surgeons performing 87.5% of all procedures (793 of 906). The average age was 59 years, and 83% were male and 17% were female. Previous treatment was documented in 7.6% of all patients (69 of 906) with 58 previously treated with irradiation and 11 undergoing revision surgery. Primary tumor T stage was documented according to the 2010 American Joint Committee on Cancer (AJCC) TNM staging system. Of the 906 patients reviewed, 36.4% had stage T1 tumors; 41.6%, stage T2; 14.9%, stage T3; and 7.2%, stage T4. All of the resections were performed transorally without reconstruction. When appropriate, neck dissection and vessel ligation were performed concurrently with primary site resection. Significantly higher T stages were treated with TLM when compared with TORS with pairwise comparison methods. This was seen when looking at the group with stage T1 tumors vs the group with stage T3 tumors (P < .001) and the group with stage T2 tumors vs the group with stage T3 tumors (P < .001).

All 906 primary tumors were located in the oropharynx, with a specific subsite documented in 88.5% of patients (802 of 906). When the tumors were documented, we found most to be located in the palatine tonsil (51.0%) followed by location in the tongue base (46.0%), with the remaining 3.0% located in the soft palate or pharyngeal wall. Pathologic results were present in all 906 patients, showing SCC in 97.8%, with the remaining 18 cases consisting of mucoepidermoid carcinoma (7), lymphoma (4), adenocarcinoma (3), adenoïd cystic carcinoma (2), and plasmacytoma (2).

### Table 1. Classification System for Postoperative Hemorrhage

<table>
<thead>
<tr>
<th>Classification</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Patient noting the presence of blood-tinged mucus, flecks of blood, brown mucus, or red streaks</td>
</tr>
<tr>
<td>Minor</td>
<td>Any description of bright red blood or blood clots Resolved without operative management whether or not physician evaluation or hospitalization occurred</td>
</tr>
<tr>
<td>Intermediate</td>
<td>Diffuse venous oozing or small arterial source bleeding resulting in operating room evaluation or intervention Managed with monopolar or bipolar cautery</td>
</tr>
<tr>
<td>Major</td>
<td>brisk or copious bleeding requiring operative intervention Managed with transoral or transcervical vessel ligation, or interventional radiology embolization</td>
</tr>
<tr>
<td>Severe</td>
<td>Bleeding resulting in life-threatening medical complications such as: Cardiopulmonary arrest Hypoxia/airway compromise requiring tracheostomy Hemodynamic instability requiring blood transfusion</td>
</tr>
</tbody>
</table>

Table 1
Tracheostomy was performed in 14.8% of patients (134 of 906), and a nasogastric tube was placed intraoperatively in 52.9% (479 of 906). Laser treatment was used in 53.0% surgical procedures, robotic surgery in 29.7%, and handheld electrocautery in 12.9%, with only 5 of 906 (0.55%) documented as laser-robotic or laser-cautery hybrid cases. No specific surgical technique was documented in 34 patients. Modified radical neck dissection or selective neck dissection most often included nodal levels II, III, and IV and was performed in 79.0% of all patients (717 of 906). These consisted of 569 ipsilateral neck dissections (62.8%), 11 contralateral neck dissections (1.2%), and 137 bilateral neck dissections (15.1%). Radical neck dissection was performed in 54 of 906 of all patients (6%).

Documentation of single or multiple external carotid artery branch ligation was present in 95.0% of medical charts and was performed in 15.6% of these cases (134 of 860). Ligation was performed at the time of concurrent neck dissection with the ipsilateral lingual arteries (80 of 134) and facial arteries (71 of 134) most frequently addressed. Also ligated were the ipsilateral superior thyroid (37 of 134), ascending pharyngeal (12 of 134), superior laryngeal (2 of 134), occipital artery (2 of 134), or main external carotid trunk (28 of 134). Only once was a contralateral vessel (lingual artery) ligated. There were no reported complications from vessel ligation.

### Postoperative Bleeding Details

The postoperative course in all patients revealed a 5.4% overall TOS resection site bleeding rate (49 of 906 patients). Operative intervention was required in 3.6% of all patients (33 of 906). Based on our classification system (Table 1), we found that 32.7% of bleeding episodes were classified as minor, 34.7% as intermediate, 12.2% as major, and 20.4% as severe. Therefore, 67% of bleeding episodes required operative intervention. The mean postoperative day of bleeding was 10, broken down to day 11 for minor episodes, day 10 in intermediate episodes, day 10 in major episodes, and day 9 in severe episodes (Table 2).

Tonsillar primaries were more likely to bleed (32 of 49 [65.3%]) compared with tongue base primaries (16 of 49 [32.7%]) (P = .04). Male patients were more likely to require operative intervention for bleeding than female patients (P = .02).

Of bleeding episodes requiring operative intervention, 64% (21 of 33) were treated by the patient’s primary surgeon with 36% (12 of 33) treated by either a local emergency department physician or otolaryngologist.

Transcervical external carotid system vessel ligation was performed in 15.6% of patients and was always performed at the time of the primary resection. No significant difference in overall bleeding rate was found between the ligated (6.7%) and nonligated (5.5%) groups (P = .21). Regarding bleeding severity, only 1 ligated patient developed severe bleeding. Ten percent of severely bleeding patients (1 of 10) underwent vessel ligation vs 20.5% of nonseverely bleeding patients (8 of 39); this difference was not statistically significant (P = .66). Higher T-stage tumors were more likely to bleed, as seen with pairwise comparison methods. This was notable in T1 tumors vs T3 tumors (P < .005) and T1 tumors vs T4 tumors (P = .001). The bleeding rate was no different between the TLM (5.6%) and TORS (5.9%) subgroups (P = .80); however, of the 2 surgical modalities, TLM T-stage cancers were significantly higher (stage T1 vs T3, P < .001; and stage T2 vs T3, P < .001).

Prior radiation therapy or surgery did not correlate with a significant increase in postoperative bleeding rate (7.8%) compared with previously untreated patients (5.4%) (P = .51). Although not statistically significant, 3 of the 5 patients with previous radiation and/or surgery that bled had severe bleeding (P = .15).

### Bleeding Classification

#### Minor Bleeding

Of all patients, minor bleeding occurred in 1.8% (16 of 906). The bleeding resolved without the need for operative intervention whether or not a physician evaluation, emergency department visit, or hospital admission occurred. In 5 of these patients, bleeding was managed via telephone conversation only. Reported estimated blood loss (EBL) ranged from 5 to 240 mL. Interestingly, 4 of the 16 cases documented use of an ice water gargle or placement of a cold compress neck to the anterior neck.

#### Intermediate Bleeding

Intermediate bleeding occurred in 1.88% of patients (17 of 906), with all taken to the operating room for control or evaluation.

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**Table 2. Postoperative Bleeding Details**

<table>
<thead>
<tr>
<th>Patient/Surgical Characteristic</th>
<th>Minor</th>
<th>Intermediate</th>
<th>Major</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, No.</td>
<td>16</td>
<td>17</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>T-stage: unknown primary</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>T1</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>T2</td>
<td>6</td>
<td>8</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>T3</td>
<td>7</td>
<td>4</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>T4</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Patients treated with revision surgery or radiation therapy, No.</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Patients treated with transcervical ligation, No.</td>
<td>2</td>
<td>5</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Postoperative day of bleeding, mean</td>
<td>11</td>
<td>10</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Transoral laser microsurgery</td>
<td>11</td>
<td>6</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Transoral robotic surgery</td>
<td>4</td>
<td>7</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Handheld electrocautery</td>
<td>1</td>
<td>4</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

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Eleven patients had a bleeding source identified; arterial in 4 patients and diffuse venous oozing in 7. The EBL ranged from 100 to 500 mL. No patients experienced another episode of bleeding following intervention. The only 2 patients to develop bleeding on the day of their primary resection fell into this group.

**Major Bleeding**

Major bleeding occurred in 0.66% of patients (6 of 906). Four of the 6 patients had “arterial spasm bleeding” or “sentinel bleeding” episodes documented up to 2 days prior to definitive intervention. The EBL leading up to and including exploration ranged from 500 to 700 mL, with the bleeding vessel identified as an arterial vessel in 4 cases, twice as many as in the superior laryngeal artery. Two patients underwent interventional radiologic embolization, 1 as primary hemorrhage management, and 1 owing to an unidentifiable bleeding source on direct laryngoscopy. Two patients had arterial bleeding with vessels that were too large for bipolar cautery; therefore, hemoclips were placed transorally. Owing to negative results from a transoral examination, the remaining 2 patients underwent transcervical vessel ligation utilizing their neck dissection incision with ligation of the lingual, facial, and superior thyroid artery performed.

**Severe Bleeding**

Severe bleeding occurred in 1.1% of patients (10 of 906). Three had a history of radiation therapy, 2 also undergoing previous surgery. Six patients received a blood transfusion, ranging from 2 to 8 U. Six patients underwent an urgently performed awake tracheostomy for airway compromise, and 5 underwent neck exploration with ligation of either the external carotid (4 patients) or facial and lingual arteries (1 patient). All patients experienced a return to preoperative function and quality of life except for 1 patient who developed an anoxic brain injury and died 8 months postoperatively (Table 3).

**Discussion**

Transoral surgical resection for oropharyngeal OPSCC carries many advantages, including its excellent oncologic and functional outcomes in addition to decreased hospitalization length and complication rate. Unfortunately, the risk of acute life-threatening postoperative hemorrhage is increased in TOS compared with open surgery. This specifically applies to the oropharynx, where an intricate network of named vessels exists with multiple branches crossing tissue planes, accompanying nerves, and penetrating into various muscular, fascial, and mucosal layers (Figure 1 and Figure 2). Unfortunately, the traditional anatomic dissection approach to head and neck structures from the outside-in is reversed, and sound knowledge of the inside-out anatomy is needed. As the oropharyngectomy resection progresses deeper into the lateral pharyngeal tissues, large vessels are cauterized, clipped, and ligated, and the open wound is left to heal by secondary intention. These insensitive tissues with altered swallow and compromised air-
way protection mechanisms can persist for several weeks to months as healing ensues. In the event of postoperative hemorrhage, the mechanism of morbidity or mortality is typically aspiration and asphyxiation, not exsanguination (as evidenced by our description of patient 9 in Table 3). This occurs as blood rapidly obscures visualization in the pharynx, impeding intubation and resulting in aspiration and hypoxia. The aspirate coagulates then accumulates in the distal bronchopulmonary tree and can result in prolonged anoxia, acidosis, cardiac arrhythmia, cerebral hypoperfusion, anoxic encephalopathy, and death.

The main outcome measures of the study were to evaluate our experience of postoropharyngectomy hemorrhage, address factors associated with increased bleeding risk, and propose methods to treat these patients with an elevated risk. In doing so we address many questions: specifically, the relationship between bleeding rate and severity with patient sex, previous treatment, tumor size, surgical technique, external carotid system vessel ligation, and concern about staged oropharyngectomy with neck dissection or ligation.

**Risk Factors for Bleeding**

Age and sex have no effect on bleeding frequency; however, we found that males are more likely than females to have a bleeding episode requiring operative intervention ($P = .02$). This is unlikely to be related to anatomy or pathologic findings but could possibly be the result of increased postoperative exertion or activity. As anticipated, the greatest bleeding risk is present 7 to 14 days postoperatively (mean [SD], 10.1 [5.9] days).
Previous Treatment and Bleeding
We did not find that previous head and neck radiation and or surgery increased the risk of postoperative bleeding ($P = .41$). We found differences in bleeding severity, with a history of previous treatment present in 3 of 10 severe bleeding episodes (30.0%) vs 2 of 39 nonsevere bleeding episodes (5.1%) ($P = .05$). Diminished or delayed wound healing, radiation-induced blood vessel or microvasculature changes, fibrosis, or anatomic variations resulting from previous surgery are all possible factors leading to an increased severity of bleeding. Although based on a small number of patients, this difference in bleeding severity (30.0% vs 5.1%) seen with previous treatment warrants discussion of vascularized flap coverage.

Tumor Size and Bleeding
Higher T-stage tumors were more likely to bleed ($P = .02$) and trended toward having a more severe episode of bleeding ($P = .07$). This comparison was statistically significant when looking at both T1 vs T3 tumors ($P < .005$) and T1 vs T4 tumors ($P = .001$). This difference likely results from larger tumors involving multiple named arteries, such as the ascending pharyngeal, facial, lingual, and superior laryngeal arteries. In large resections required for advanced T-stage tonsillar and tongue base tumors, the tonsillar and ascending palatine branches of the facial artery and dorsal lingual branch of the lingual artery are typically encountered and ligated transorally.

Surgical Modality and Bleeding
Analysis comparing different techniques showed that no statistical difference in bleeding rate existed when comparing TLM resections (5.9%), TORS resections (6.3%), and handheld monopolar electrocautery resections (4.5%) ($P = .80$). Comparison of bleeding severity also showed no significant differences among the 3 primary resection methods ($P = .54$). Although no increase in bleeding rate or bleeding severity was present between the different resection techniques, tumors with higher T stages were more often resected with laser than robotic techniques ($P < .001$). The 2 specific comparisons that were statistically significant were between T1 and T3 tumors as well as between T2 and T3 tumors ($P < .001$ for both comparisons). Although additional variables may be present, that higher T-stage tumors have an increased bleeding rate, and larger tumors more often resected by TLM warrants mention. This and other potential differences between resection modalities prompted further study.

Vessel Ligation and Bleeding
All vessel ligations were performed transcervically at the time of the primary transoral resection. The 15.6% documented ligation rate likely underrepresents the true frequency as a result of variability in operative note dictation detail. Despite this deficiency, vessel ligation was not found to be associated with decreased overall rate of bleeding ($P = .21$), but it also was not found to be related to increased bleeding. Although severe bleeding seemed to be less frequent in patients with vessel ligation (1 of 9 [11.1%] vs 8 of 31 [25.8%]), this difference was not statistically significant ($P = .66$). While the overall bleeding rate was not different between patients who had undergone ligation and those who had not, we observed that tumors with higher T stages were more often ligated ($P = .002$). This comparison is statistically significant when comparing T1 and T3 tumors ($P = .005$) and comparing T1 and T4 tumors ($P = .001$). This likely represents the surgeon’s calculated effort to minimize the bleeding risk in a more complex wound that will take longer to heal.

Simultaneous neck dissection was performed in 79.1% of cases; therefore, most of our patients had accessible external carotid artery branches at the time of the primary surgery, facilitating ligation. Despite this increased rate of ligation in larger tumors and the increased rate of bleeding in higher T-stage tumors, we are unable to measure the precise impact of vessel ligation in this subgroup regarding the overall bleeding rate. While there are theoretic concerns about regional necrosis or vascular insults with ligation, none were noted, even in previously radiated patients. An additional risk with large resections performed in conjunction with neck dissection is fistula formation. Fistulas occurred rarely with neck dissection technique modified to prevent their occurrence. In the rare circumstance that a communication occurred between the oropharynx and neck following a large resection with neck dissection, it was closed with local tissue or by suture impaction.

Simultaneous vs Staged Resection With Neck Dissection
Owing to time and facility constraints, the practice of staging the margin-clearing resection and neck dissection with vessel ligation is becoming more frequent. With a hospital’s investment in expensive equipment, such as surgical robotic systems, lasers, or microscopes, comes the pressure to maximize productivity. This may result in scheduling multiple resections around equipment or block time availability, which does not allow time for additional procedures, such as a neck dissection. Patients then return to the operating room days to weeks later for a second anesthetic and neck dissection with or without vessel ligation. We report that postoperative day 10 is the mean postoperative day for oropharyngeal hemorrhage, with 83.6% of bleeding episodes occurring within 2 weeks or surgery.

Additional Recommendations
Our standard practice during oropharyngectomy is to use hemoclips on all arteries 2 mm or larger and suture ligature on arteries larger than 4 mm. When cautery is needed, we find the bipolar hemoclip superior to the monopolar hemoclip owing to its ability to seal vessel ends rather than create a charred coagulum that imitates a “spot weld.” If neck dissection is performed and there is concern for increased postoperative bleeding or any question of exposed arterial vessels, we perform vessel ligation. The specific branches of the external carotid artery to be ligated are those directly involved in the resection bed, typically including the lingual and facial arteries in oropharyngeal resections. If a large resection continues inferiorly near the hypopharyngeal ligation of the superior thyroid artery is also performed.

We prefer not to stage the neck dissection because we feel it allows for concurrent vessel ligation, is more efficient, and
is cost-effective. Although not assessed in this study, in our experience, detailed appreciation of the inside-out anatomy is critical to performing safe TOS. Although rarely performed, planned tracheostomy is utilized in selected patients, often those undergoing concomitant TOS and bilateral neck dissection with a history of radiotherapy or previous surgery.

Known study limitations include its retrospective nature, as well as lack of additional risk factor assessment, such as antiplatelet or anticoagulation therapy discontinuation, human papillomavirus status, or smoking history.

In conclusion, transoral resection of oropharyngeal carcinoma is safe and effective with a predictable rate of postoperative hemorrhage. Severe life-threatening hemorrhage is very rare. Bleeding rates were equivalent between TLM- and TORS-treated patients. Although transcervical vessel ligation did not result in an overall decrease in bleeding rate, we feel it is a safe technique to use in selected cases. For higher T-stage tumors, primary tonsil tumors, or previously treated patients, simultaneous multivessel ligation may reduce the severity of a severe episode of bleeding.

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REFERENCES