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First Bite Syndrome Following Transcervical Arterial Ligation After Transoral Robotic Surgery

Michael C. Topf, MD; Ethan Moritz, BA; John Gleysteen, MD; Joseph M. Curry, MD; David M. Cognetti, MD; Adam J. Luginbuhl, MD

**Objective:** To assess the incidence of first bite syndrome (FBS) in transoral robotic surgical (TORS) patients undergoing transcervical arterial ligation.

**Methods:** Retrospective case series of all patients diagnosed with FBS following prophylactic transcervical arterial ligation of branches of the external carotid system between March 2010 and December 2016 at a single academic center.

**Results:** Six patients with FBS after TORS with transcervical arterial ligation were evaluated, representing 7% of all patients who underwent neck dissection with concomitant transcervical arterial ligation (6 of 83). Median presentation of FBS was 63 days, with an average duration of 66 days. Treatment ranged from observation to botulinum toxin injection.

**Conclusion:** Patients who undergo transcervical arterial ligation to minimize bleeding complications following TORS are at risk of developing first bite syndrome.

**Key Words:** Transoral robotic surgery (TORS), robotic surgery, first bite syndrome, arterial ligation, bleeding.

**Level of Evidence:** 4.

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**INTRODUCTION**

Since the initial approval of transoral robotic surgery (TORS) in 2009 by the Food and Drug Administration for the treatment of tumor (T1 and T2 oropharyngeal cancer, multiple centers have adopted the use of the surgical robot for the treatment of oropharyngeal cancer.\(^1,2\) TORS has been shown to offer excellent oncologic outcomes and low incidence of positive margins,\(^3,4\) with promising functional outcomes\(^5\) at multiple subsites of the head and neck. The indications for TORS have expanded to include the surgical treatment of benign lesions and obstructive sleep apnea.\(^6,7\) TORS is recognized as a safe procedure, with a retrospective, multi-institutional study on the safety of TORS for oropharyngeal tumors reporting a relatively low 30-day mortality rate of 0.7% with a complication rate of 7.9%.\(^8\)

Previous studies have examined postoperative complications following TORS, which include tooth injury, percutaneous endoscopic gastrostomy tube dependency, pharyngocutaneous fistula, airway obstruction, aspiration, hypoglossal nerve injury, lingual nerve injury, and dehydration requiring readmission.\(^3,9,10\) Perhaps the most formidable complication after TORS is postoperative hemorrhage, owing to the risk of possible airway compromise and death. Previously published large retrospective studies report postoperative bleeding rates after TORS ranging from 3.1% to 13.2%.\(^9,11–16\) Of these, 2% to 5% are major or severe bleeds, defined as brisk or copious bleeding requiring vessel ligation or embolization; or bleeding resulting in life-threatening medical complications such as airway compromise, hemodynamic instability, and cardiopulmonary arrest.\(^11,13–15\) A study by Chia et al.\(^9\) queried 45 TORS surgeons throughout the United States to evaluate postoperative complications with a reported 30-day mortality of 0.3%; however, all six deaths were secondary to postoperative hemorrhage.

In an attempt to limit the risk of this catastrophic outcome, many surgeons have advocated prophylactically ligating selected branches of the external carotid artery (ECA) during concomitant neck dissection. Although the impact of prophylactic transcervical arterial ligation on overall bleeding rates is unclear, studies have shown a trend toward decreased hemorrhage severity in ligated patients.\(^13,14,16,17\) To date, none of the retrospective studies have noted complications, such as neurologic changes, cranial nerve palsies, major vascular injuries, and delayed wound healing attributable to ipsilateral ECA ligation.\(^15,16,17\) There is a theoretical concern that ECA ligation may increase tumor site hypoxia and thus impair the efficacy of postoperative radiation therapy. However, given the decreased risk of severe bleeding following transcervical arterial ligation, most authors advocate its routine use.

Since adopting the practice of ligating portions of the external carotid system during concurrent neck dissection, we have noted the presentation of First Bite Syndrome.
Syndrome (FBS) in several of our patients. FBS was first described by Netterville in 1998 as facial pain and cramping in the parotid region that occurs on the first bite of a meal and diminishes with each subsequent bite. It has been associated with surgeries of the infratemporal fossa, parapharyngeal space, and or deep lobe of the parotid gland. Although the etiology of FBS is not entirely clear, it is believed to be secondary to unopposed parasympathetic innervation to the parotid gland. It is our belief that the ligation of the ECA branches may cause denervation of the postganglionic sympathetic fibers to the parotid gland. Details regarding the clinical course of six patients who developed FBS following TORS resection of oropharyngeal tumors with prophylactic ligation of branches of the ECA during neck dissection are outlined.

MATERIALS AND METHODS

Following institutional review board approval, our retrospective TORS clinical database was queried from March 2010 to December 2016 for all patients who underwent TORS for squamous cell carcinoma (SCC). All patients who underwent TORS and neck dissection and developed FBS, as noted in postoperative follow-up visits, were identified. First bite syndrome was defined as sharp pain in the parotid region that occurred with commencement of eating and resolved after a few seconds. The electronic medical records were then examined to describe the cases. Data collection included tumor stage, tumor subsite, timing of neck dissection, ECA vessels ligated, adjuvant treatment, onset, duration of FBS symptoms, and treatment parameters. Univariate analysis of patient demographic and baseline clinical data was carried out using Fisher’s exact test and Wilcoxon rank sum test, with significance defined a priori as \( P < .05 \).

Transcervical arterial ligation was performed in all cases at the time of primary neck dissection. Silk sutures were used to ligate vessels. Transcervical arterial ligation was performed using two general approaches: the first method was dissection of individual branches of the ECA with ligation of that individual branch or branches, most commonly the lingual artery; the second method was ligation of a more proximal stump of the ECA resulting in ligation of two or more branches of the ECA.

RESULTS

Six patients with FBS after TORS with transcervical arterial ligation were identified, representing 7% of all patients who underwent neck dissection and transcervical arterial ligation (6 of 83). In contrast, none of the patients who underwent TORS or TORS with neck dissection without undergoing transcervical arterial ligation developed FBS (0 of 214). Patient demographic and baseline clinical data for the transcervical arterial ligation group and non-ligated group are shown in Table I. Of note, none of the patients who had a history of prior radiation therapy to the head and neck or prior chemotherapy underwent transcervical arterial ligation. Patients who were p16-positive were more likely to undergo transcervical arterial ligation. Of the patients who underwent transcervical arterial ligation, concurrent procedures were performed in 58 patients and staged procedures were performed in 25 patients. Of the staged patients, 17 patients had neck dissection with transcervical arterial ligation followed by TORS, and eight patients had TORS followed by neck dissection and transcervical arterial ligation. Vessels of the ECA system ligated included the lingual artery in 67 patients (81%), facial artery in 33 patients (40%), ascending pharyngeal artery in 14 patients (17%), internal maxillary artery in one patient (1%), and superior thyroid artery in one patient (1%). Twenty-eight patients (34%) underwent ligation of two branches of the ECA at the time of neck dissection, and three patients (4%) had three vessels ligated. None of the patients who had only one branch of the ECA ligated developed FBS.

Age, sex, tumor stage, tumor subsite, vessel ligated, adjuvant treatment, time to presentation, duration of symptoms, and treatment for FBS for the identified patients is listed in Table II. Of note, all six patients were males. Five of the six patients underwent tonsillectomy. All patients underwent transcervical ligation of multiple branches of the ECA system with the lingual artery being ligated in all patients. Three of the six patients had three vessels of the ECA system ligated. None of the six patients underwent retropharyngeal node dissection. All patients who developed FBS received postoperative radiation, although FBS preceded the start of radiation therapy in three of the six.

<table>
<thead>
<tr>
<th>TABLE I.</th>
<th>Patient Demographic and Baseline Clinical Data.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic</td>
<td>No Transcervical Arterial Ligation</td>
</tr>
<tr>
<td>----------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>Total</td>
<td>214 (72)</td>
</tr>
<tr>
<td>Age, years</td>
<td>60.7</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>169 (79)</td>
</tr>
<tr>
<td>Female</td>
<td>45 (21)</td>
</tr>
<tr>
<td>Prior RT</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>26 (12)</td>
</tr>
<tr>
<td>No</td>
<td>188 (88)</td>
</tr>
<tr>
<td>Prior chemotherapy</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>No</td>
</tr>
<tr>
<td>Tumor subsite</td>
<td>Tonsil</td>
</tr>
<tr>
<td></td>
<td>Base of tongue</td>
</tr>
<tr>
<td></td>
<td>Hypopharynx</td>
</tr>
<tr>
<td></td>
<td>Unknown primary</td>
</tr>
<tr>
<td></td>
<td>Soft palate</td>
</tr>
<tr>
<td></td>
<td>Supraglottic larynx</td>
</tr>
<tr>
<td>T stage</td>
<td></td>
</tr>
<tr>
<td>Tx</td>
<td>7 (3)</td>
</tr>
<tr>
<td>T1</td>
<td>95 (44)</td>
</tr>
<tr>
<td>T2</td>
<td>82 (38)</td>
</tr>
<tr>
<td>T3</td>
<td>28 (13)</td>
</tr>
<tr>
<td>T4</td>
<td>2 (1)</td>
</tr>
<tr>
<td>p16 status</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td>Negative</td>
</tr>
</tbody>
</table>

RT = radiation therapy; T = tumor.
patients. The median time to presentation of FBS following transcervical arterial ligation was 63 days with a range of 21 to 951 days. Treatment ranged from observation to neuroleptic medications to botulinum toxin. Five of the six patients had resolution of symptoms. For these five patients, the mean duration of FBS was 66 days, with a range of 35 to 111 days.

The following patients are summarized in Table II:

Patient 1 is a 45-year-old male with T1N2b SCC of the tonsil who underwent concomitant TORS radical tonsillectomy with neck dissection and ligation of the lingual, facial, and ascending pharyngeal vessels. Four days postoperatively, he developed trismus, with FBS evolving 2 weeks later, with the classic presentation of sharp pain on the first bite of a meal lasting 20 to 30 seconds. The patient was treated with pregabalin, which helped relieve his symptoms, and he was titrated off the medication at 3.5 months without further incident.

Patient 2 is a 43-year-old male with a p16-positive T1N2b SCC of the left base of the tongue who underwent bilateral neck dissection, followed by a TORS left radical tonsillectomy and base of tongue resection. During the neck dissection, the left lingual, facial, and ascending pharyngeal vessels were ligated. The patient presented 4 weeks postoperatively with evidence of FBS localized to the left side only. This pain lasted 42 days and then resolved without intervention. Treatment was not initiated because symptoms were tolerable, and the patient declined out of concern for possible side effects from medical treatment. Seven months postoperatively, there were complaints of a mild recurrence of FBS.

Patient 3 is a 67-year-old male with a p16-positive T1N2a SCC of the right base of tongue. The patient underwent concurrent TORS resection of the right base of tongue with right neck dissection and ligation of the lingual and facial arteries. The patient reported mild signs of FBS 3 months postoperatively. One month later, his FBS was resolving but remained following ingestion of acidic or tart foods. The patient did not receive any treatment for his FBS, and the symptoms subsided after a total duration of 3 months.

Patient 4 is a 67-year-old male with T2N2b SCC of the right palatine tonsil and pharyngeal wall. The patient initially underwent bilateral neck dissection with ligation of the lingual and ascending pharyngeal branches of the ECA on the right side. Two days later, a TORS radical tonsillectomy was performed. Two to 3 months postoperatively, he presented to a radiation oncology appointment with signs of FBS. The patient was prescribed opioids for the pain and his FBS symptoms had fully resolved 5 weeks after the onset.

Patient 5 is a 65-year-old male with p16-positive T3N0 SCC of the palatine tonsil. A TORS radical tonsillectomy with partial glossectomy was performed with concomitant neck dissection and ligation of the lingual, ascending pharyngeal, and maxillary arteries. The patient presented with the symptoms of FBS 41 days postoperatively. He was observed and did not receive any medical treatment for his FBS. His FBS lasted for 60 days and was self-resolved.

Patient 6 is a 66-year-old male with p16-positive T2N2b SCC of the tonsil who underwent TORS radical tonsillectomy with partial glossectomy with concurrent right neck dissection and ligation of the lingual and facial arteries. Nearly 3 years after surgery, the patient first complained of symptoms consistent with FBS. The patient was initially treated with gabapentin, but he returned 4 months later because he was unable to tolerate the medication with only minimal alleviation of his pain. The patient received an injection of botulinum...
Fig. 1. Intraoperative photograph of lingual artery with lacy postganglionic sympathetic fibers. [Color figure can be viewed at www.laryngoscope.com.]

toxin to the parotid gland and experienced improvement in symptoms.

DISCUSSION

The pendulum of treatment for oropharyngeal squamous cell carcinoma is swinging back toward primary surgical intervention. The increase in use of both TORS and transoral laser microsurgery techniques over the past 5 to 10 years has resulted in excellent oncologic and functional outcomes. However, with this paradigm shift comes adverse events and complications that were not previously seen in this population. Fatal oropharyngeal hemorrhage is the most feared complication of TORS. To mitigate this, many authors have advocated prophylactic ligation of branches of the ECA during concomitant neck dissection, which may decrease the risk of major and severe bleeding. We present FBS as a rare yet potential complication of the empiric ligation of the portions of the external carotid system. In our database of TORS patients, 214 patients underwent TORS for malignant lesions without transcervical arterial ligation, with none of these patients developing FBS. This is in comparison to the more recent subset of 83 patients who underwent transcervical arterial ligation during neck dissection with a FBS rate of 7%. The authors used no routine questionnaire regarding postoperative complaints, therefore the incidence of patients with mild FBS symptoms may be underestimated. In our experience, FBS presented at a median of 2 months postoperatively.

The course of the sympathetic innervation of the head and neck has a circuitous route: the rootlets exit the thoracic spine (T1-6), traveling superiorly as the sympathetic chain to the superior sympathetic ganglion, at which point it sends postganglionic fibers to the carotid system to bring autonomic innervation to target organs along the arterial vasculature. The architecture of these postganglionic fibers forms a lacy pattern surrounding the external carotid artery and its branches (Fig. 1). Our working hypothesis of the pathophysiology of FBS is predicated on the unopposed parasympathetic innervation of the parotid gland after disruption of the sympathetic innervation during dissection of the carotid artery. All patients who developed FBS had multiple branches of the ECA ligated, whereas no patients who had only one branch ligated developed FBS. Furthermore, all three patients who had three branches of the ECA ligated developed FBS. Finally, the symptoms were more intense and debilitating in patients who had greater dissection of the external carotid system. Therefore, the authors feel that surgeons should consider minimizing the number of ligated vessels because ligating only one branch of the ECA may decrease the risk of catastrophic bleeding with limited risk of postoperative FBS.

Previous studies have linked dissection in the parapharyngeal space and resection of the deep lobe of the parotid to FBS. Interestingly, we have not had any documented case of FBS in our TORS resections of parapharyngeal space tumors via a transoral approach with or without TORS. Although possibly underreported, none of the patients who underwent TORS without transcervical arterial ligation developed FBS. It is our hypothesis that FBS is secondary to vessel ligation and not due to dissection into the parapharyngeal space during the primary tumor resection.

A confounding group is patients who undergo free flap reconstruction, where FBS has not been recognized. We would expect to see FBS in this population more often due to extensive carotid dissection to obtain donor arterial supply. Garg et al. presented their series of 200 external carotid artery dissections for free flap surgery donor vessels without a single case of FBS. Two unproven but postulated explanations include: 1) underreporting/underdiagnosing of FBS; and 2) high percentage of patients requiring free flaps with a previous history of radiation, potentially resulting in loss of parotid gland function and a muted autonomic response. Of the 28 patients with prior history of radiation to the head and neck who underwent TORS for malignant lesions at our institution, none underwent prophylactic transcervical arterial ligation; therefore, we cannot comment on the prevalence of FBS in patients with prior radiation. On the contrary, a large series of 500 patients who underwent parapharyngeal or infratemporal fossa surgical procedures reported a 10% incidence of FBS. This confirms that the penetrance of this syndrome postoperatively is variable and thus the mechanism is not well-established.

Observation is an appropriate treatment option in milder cases because the symptoms of FBS are often not debilitating. As seen in the majority of the patients in our series, symptoms tend to resolve within months without intervention. In cases for which FBS is causing an aversion to eating, therapeutic options should be considered. Strategies for treatment of FBS include pain medications such as nonsteroidal anti-inflammatory drugs.
drugs, acetaminophen, and narcotics; however, these have been previously reported to have limited success.\textsuperscript{23} Neuroleptic medications such as gabapentin, nortriptyline, and pregabalin have been shown to decrease the intensity and duration of symptoms.\textsuperscript{24} Botulinum toxin injections over the painful parotid area have shown to improve the intensity of symptoms and reduce the need for further intervention.\textsuperscript{25} One group studied a low dose of radiation to the parotid gland to treat FBS with some success.\textsuperscript{26} This finding is in contrast to three of our patients who developed FBS after the completion of adjuvant radiation.

Despite the identified trend of FBS in our patient population, we agree with the recommendation of vessel ligation following TORS. If prophylactic vessel ligation can decrease the risk of developing severe or catastrophic postoperative oropharyngeal hemorrhage, the practice should continue, even at the risk of FBS. Therefore, this report of FBS in this patient population is not intended to discourage vessel ligation but rather to raise awareness of a potential sequela.

CONCLUSION

Patients who undergo ligation of branches of the ECA to minimize bleeding complications following TORS are at risk of developing FBS. Most cases of FBS in this setting are mild in nature and spontaneously resolve. First bite syndrome should be incorporated into the preoperative counseling for this patient population, and surgeons should be aware of treatment options for refractory cases. Surgeons should consider minimizing the number of branches of the ECA that they ligate because one branch may be enough to decrease catastrophic bleeding while decreasing the risk of postoperative FBS.

BIBLIOGRAPHY