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ORIGINAL RESEARCH

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Five-year survival outcomes in oropharyngeal squamous cell carcinoma following transoral laser microsurgery

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Abstract

Objective: To determine the 5-year survival outcomes of patients with oropharyngeal cancer treated with transoral laser microsurgery at our institution.

Methods: A prospective longitudinal cohort study of all cases of oropharyngeal squamous cell cancer or clinically unknown primaries diagnosed at our institution between September 1, 2014, to December 31, 2019, treated with primary transoral laser microsurgery were analyzed. Patients with a previous history of head and neck radiation were excluded from analysis. Kaplan–Meier survival curves were used to estimate 5-year overall survival, disease-specific survival, local control, and recurrence free survival rates in oropharyngeal squamous cell carcinoma.

Results: Of 142 patients identified, 135 met criteria and were included in the survival analysis. Five-year local control rates in p16 positive and negative disease were 99.2% and 100%, respectively, with one locoregional failure in the p16 positive cohort. Five-year overall survival, disease-specific survival, and recurrence free survival in p16 positive disease were 91%, 95.2%, and 87% respectively ($n = 124$). Five-year overall survival, disease-specific survival, and recurrence free survival in p16 negative disease were 39.8%, 58.3%, and 60%, respectively ($n = 11$). The permanent gastrostomy tube rate was 1.5% and zero patients received a tracheostomy at the time of surgery. One patient (0.74%) required a return to the OR for a post-operative pharyngeal bleed.

Conclusion: Transoral laser microsurgery is a safe primary treatment option for oropharyngeal squamous cell carcinoma with high 5-year survival outcomes, notably in p16 positive disease. More randomized trials are needed to compare survival outcomes and associated morbidity in transoral laser microsurgery compared to treatment with primary chemoradiation.

Level of Evidence: 3

Brooke Turner and Colin MacKay are the co-primary authors.

OCEBM Levels of Evidence Working Group*. "The Oxford Levels of Evidence 2". Oxford Centre for Evidence-Based Medicine. https://www.cebm.ox.ac.uk/resources/levels-of-evidence/ocebm-levels-of-evidence

KEYWORDS
HPV-mediated, oropharynx, squamous cell carcinoma, survival outcomes, Transoral laser microsurgery

1 | INTRODUCTION

The incidence of oropharyngeal squamous cell carcinoma (OPSCC) is rising by 0.8%–3% per year as a consequence of increasing rates of human papilloma virus (HPV) infections.[1–6] HPV infection is estimated to account for up to 80% of cancers of the oropharynx, with patients being diagnosed younger.[2,7,8] HPV strains 16 and 18 are the most common high-risk subtypes, with most infections clearing within 2 years.[1,7,9–11] HPV-mediated oropharynx tumors are known to be treatment sensitive; however, this mechanism is not fully understood.[3,12–15] Given superior treatment response and survival, the 8th edition of the American Joint Committee on Cancer (AJCC) stratifies OPSCC staging by p16 status, an identifiable surrogate marker for HPV infection.

Primary radiation therapy in OPSCC is often associated with treatment-related toxicities, particularly chronic xerostomia, reduced voice quality, osteoradionecrosis, and long-term swallowing dysfunction.[5,16,17] Quality of life responses from 56 patients who received radiation to the oropharynx found late-onset xerostomia and mucositis in 59% and 24% of respondents, respectively, with a significant dose-dependent relationship between radiation dose to the superior constrictor and absence of dysphagia symptoms.[18] Long-term toxicities are partially alleviated with intensity-modulated radiation therapy (IMRT), which allows for delivery of a reduced radiation dose to regions in the head and neck at lower risk of recurrence.[19–21] One-year gastrostomy tube (G-tube) dependence rates in patients with stages I and II disease receiving IMRT are low at 5%,[22] with 1-year G-tube dependence rates of 6%–8.8% in patients with stages III–V disease treated with primary IMRT.[19,20,22]

The use of transoral laser microsurgery (TLM) and transoral robotic surgery (TORS) is becoming more common in the treatment of oropharyngeal cancer. Patient selection is important in transoral surgery as access can be limited in patients with severe trismus, limited neck extension, and more advanced local tumor stage.[23] Following the adoption of TLM in OPSCC treatment, several studies have reported on survival outcomes in patients receiving primary TLM treatment plus or minus adjuvant therapy. In a study of 69 patients with OPSCC, patients treated with primary TLM without adjuvant therapy, 5-year OS estimate was 86%.[24] Five-year LC rates for stages I–IV oropharyngeal cancer treated with TLM with or without adjuvant therapy range from 92.3%–94%.[24,25] After stratifying by p16 status, 5-year OS and DSS in p16 OPSCC ranges from 80.7%–90% and 91%–93%, respectively.[26–28] Survival outcomes in advanced stages III and IV disease treated with primary TLM are also promising. In a study of 204 patients with stages III and IV p16 positive OPSCC treated with TLM with or without adjuvant therapy, 5-year OS was 90%.[5] This study contains an overlapping patient cohort from Rich et al., who reported 86% 5-year OS in 84 patients with stages III and IV p16 positive OPSCC treated with primary TLM.[23] Similar survival outcomes have been reported in early and late-stage p16 positive disease treated with primary TORS. A retrospective review of 628 patients with p16 positive oropharyngeal cancer who underwent TORS found that 5-year OS and RFS in the early T-stage I and II cohort ($n = 589$) was 91% and 86%, respectively.[29] In the late T-stage III and IV cohort ($n = 39$), 5-year OS and RFS rate was 87% and 84%, respectively; there was no significant difference in OS ($p = .75$) and RFS ($p = .60$) between early (stages I and II) and late (stages III and IV) stage disease.[29]

P16 negative status remains a poor predictor of OS, with few studies assessing the use of transoral surgery in this cohort.[30] Five-year OS rates in stages I–IV p16 negative OPSCC treated with TLM range from 54.4% to 57%,[26,27] with Haughey et al., and Rich et al., reporting 5-year OS rates of 25% and 30%, respectively, for stages III and IV p16 negative disease.[5,23] One recent study found TORS to be superior to primary radiation in a case-matched comparison of 206 patients with p16 negative disease; 3-year OS was 84% (95% CI 76%–91%) in TORS compared to 66% (95% CI 57%–77%) in patients treated with primary radiation ($p = .1$).[31]

The use of transoral surgery compared to open surgical approaches has gained favor due to significantly shorter length of stay in hospital, lower risk of free flap reconstruction and lower odds of post-treatment G-tube use.[32,33] ORATOR: an open-label, phase 2 trial aimed to compare swallowing-related quality of life scores in 68 patients with T1-2, N0-2 OPSCC 1 year after primary radiotherapy (70 Gy in 35 fractions) with or without chemotherapy versus primary TORS with neck dissection plus or minus chemoradiotherapy (CRT).[34] The authors observed that the mean MD Anderson Dysphagia Inventory (MDADI) scores were significantly higher in the cohort receiving primary radiation ($p = .042$), however, this difference in mean MDADI scores was not clinically significant based on the 10-point threshold determined prior to study initiation.[34] On long-term follow-up, rates of chronic xerostomia were significantly higher in the primary radiation arm ($p = .041$) with no significant differences in 5-year overall survival (OS) ($p = .99$) and progression-free survival (PFS) ($p = .73$).[35]

Pooled analysis of post-operative bleeding rates following TORS is low at 2.4%, with post-operative bleeding resulting in significant sequelae being rare, notably if external carotid artery vessels are ligated during neck dissection.[36–38] Despite reduced morbidity and improved functional outcomes compared to open surgical techniques, transoral surgery is not without risk, and routine external carotid artery branch ligation is recommended. Unfortunately, ORATOR2, a randomized phase II trial comparing IMRT 60 Gy plus or minus Cisplatin and trans-oral surgery, mainly completed using TORS, plus or minus deintensified adjuvant radiation was ended because of two patient deaths in the surgical arm.[39,40] Additional studies aim to elucidate differences in morbidity and quality-of-life outcomes following

transoral surgery versus IMRT in early-stage OPSCC (QoLATI, NCT04124198; EORTC 1420, NCT02984410).

Several clinical trials have examined or are currently examining the role of de-intensified adjuvant radiation following transoral surgery on survival outcomes and/or functional morbidity in OPSCC (E3311 (NCT01898494),[41] PATHOS (NCT02215265),[42] AVOID (NCT02159703),[43] SIRS trial (NCT02072148)[44]). E3311, a randomized phase II trial, sought to examine PFS rates in patients with stages III and IVA p16 positive OPSCC assigned to receive transoral surgery plus adjuvant treatment in the form of 50 Gy, 60 Gy, 66 Gy with Cisplatin, or no radiation based on the abscence of predetermined pathologic risk factors for recurrence.[41] Two-year PFS rates in intermediate risk patients, defined by close margins <3 mm, 2–4 involved lymph nodes, presence of lymphovascular invasion (LVI), perineural invasion (PNI), or extranodal extension (ENE) ≤ 1 mm, who received 50 Gy (Arm B) or 60 Gy (Arm C) were 94.9% (90% CI = 91.3%–98.6%) and 96.0% (90% CI = 92.8%–99.3%), respectively, with a significant difference in grades III–V treatment toxicities between the intermediate risk arms ($p = .030$), supporting de-escalation of adjuvant radiotherapy in patients with p16 positive disease.[41] More long-term data is necessary to determine safe, patient specific guidelines for de-escalated primary and adjuvant radiotherapy.[45]

As Halifax, Nova Scotia is the primary center in Atlantic Canada for minimally invasive oropharynx surgery, we sought to determine the 5-year survival outcomes for OPSCC treated with primary TLM, with or without adjuvant therapy, at our institution.

2 | METHODS

A prospective analysis of patients with primary OPSCC treated with curative TLM from September 1, 2014 to December 31, 2019, at our institution was performed. Patients with a malignancy other than squamous cell carcinoma (SCC) of the oropharynx or who previously received head and neck radiation were excluded. Clinically unknown primaries were treated according to our institution's unknown primary protocol.[46,47] Pathologic unknown primaries were excluded if non-oropharyngeal origin was suspected. Following TLM, the role of adjuvant therapy was decided by a multi-disciplinary tumor board based on TNM staging, final margin status, presence of adverse pathologic features and additional patient comorbidities that might impact treatment. Patients were staged and treated per the 7th or 8th edition of the AJCC, depending on the edition in effect at the time of diagnosis. All patients were restaged according to the AJCC 8th edition for data analysis. Kaplan–Meier survival curves were used to estimate 5-year overall survival (OS), disease-specific survival (DSS), local control (LC), and recurrence free survival (RFS), defined as length of time after surgery in which there was no evidence of recurrence. Survival outcomes were stratified by p16 status and early versus late-stage disease. Institutional review board approval was obtained from the Nova Scotia Health Authority Research Ethics Board (ROMEO#1020643). All participants provided written informed consent.

3 | RESULTS

One-hundred forty-two patients were treated with curative TLM to the oropharynx. Three patients were excluded due to pathology other than SCC, and two patients were excluded due to previous head and neck radiation. Additionally, two patients with clinically unknown primaries were excluded from analysis as after TLM, SCC was felt to be cutaneous in origin. In total, 135 patients were included in the survival analysis (Table 1). Data from three patients overlaps with data previously published at our institution by Melong et al.[48] Mean patient age was 61.0 (SD 9.0), of whom the majority were male (80.0%). Of the 135 patients analyzed, 124 (91.9%) were p16 positive. Of 73 patients with a clinically unknown primary, SCC was found in the base of tongue in 34 patients and in the palatine tonsil(s) in 30 patients. In two patients with unknown primaries, SCC was found in both tonsil and base of tongue, and seven patients had a true unknown primary following surgery using our institution's unknown primary protocol.[46,47] Final pathologic distribution of OPSCC subsite was tonsil in 74 patients (54.8%), base of tongue in 49 patients (36.3%), both tonsil and base of tongue in 2 patients (1.5%), a pathologic unknown primary in 7 patients (5.2%) and soft palate in 4 patients (3.0%).The permanent G-tube rate in our cohort was 1.5% (2 of 135 patients). There were no tracheostomies performed perioperatively. Four patients (3.0%) experienced post-operative pharyngeal bleeding; two of whom required no intervention. One patient returned to the operating room on post-operative day five for definitive surgical management. The other patient underwent inital stabilization at an outside hospital and received no operative intervention, but did receive a blood transfusion. There were no peri-operative deaths observed in our cohort.

Kaplan–Meier estimates of 5-year survival for our cohort of oropharyngeal cancer patients treated with primary TLM ($n = 135$) are presented in Figures 1–4 and are summarized in Table 2.

3.1 | P16 positive

Five-year OS in stages I and II ($n = 117$) was 93.6% (SE = 3.2%, 95% CI = 87.9–99.7) while 5-year OS in stages III and IV ($n = 7$) was 57.1% (SE = 32.7%, 95%CI = 30.1–100.0). Five-year DSS in stages I and II was 96.2% (SE = 2.8%, 95%CI = 91.0–100.0) while 5-year DSS in stages III and IV was 85.7% (SE = 15.4%, 95%CI = 63.3–100.0). Five-year LC in stages I and II was 99.1% (SE = 0.9%, 95% CI = 97.4–100.0) and 5-year LC in stages III and IV was 100.0% (SE = 0.0%). Finally, 5-year RFS in stages I and II was 87.0% (SE = 4.5%, 95%CI = 79.6–95.1) and 85.7% (SE = 15.4%, 95%CI = 63.3–100.0) in stages III and IV. In the p16 positive cohort, there were no significant differences in OS ($p = .97$), DSS ($p = .42$), LC ($p = .85$), or RFS ($p = .51$) based on oropharyngeal subsite.

3.2 | P16 negative

Five-year OS, DSS, and RFS in p16 negative stages I and II are of minimal statistical value due to a small sample size ($n = 3$), of which one patient died

TABLE 1 Patient demographics for p16 Positive ($n = 124$) and p16 Negative ($n = 11$) patients

	p16 positive	p16 negative	Total
Age at treatment			
Mean (SD)	60.3 (8.8)	68.8 (7.7)	61.1 (9.0)
Range	35.0–84.0	58.8–83.0	35.0–84.0
Gender (%)			
Male	100 (80.6)	8 (72.7)	108 (80.0)
Female	24 (19.4)	3 (27.3)	27 (20.0)
Smoking (%)			
Non-smoker	33 (26.6)	0	33 (24.4)
< 10 pack year	2 (1.6)	0	2 (1.5)
> 10 pack year	19 (15.3)	6 (54.5)	25 (18.5)
Ex-smoker <10 pack year	12 (9.7)	0	12 (8.9)
Ex-smoker >10 pack year	35 (28.2)	3 (27.3)	38 (28.2)
Ex-smoker pack year unknown	17 (13.7)	2 (18.2)	19 (14.1)
Unknown	6 (4.8)	0	6 (4.4)
Alcohol (%)			
<1–7 drinks/week	90 (72.6)	6 (54.5)	96 (71.1)
7–14 drinks/week	16 (12.9)	1 (9.1)	17 (12.6)
15–21 drinks/week	6 (4.8)	1 (9.1)	7 (5.2)
>21 drinks/week	5 (4.0)	2 (18.2)	7 (5.2)
Unknown	7 (5.6)	1 (9.1)	8 (5.9)
Adjuvant treatment (%)			
None	41 (33.1)	4 (36.4)	45 (33.3)
Radiation	58 (46.8)	5 (45.5)	63 (46.7)
Chemoradiation	25 (20.2)	2 (18.2)	27 (20.0)
AJCC 8th cTstage (%)			
Tx	0	3 (27.3)	3 (2.2)
T0	68 (54.8)	0	68 (50.4)
T1	10 (8.1)	2 (18.2)	12 (8.9)
T2	36 (29.0)	4 (36.4)	40 (29.6)
T3	9 (7.3)	2 (18.2)	11 (8.1)
T4a	1 (0.8)	0	1 (0.7)
AJCC 8th cN stage (%)			
N0	11 (8.9)	4 (36.4)	15 (11.1)
N1	103 (83.1)	1 (9.1)	104 (77.0)
N2	4 (3.2)	0	4 (3.0)
N2a	0	2 (18.2)	2 (1.5)
N2b	0	2 (18.2)	2 (1.5)
N2c	0	1 (9.1)	1 (0.7)
N3	6 (4.8)	0	6 (4.4)
N3a	0	1 (9.1)	1 (0.7)

following a second head and neck primary of the mandible, and one patient was lost to follow-up. In p16 negative stages III and IV disease ($n = 8$), 5-year OS was 45.0% (SE = 41.8%, 95%CI = 19.8–100), 5-year DSS was 80.0% (SE = 22.4%, 95%CI = 51.6–100) and 5-year RFS was 71.4% (SE = 23.9%, 95%CI = 44.7–100) ($n = 8$). Kaplan–Meier estimates of 5-year LC in all stages was 100.0% (SE = 0.0%). With small sample sizes and large confidence intervals, the outcomes in p16 negative patients should be interpreted cautiously and are limited in clinical value or predictive utility.

3.3 | Recurrences

Thirteen patients (9.6%) suffered one or more recurrences (Table 3). One of the distant recurrences among stage I patients was the same individual who suffered a locoregional recurrence (LRR); the multidisciplinary tumor board did not recommend adjuvant therapy. The patient was salvaged with radiotherapy 70 Gy in 35 fractions to the primary site and bilateral neck irradiation, with concurrent high dose

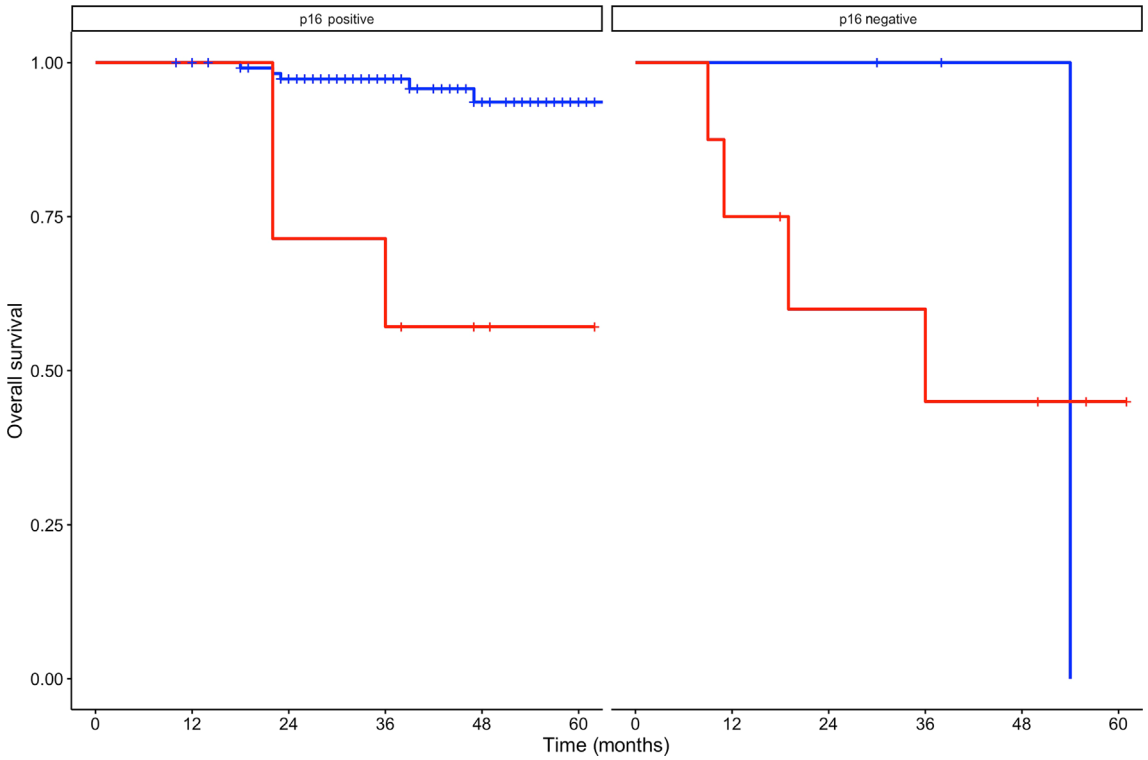

FIGURE 1 Five-year overall survival of patients with oropharyngeal squamous cell carcinoma stratified by p16 status in early (blue) and late (red) stage disease. Due to small sample size ($n = 11$), p16 negative plots should be interpreted with caution.

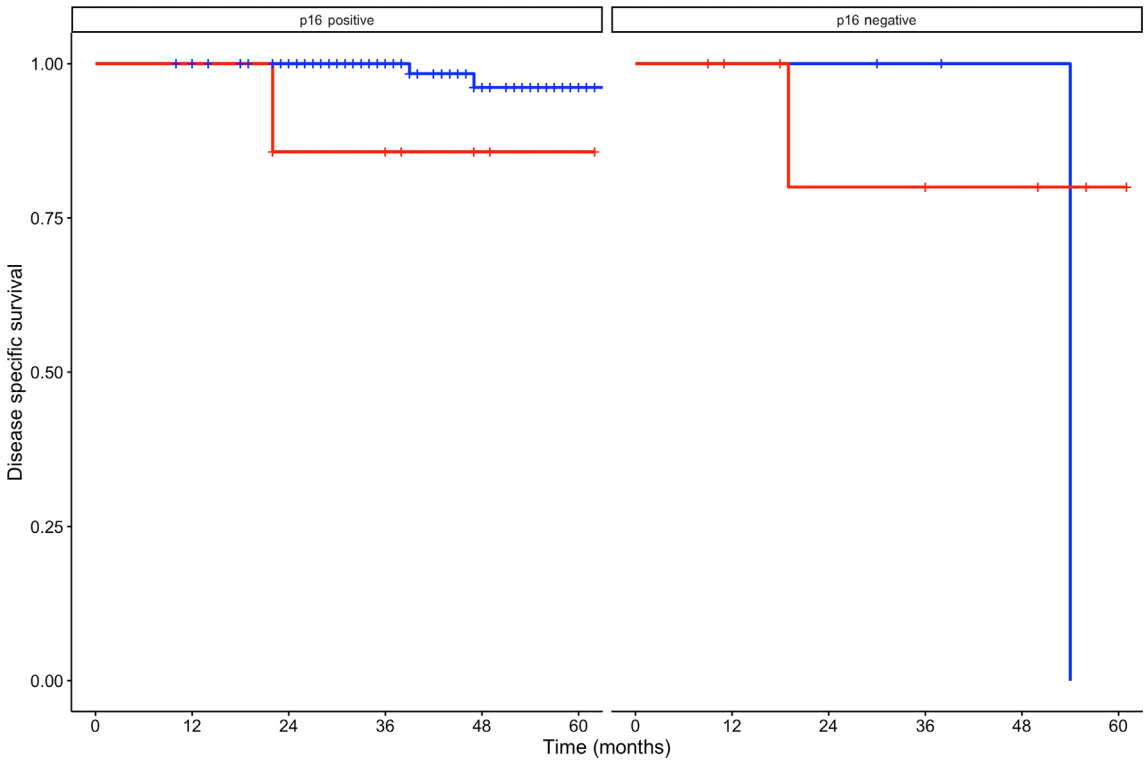

FIGURE 2 Five-year disease-specific survival of patients with oropharyngeal squamous cell carcinoma stratified by p16 status in early (blue) and late (red) stage disease. Due to small sample size ($n = 11$), p16 negative plots should be interpreted with caution.

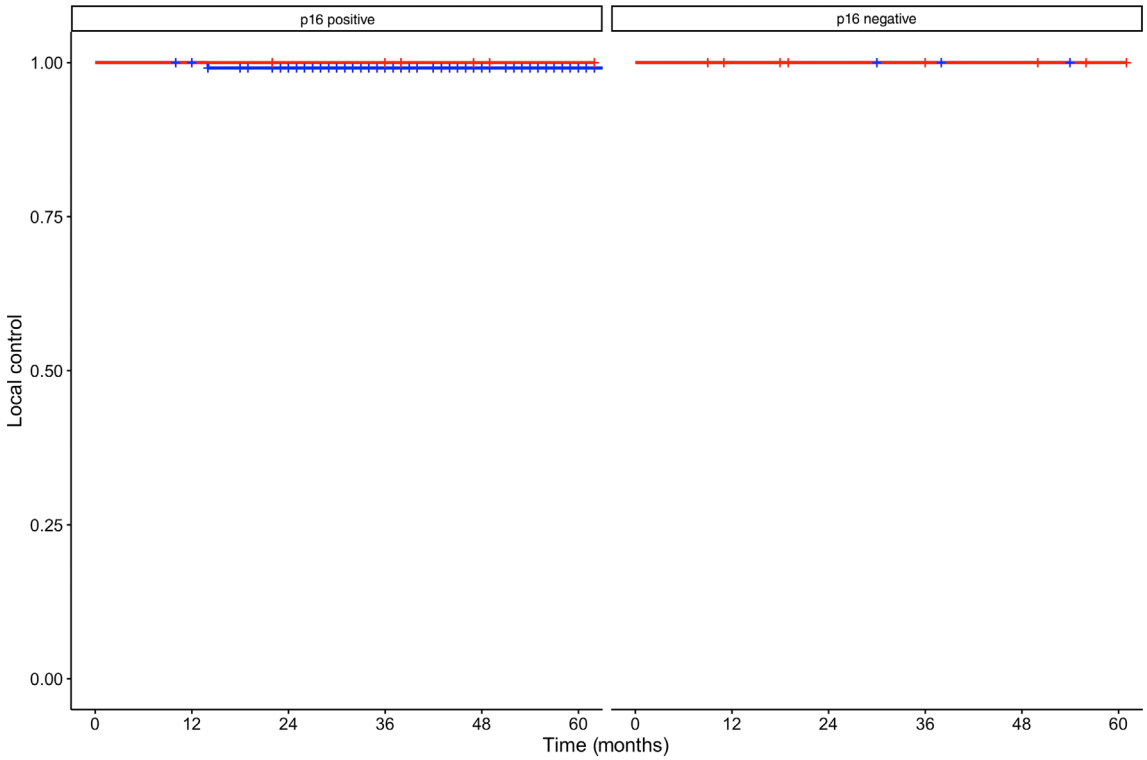

FIGURE 3 Five-year local control of patients with oropharyngeal squamous cell carcinoma stratified by p16 status in early (blue) and late (red) stage disease. Due to small sample size ($n = 11$), p16 negative plots should be interpreted with caution.

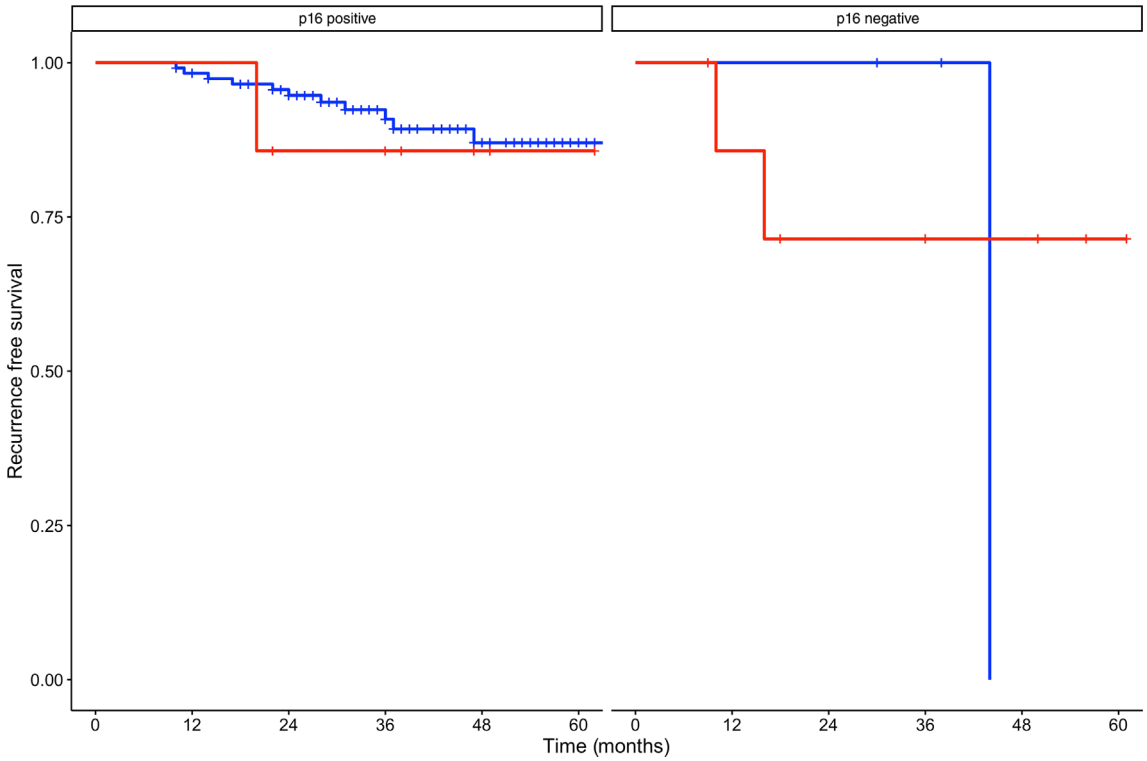

FIGURE 4 Five-year recurrence free survival of patients with oropharyngeal squamous cell carcinoma stratified by p16 status in early (blue) and late (red) stage disease. Due to small sample size ($n = 11$), p16 negative plots should be interpreted with caution.

TABLE 2 Two- and 5-year OS, DSS, LC, and RFS outcomes stratified by p16 status

	p16 positive ($n = 124$)			p16 negative ($n = 11$)		
	Value (%)	SE (%)	95%CI	Value	SE	95%CI
2-year OS	95.8	1.9	92.3–99.5	71.6	19.5	48.8–100
5-year OS	91.0	3.6	84.9–97.6	39.8	48.8	15.3–100
2-year DSS	99.2	0.9	97.5–100	87.5	13.4	67.3–100
5-year DSS	95.5	2.8	90.5–100	58.3	43	25.1–100
2-year LC	99.2	0.8	97.6–100	100	13.4	100–100
5-year LC	99.2	0.8	97.6–100	100	0	100–100
2-year RFS	94.1	2.3	90.0–98.5	80	15.8	58.7–100
5-year RFS	87.0	4.3	80.0–94.7	60	32.9	31.5–100

Abbreviations: DSS, disease-specific survival; LC, local control; OS, overall survival; RFS, recurrence free survival.

TABLE 3 Comparison of AJCC 8th edition clinical stage and type of recurrence

AJCC stage (n)	Recurrences/stage (%)	Local	Locoregional	Regional	Regional and distant	Distant
I (106)	9 (8.5)	0	1	2	1	5
II (14)	2 (14.3)	0	0	2	0	0
III (9)	1 (11.1)	0	0	0	0	1
IVA (4)	2 (50.0)	0	0	0	0	2
IVB (2)	0	0	0	0	0	0

Cisplatin. Less than 3 months after completing CRT, the patient presented with a distant lung metastasis. The patient was treated with 9 cycles of Nivolumab and 8 cycles of Carboplatin plus Paclitaxel. The two regional recurrences within the stage I cohort were ipsilateral recurrences in patients who did not receive adjuvant radiotherapy. The two regional recurrences in the stage II cohort were clinically T3 who received post-operative radiotherapy to the primary site and ipsilateral neck and recurred in the contralateral neck. However, one of the two patients was recommended 60 Gy in 30 fractions to the primary site and bilateral neck but declined. The patient agreed to 50 Gy to the primary site and ipsilateral neck but only completed 38 Gy. The individual with both regional and distant recurrence received adjuvant radiation to the primary site and ipsilateral neck. The patient recurred in the contralateral neck and lung; time to recurrence was 13 months following radiation completion.

3.4 | De-escalation of adjuvant therapy

Ninety patients (67%) received adjuvant therapy following TLM; 64 patients received adjuvant radiation while 26 patients received adjuvant chemoradiation. Between 2014 and 2019, there was a trend toward de-escalation of addition of chemotherapy (Figure 5A) and radiation dose administered (Figure 5B).

4 | DISCUSSION

Our strong survival outcomes, specifically OS and DSS, are consistent with pre-existing literature on primary TLM in p16 positive OPSCC.[5,23,26–28] Our LC rates of >99% in both p16 positive and negative disease across all stages compare favorably with studies that report 5-year LC rates following TLM in OPSCC.[24,25] Our institution has utilized a specimen-oriented margin sampling method since 2017, which significantly reduced our margin positivity rate.[49] This may be a contributing factor to our high local control rate. Our p16 positive RFS rates of >85% in all stages are superior to that of Canis et al., who reported a 64% RFS rate in stages I and II disease, and a 60% RFS rate in stages III and IV disease in their cohort of 102 patients with p16 positive OPSCC treated with primary TLM.[17] However, their study population dates back to 1987, which may partially account for reduced survival outcomes.

As the incidence of HPV-associated OPSCC in younger patients rises, treatment de-escalation while maintaining high survival outcomes is becoming increasingly more important. Between 2014 and 2019, there was a trend toward adjuvant therapy de-escalation at our institution, notably after 2016. At 5 years, there was one LRR in our cohort; time to recurrence was 14 months in a patient who had no adjuvant therapy. Due to our strong survival outcomes, our study lacks power to detect a statistical difference in variables that potentially contribute to recurrence such as PNI, LVI, or ENE (not reported). In a retrospective review of LRR rates in p16 OPSCC treated with TORS, patients who received adjuvant therapy due to higher risk pathologic features were at a lower risk of LRR (HR = 0.28, 95% CI = 0.09–0.83, $p = .023$). However, there were no specific pathologic features such as PNI, LVI, or ENE that were associated with LRR and there was no difference in DFS ($p = .21$) or OS ($p = .86$) between patients who did and did not receive adjuvant therapy.[50] There was a significant difference in 5-year OS in patients who suffered LRR (67.1% vs. 93.9%, $p < .001$).[50] Fortunately, surgery and/or CRT remains an effective salvage treatment option for the majority of p16

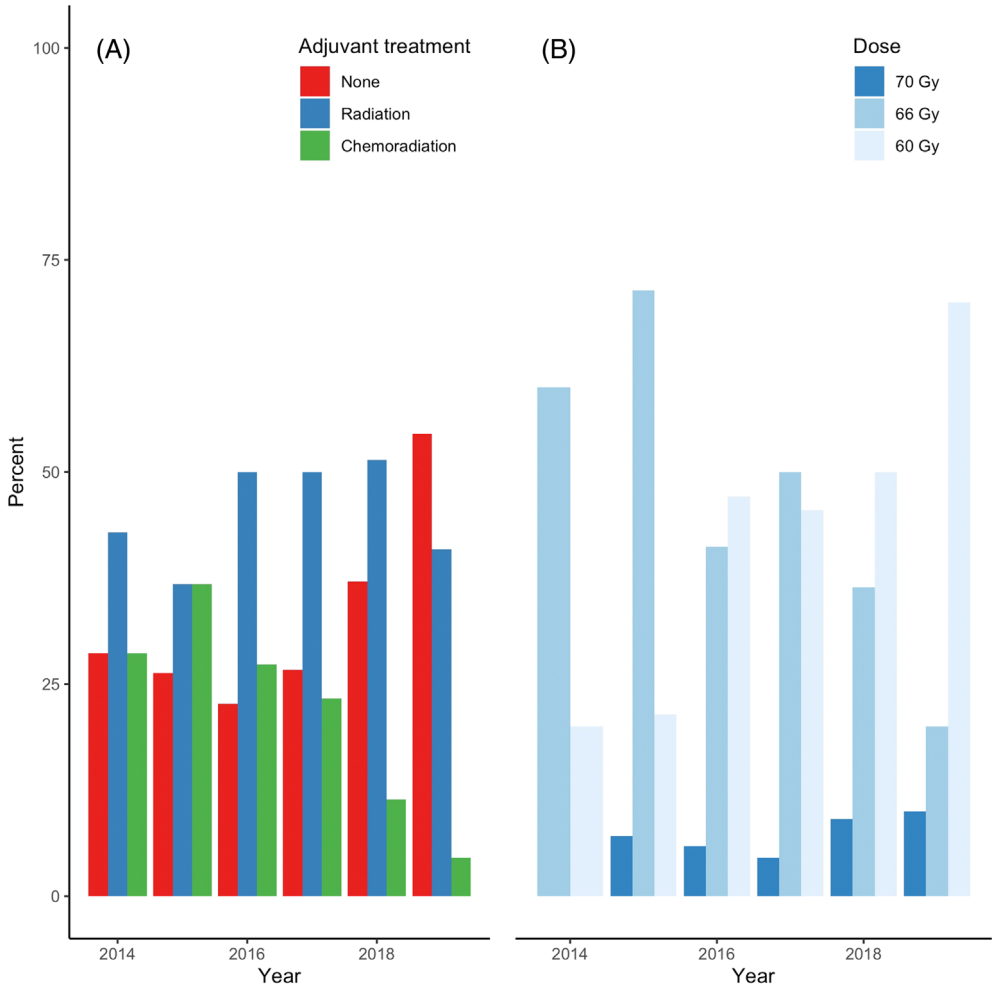

FIGURE 5 (A) Trend in de-escalation of adjuvant therapy by year. (B) Percentage of patients receiving 70, 66, and 60 Gy adjuvant radiation by year

positive patients with LRR; 15 of 23 patients with LRR were alive at last follow-up.[50]

There were two contralateral neck recurrences among nine p16 positive patients with cT3 disease of the tonsil. Of the seven p16 positive cT3 patients without recurrence, each patient received treatment to the contralateral neck, either in the form of a neck dissection, postoperative radiation, or both. Time to recurrence was <1 year in both patients. Considering these findings, we have since changed our practice and now perform a limited contralateral level II and III neck dissection in p16 positive T3 disease involving the tonsil. This ensures patients receive some form of contralateral neck treatment, in cases in which the multidisciplinary tumor board elects not to radiate a clinically node negative contralateral neck. Future work will assess whether this change in practice significantly affects recurrence rates in cT3 disease.

The degree of significant difference in survival outcomes between p16 positive and negative patients, as well as worse survival outcomes in the p16 negative cohort, is partially impacted by a small p16 negative sample size. Large confidence intervals with a standard error in some survival estimates as much as 41.8% warrants caution on conclusions drawn about survival outcomes in the p16 negative cohort at our institution. Mahmoud et al., found a significant difference in 3-year overall survival in patients with p16 negative disease treated with TORS compared to primary radiation; 3-year OS in the TORS arm was 84% (95% CI = 76%–91%), compared to 66% (95%CI = 57%–77%) in patients treated with primary radiation ($p = .01$).[31] Our small p16 negative cohort limits comparison with this study, which is currently the largest case–control study examining transoral surgery in p16 negative disease.

There were no tracheostomies performed in the study group. Additionally, our permanent G-tube rate of 1.5% was consistent with the reported literature. One-year G-tube dependence reported by Wilkie et al. was 1.3%,[51] while Woods et al. reported one patient of 26 required a G-tube during radiation therapy, and was not feeding tube dependent at last follow-up.[25] In a survey of 150 patients with head and neck cancer, Windon et al. found that cure was the highest priority for respondents, followed by overall survival longevity and subsequently swallowing.[52] Notably, priority of survival varied by age, with younger patients valuing long-term survival compared to older patients valuing quality of remaining years of life over quantity. Patients who received dual modality or triple modality therapy reported higher regret scores on the Ottawa Decision Regret Scale compared to single modality treatment. Subjective functional outcomes such as dysphagia and chronic xerostomia were not assessed in our cohort, therefore we are unable to comment on the percent of patients who experienced moderate to severe functional morbidity. Although chronic xerostomia is reported by a high number of patients receiving either primary or adjuvant radiation therapy,[18,35] the absence of xerostomia, ranked as

priority of a moist mouth on the Functional Assessment for Cancer Treatment-General (FACT-G), was among the functional outcomes routinely ranked low by respondents.[52] Despite cure and survival being ranked as the highest and second highest priorities respectively by respondents, head and neck cancer patients continue to regret escalating treatment required to achieve long-term survival.[52]

5 | CONCLUSION

TLM is a safe and effective primary treatment option in OPSCC with strong local control rates in p16 positive and negative disease. Our high 2- and 5-year RFS rate in early p16 positive disease and low 1-year G-tube dependence rate supports our institution's trend toward de-escalation of adjuvant therapy. Our institution now routinely performs a limited level II and III contralateral neck dissection in cT3 p16 positive disease to reduce the risk of recurrence.

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CONFLICTS OF INTEREST

We have no conflicts of interest to disclose.

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