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R. Rahmati

S. Dogan

O. Pyke

F. Palmer

M. Awad

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Authors

R. Rahmati, S. Dogan, O. Pyke, F. Palmer, M. Awad, N. Lee, D. Kraus, J. P. Shah, S. G. Patel, and I. Ganly



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Squamous cell carcinoma of the tonsil managed by conventional surgery and postoperative radiation

Rahmatullah Rahmati, MD^{1,4}, Snjezana Dogan, MD², Owen Pyke, BSc^{1,5}, Frank Palmer, BA¹, Mahmoud Awad¹, Nancy Lee, MD³, Dennis H. Kraus, MD^{1,6}, Jatin P. Shah, MD¹, Snehal G. Patel, MD¹, and Ian Ganly, MD, PhD^{1,*}

¹Head and Neck Service, Department of Surgery, Memorial Sloan–Kettering Cancer Center, New York, New York

²Department of Pathology, Memorial Sloan–Kettering Cancer Center, New York, New York

³Department of Radiation Oncology, Memorial Sloan–Kettering Cancer Center, New York, New York

⁴Department of Otolaryngology–Head and Neck Surgery, Columbia University Medical Center, New York, New York

⁵State University of New York – Stony Brook, School of Medicine, Stony Brook, New York

⁶Head and Neck Institute, North Shore Health System, Great Neck, New York

Abstract

Background—The purpose of this study was to report the long-term outcome of patients with squamous cell cancer (SCC) of the tonsil managed by surgery followed by postoperative radiotherapy (PORT).

Methods—Eighty-eight patients treated between 1985 and 2005 were analyzed. Overall survival (OS), disease-specific survival (DSS), and recurrence-free survival (RFS) were determined by the Kaplan–Meier method. Factors predictive of outcome were determined by univariate and multivariate analysis.

Results—Forty-eight percent of patients had T3 to T4 disease and 75% had a positive neck. Five-year OS, DSS, and RFS were 66%, 82%, and 80%, respectively. The status of the neck was not predictive of outcome (DSS 80% for N0 vs 82% for N+; $p = .97$). Lymphovascular invasion was an independent predictor of OS, DSS, and RFS on multivariate analysis.

Conclusion—Lymphovascular invasion but not pathological stage of the neck is an independent predictor of outcome in patients with tonsillar SCC.

Keywords

tonsil; squamous cell carcinoma (SCC); prognostic factors; human papillomavirus (HPV); oropharynx; surgery

*Corresponding author: I. Ganly, Head and Neck Service, Department of Surgery, Memorial Sloan–Kettering Cancer Center, 1275 York Avenue, New York, NY 10021. ganlyi@mskcc.org.

INTRODUCTION

Over the past 20 years, the incidence of squamous cell carcinoma (SCC) of the oropharynx has increased.¹ This increase has been due to a change in etiology of oropharyngeal cancer from a smoking and alcohol-related disease to a disease caused by human papillomavirus (HPV).¹⁻⁵ It is now estimated that up to 70% of oropharyngeal cancers are due to HPV.^{2,3} The majority of these patients with oropharyngeal SCC are young patients who are usually nonsmokers and nondrinkers.^{3,5,6}

Before the development of organ-preservation protocols involving concurrent chemoradiation therapy, surgery followed by radiation therapy (RT) was the mainstay of treatment for patients with tonsillar SCC, with 5-year disease-specific survival (DSS) rates ranging from 61% to 75%.⁷⁻⁹ Over the past 15 years, improvements in chemoradiation have resulted in excellent locoregional control rates and DSS rates that are comparable to outcome results reported for traditional surgery.¹⁰⁻¹³ As a result, surgery for patients with advanced-stage tonsillar SCC is now rarely carried out. However, 3 observations have resulted in a renewed interest in the surgical management of tonsillar SCC. First, recent advances in robotic and transoral laser microsurgery have meant that some tonsil tumors previously requiring mandibulotomy and free flap surgery can now be treated surgically in a more minimally invasive fashion resulting in less morbidity for the patient.¹⁴ Second, the short-term high-grade acute toxicity of chemoradiation, and the long-term sequelae with fibrosis and swallowing difficulties, have dampened the enthusiasm for concurrent chemoradiation. Finally, it is now widely accepted that patients with HPV-related tonsillar SCC have a superior outcome compared with patients with HPV-negative disease.^{13,15-17}

There is now considerable interest in deintensifying chemoradiation treatments for patients with HPV-positive tonsillar SCC by using lower doses of radiation, smaller radiation fields, and using alternate chemotherapy agents. These deintensifying treatments may spare patients the acute and long-term toxicities associated with platinum-based chemoradiation therapy.^{18,19} A phase 3 trial (Radiation Therapy Oncology Group [RTOG] 1016) randomizing patients to concurrent chemoradiation therapy with cisplatin versus cetuximab for the treatment of HPV-positive oropharyngeal cancer has recently been initiated.²⁰ An alternative approach to deintensifying treatment could be to select patients for minimally invasive transoral surgical techniques in conjunction with adjuvant postoperative radiotherapy (PORT). Therefore, the purpose of our study was to analyze our experience in the management of tonsillar cancer managed by conventional surgery and PORT and determine the impact of lymph node status, margin status, extracapsular spread (ECS), and HPV status on outcomes.

PATIENTS AND METHODS

After institutional review board approval, patients with tonsillar SCC were identified from an institutional database of oropharyngeal cancer treated at Memorial Sloan-Kettering Cancer Center between January 1985 and December 2005. Two hundred thirteen patients received primary treatment of which 105 had definitive surgery, 81 chemoradiation, 26 radiation alone, and 1 chemotherapy alone. Of the 105 patients treated with definitive

surgery, 13 patients had open neck biopsy for unknown primary, 2 patients had prior head and neck radiation, 1 patient had synchronous primaries, and 1 patient had received non-standard treatment for tonsillar SCC. These patients were excluded, leaving 88 patients available for analysis. All patients were treated with surgery and PORT (1 patient did not have radiation). No patients had postoperative chemoradiation, as this was before the publications by Bernier et al.²¹ and Cooper et al.²² Details on patient, tumor, and treatment characteristics were recorded by retrospective review of patient charts. Pathological review was carried out by a pathologist specialized in head and neck pathology (S.D.). To assess HPV status of each tumor, we used p16 immunohistochemistry, which is now recognized as a surrogate marker for HPV.²³ Paraffin blocks were available on 66 patients. Four-micrometer tumor sections were deparaffinized, and after heat-induced epitope retrieval, immunohistochemistry for p16^{INK4a} was performed with the primary antibody dilution of 1:7 as per manufacturer's protocol (CINtec Histology Kit, catalog #9517, Roche mtm Laboratories AG, Heidelberg, Germany). Cases with nuclear and cytoplasmic immunolabeling in at least 70% of the tumor cells were considered positive for p16. Any association between survival outcome and p16 status was determined using the chi-square test.

Patient, tumor, and treatment characteristics are summarized in Table 1. Median age for the entire cohort was 55 years (range, 35–78 years) and 64 (73%) were men. Seventy-seven percent of patients were smokers and 70% alcohol drinkers. The p16 status was available in 66 patients with 48 p16-positive (73%) and 18 p16-negative (27%). Forty two patients (48%) had advanced T3/T4 tumors and 75% had a clinically positive neck. Surgical approach was transoral in 38%, whereas the remainder required an open approach. Mandibulotomy and composite resection was used in 56% and 44% of open approaches, respectively. All but 1 patient underwent neck dissection; with 51% receiving a modified comprehensive neck dissection, 33% radical neck dissection, and 16% selective neck dissection. Sixty-two percent of patients required reconstruction entailing a free flap (40%) or pectoralis major myocutaneous flap (20%).

PORT was delivered by conventional RT methods in 82 patients (93%) and by intensity-modulated radiation therapy (IMRT) in 5 patients (6%). Details regarding target delineation, dose specifications, and guidelines used at our center have been previously described in detail for both conventional RT²⁴ and IMRT approaches.²⁵ In brief, the median prescription dose delivered to the postoperative bed was 63 gray (Gy). If margins were positive, this dose was 66 Gy. The radiation dose to the positive neck was 63 Gy and to the contralateral negative neck it was 54 Gy. For IMRT patients, the high-risk clinical target volume included the preoperative gross disease and the postoperative tumor bed at the primary site, along with any nodal regions with disease involvement. The margin for high-risk clinical target volume was generally 0.5 cm.

Pathologic staging consisted mainly of T1/T2 tumors, 33% and 49%, respectively. Final pathology reports downstaged 10 cT2 and 20 cT3 tumors, as shown in Table 2. The majority of tumors were either moderately or poorly differentiated, 41% and 45%, respectively. Other important findings included the presence of close (defined as <5 mm) or positive resection margins in 49 patients (56%; 20 close and 29 positive), perineural invasion in 14% patients,

necrosis in 15% of patients, and lymphovascular invasion in 15% of patients. Seventy-eight percent of patients had a pathological positive neck with the majority containing N2 disease (64%). In patients with positive neck disease (68 of 88 patients), ECS was present in 41% of patients.

Overall survival (OS), DSS, and recurrence-free survival (RFS), were calculated using the Kaplan–Meier method. Patients lost to follow-up were censored from analysis at the last date of follow-up. Factors predictive of outcome were analyzed by univariate analysis using the log-rank test. Factors with a p value of $< .05$ on univariate analysis or deemed to be of clinical significance were then assessed by multivariate analysis using a Cox proportional hazards model. Statistical analysis was carried out using commercially available software (IBM SPSS for Windows, version 19.0; SPSS, Chicago, IL).

Because of the retrospective nature of the study, assessment of functional outcome of speech, airway, diet, and swallowing could not be accurately determined from chart review. We therefore used percutaneous endoscopic gastrostomy (PEG) tube dependency as a surrogate marker for swallowing dysfunction and tracheostomy dependency as a surrogate marker for airway dysfunction.

RESULTS

The median follow-up time was 74 months (range, 1–241 months). OS, DSS, and RFS at 5 years were 66%, 82%, and 80%, respectively (Figure 1). Seventeen patients had recurrence of which 7 were local alone, 2 locoregional, and 8 distant. There were no cases of isolated neck recurrence. The 5-year local RFS, regional RFS, locoregional RFS, and distant RFS were 89%, 98%, 88%, and 90%, respectively.

Age >60 years, female sex, clinical and pathological T classification, margin status, lymphovascular invasion (LVI), and p16 status were predictive of OS on univariate analysis. In a multivariate model of the 4 most significant variables (age, pT classification, margin status, and LVI), only LVI remained a significant independent predictor (Table 3). Patients with LVI were 2.4 times more likely to die compared with those without LVI (5-year OS 23% vs 73%; $p = .04$).

LVI and ECS were factors predictive of DSS on univariate analysis, whereas only LVI remained significant on multivariate analysis (Table 3). Patients with LVI were 6.9 times more likely to die compared to those without LVI (5-year DSS 43% vs 89%; $p = .003$; Figure 2).

Clinical T classification and LVI were factors predictive of RFS on univariate analysis. Once again, only LVI held significance on multivariate analysis (Table 3). Patients with LVI were 5.5 times more likely to have a recurrence compared to those without LVI (5-year RFS 37% vs 88%; $p = .005$).

An important observation was that 64% of patients had N2 disease, yet nodal status was not a predictor of DSS or RFS. The 5-year DSS for patients with pathological N0, N1, and N2

disease were 80%, 82%, and 83%, respectively. The 5-year RFS for patients with pathological N0, N1, and N2 disease were 75%, 81%, and 81%, respectively.

With regard to p16 status, patients who were p16-positive had superior OS and DSS compared with patients who were p16-negative (5-year OS 74% vs 47%; $p = .04$ and 5-year DSS 89% vs 66%; $p = .08$; Figure 3).

For functional outcome, 59 patients (67%) required tracheostomy at the time of initial surgery. However, only 1 patient (1.1%) had the tracheostomy still in place at 1 year after surgery (Table 4). PEG tube insertion was carried out in 27 patients (31%) either during or after primary surgical procedure. Of these, 11 patients (12%) were still PEG-dependent at 1 year, 8 (9%) were PEG-dependent at 2 years, and 5 (6%) were PEG-dependent at 5 years (Table 4).

DISCUSSION

In this study, we report outcome figures for patients with tonsillar SCC managed with conventional surgery and PORT. OS, DSS, and RFS in our study were excellent at 66%, 82%, and 80%, respectively. The 5-year local, regional, and locoregional controls rates were also excellent at 89%, 98%, and 88%, respectively. Table 5 is a summary of studies published in the literature evaluating tonsillar SCC managed by primary surgery, radiation, or both.^{7–10,12,16,17,26–34} Some series have reported superior results, but these were primarily on patients with T1 and T2 primaries in which transoral tonsillectomies were carried out.^{22,23} In comparison to these studies, 48% of our patients had T3/T4 tonsil tumors. More recently, a multicenter prospective study of 204 patients with oropharyngeal cancer treated with transoral laser microsurgery, reported a 3-year OS, DSS, and disease-free survival (DFS) of 86%, 88%, and 82%, respectively.¹⁶ In a recent prospective study, Haughey et al¹⁷ reported his personal experience of 171 patients with p16-positive oropharyngeal SCC treated with transoral laser microsurgery with 5-year OS, DSS, and DFS of 91%, 94%, 88%, respectively. These excellent survival outcomes coupled with the results reported in our study make a strong argument for primary surgical therapy for selected patients whose primary tumors are amenable to surgical resection by transoral endoscopic or robotic techniques. Our outcome results also compare favorably with nonsurgical series, in which survival figures for primary radiation range from 30% to 86%.^{7–9,29} Recent articles from Memorial Sloan–Kettering Cancer Center¹⁰ and MD Anderson Cancer Center³⁵ report their outcomes in treating oropharyngeal cancer with IMRT. Setton et al¹⁰ reported on 442 patients with tonsillar (50%) and base of tongue (46%) cancer undergoing IMRT and concurrent chemotherapy (88%), achieving 3-year OS of 84.9%. Garden et al³⁵ reported on the outcomes of 776 patients with oropharyngeal cancer treated with IMRT at MD Anderson. In their cohort, 48% were tonsillar SCC and 54% received chemotherapy in either an induction or concurrent fashion. They too observed excellent outcomes with 5-year OS of 84%.

Our multivariate analysis demonstrated only LVI to be an independent predictor of survival. This would be in keeping with our observation that in over 50% of patients with recurrence, the site of recurrence was distant metastases rather than locoregional. The importance of LVI

in other tumor types (eg, breast, gastric, cervical, prostate, and bladder tumors) as a prognostic factor is well documented.^{36–41} However, the significance of LVI in head and neck cancer is less well documented with some articles reporting it to be significant^{17,42} and others not.²⁸ Interestingly, patients who were p16-negative were more likely to have LVI compared to p16-positive patients (27.8% vs 14.6%; $p = .18$). When LVI was stratified by p16 status, patients who had LVI had a statistically significant poorer DSS in both p16-positive (60% vs 94%; $p = .022$) and p16-negative tumors (30% vs 86%; $p = .023$). However, the outcome was most poor in patients with p16-negative LVI-positive tumors.

In our study, nodal involvement was not a significant predictor of survival. Nodal metastasis in head and neck cancer is generally associated with a 50% decrease in survival and numerous articles demonstrate its significance as a prognostic indicator in all sites of the head and neck.^{43–45} It is possible that nodal metastases in tonsillar cancer are of less biological importance and there is evidence from other studies that support this.^{16,29,34} The reason why nodal status is not significant on outcome in tonsillar cancer is an important observation, but the reason for this remains unclear. There are 2 possible explanations. First, tonsillar cancers are often “lymphoepithelioma like SCC” similar to nasopharyngeal cancer. These types of cancers are highly radiosensitive, and, thus, similar to nasopharynx, the status of lymph node metastases does not influence outcome.^{46–49} The other possibility is that this may be an HPV-related phenomenon and that nodal metastases in HPV-related oropharyngeal cancers are of less biological significance. In the study by Haughey et al¹⁶ in which nodal status was also reported not to be of significance for recurrence or survival outcome, 74% of patients were positive for HPV and 90% stained positive for p16. In our series, of 66 patients analyzed, p16 stained positive in 73% patients. In these patients, there was no significant difference in DSS in patients who were pN-positive compared to those who were pN0 (DSS: 91% vs 75%; $p = .26$). However, our analysis also showed that in patients with p16-negative tumors, nodal status was also not significant (DSS: 62% vs 75%; $p = .51$). This therefore suggests that positive lymph nodes in patients with tonsillar cancer does not confer a worse outcome irrespective of p16 status.

The relevance of ECS also requires some discussion. In our study, 41% of lymph nodes had ECS. None of these patients had postoperative chemoradiation as these patients were treated in an era before the RTOG and European Organization for Research and Treatment of Cancer publications by Bernier et al²¹ and Cooper et al²² that reported reduced locoregional recurrence with adjuvant chemoradiation. All patients, except 1, did receive PORT. Importantly, there were no cases of isolated neck recurrence and only 2 cases of neck recurrence in conjunction with local recurrence. ECS was also not significant on multivariate analysis, an observation recently reported by Haughey et al.¹⁶ Again, this may be an HPV-related phenomenon. To examine this further we assessed the impact of ECS on DSS by stratifying for p16 status. For patients who were p16-positive, ECS had no impact on DSS; the 10-year DSS for ECS-positive versus ECS-negative was 86% versus 92%, $p = .65$, respectively. In contrast, however, ECS had a significant negative impact in patients who were p16-negative; the 10-year DSS for ECS-positive versus ECS-negative was 31% versus 86%, $p = .03$, respectively. A similar finding was also observed when we assessed the impact of positive/close margins on DSS in patients who were p16-positive. Again, margin status was only of significance in patients who were p16-negative. In p16-positive patients, the 10-

year DSS for margin positive/close versus margin negative was 89% versus 87%, $p = .83$, respectively. In contrast, in patients who were p16-negative, the 10-year DSS for margin positive/close versus margin negative was 33% versus 86%, $p = .07$, respectively. However, it must be emphasized that our data are based upon retrospective data of a small series of patients in whom p16 status was only available on 66 patients. As such, the results have to be interpreted with some caution and require further validation on larger surgical series. It is possible that the observed lack of significance of nodal status, ECS, and margin status in patients who are p16-positive (HPV-positive) may indicate that this is a biologically less aggressive disease than p16-negative tonsillar SCC. The most important predictor of outcome in our analysis, LVI, was also less common in patients with p16-positive tumors indicating a possible association between LVI and p16 status. Our study, therefore, raises questions about whether or not there should be a new staging system for oropharyngeal cancer, with stratification based on p16 status. Indeed, the RTOG 0129 study reported by Ang et al¹³ introduced a risk stratification system based on p16 status and smoking status. In this system, patients were classified as low risk when p16-positive and smoked <10 pack-years, high risk if p16-negative and smoked >10 pack-years, and intermediate risk if p16-positive/smoker >10 pack-years, or p16-negative/smoker <10 pack-years. This system showed that low risk patients had OS at 3 years over 85%, high risk 45%, and intermediate risk 65%. It is possible that this risk classification system may be introduced in the staging system for HPV (p16)-positive tonsillar cancer. The adequacy of the current staging system is further questioned by a recent 50-year retrospective analysis of 3891 patients with oropharyngeal SCC treated at the MDACC.⁵⁰ After determining a significant survival difference between patients treated before and after 1995, patients treated after 1995 with nodal disease had significantly better prognosis compared to those without. More specific to tonsillar SCC, an Australian multicenter analysis of 489 patients with tonsillar SCC found better outcomes in HPV-positive tumors with higher N classification, suggesting that the staging is modified by HPV status.⁵¹

Our study does have the limitation that it is retrospective and, therefore, susceptible to all the problems associated with retrospective data collection and analysis. Despite this, our data does show that primary surgery and PORT offers excellent survival outcomes that are comparable to results for RT alone and chemoradiation therapy. This data helps support the recent renewed interest in the treatment of tonsillar SCC in selected patients by transoral surgery with or without the use of new techniques, such as robotic and laser surgery and can be used as benchmark data against which the results of these techniques can be compared.

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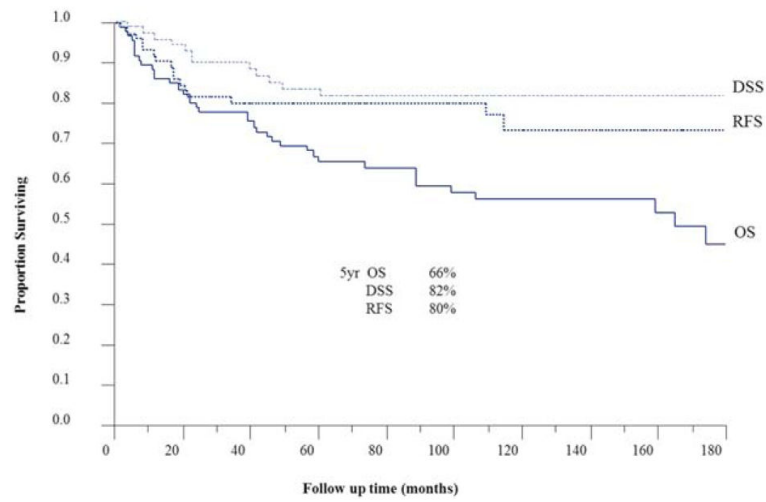


FIGURE 1. Overall, disease-specific, and recurrence-free survival in patients with squamous cell carcinoma (SCC) of the tonsil managed by surgery with postoperative radiotherapy (PORT). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

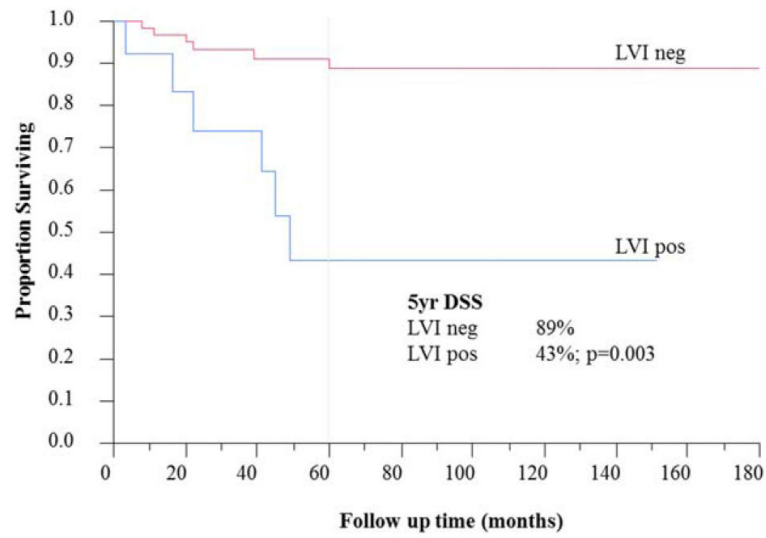


FIGURE 2. Disease-specific survival stratified by lymphovascular invasion. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

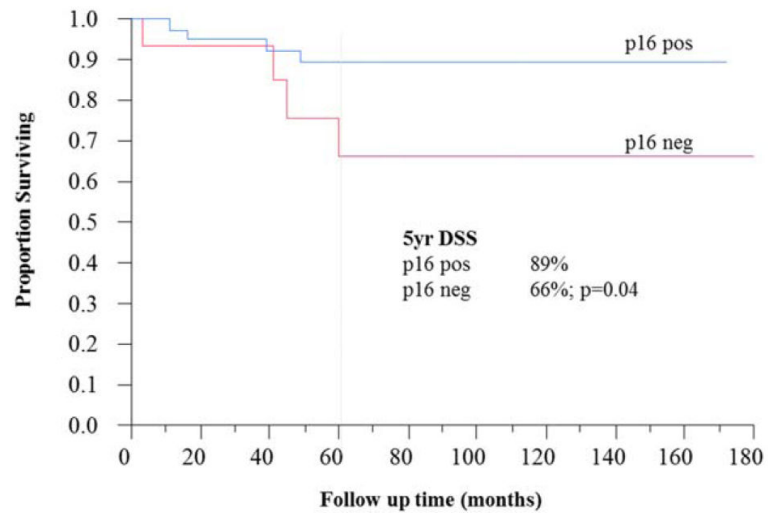


FIGURE 3. Disease-specific survival stratified by p16 status. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

TABLE 1

Clinical, pathologic, and treatment characteristics.

Clinical characteristics		Pathologic characteristics		Treatment characteristics	
Baseline characteristics	No. of patients (%)	Baseline characteristics	No. of patients (%)	Baseline characteristics	No. of patients (%)
Sex		pT classification		Primary surgery	
Male	64 (73)	pT1	28 (32)	S only	1 (1)
Female	24 (27)	pT2	38 (43)	S + PORT	87 (99)
Age, y		pT3	5 (6)	Neck dissection	
<60	64 (73)	pT4	17 (19)	Yes	87 (99)
>60	24 (27)	pN classification		Selective neck dissection	14 (16)
Smoking status		pN0	20 (23)	Modified neck dissection	44 (51)
Yes	68 (77)	pN1	12 (14)	Radical neck dissection	29 (33)
No	14 (16)	pN2a	9 (10)	No	1 (1)
Unknown	6 (7)	pN2b	46 (53)	Approach	
Alcohol status		pN2c	1 (1)	Transoral	33 (38)
Yes	62 (70)	p Overall stage		Open	55 (62)
No	18 (20)	I	4 (5)	Mandibulotomy	31 (56)
Unknown	8 (10)	II	11 (12)	Composite resection (mandibulectomy)	24 (44)
Clinical T classification		III	12 (14)	Reconstruction	
cT1	18 (20)	IV	61 (69)	Yes	55 (62)
cT2	28 (32)	Margins		Primary	22 (40)
cT3	28 (32)	Negative	33 (38)	PMMF	11 (20)
cT4	14 (16)	Positive/close	49 (56)	Free flap	22 (40)
Clinical N classification		Unknown	6 (7)	No	33 (38)
cN0	23 (26)	LVI			
cN1	23 (26)	Yes	13 (15)	PORT	
cN2a	15 (17)	No	75 (85)	Conventional	82 (93)
cN2b	22 (25)	Necrosis		IMRT	5 (6)
cN2c	3 (3)	Yes	13 (15)	None	1 (1)
cN3	2 (2)	No	75 (85)		
		PNI			
		Yes	12 (14)		
		No	76 (86)		
		ECS			
		Yes	28 (41)		
		No	40 (59)		

Abbreviations: S, surgery; PORT, postoperative radiotherapy; PMMF, pectoralis major myocutaneous flap; LVI, lymphovascular invasion; IMRT, intensity-modulated radiation therapy; PNI, perineural invasion; ECS, extracapsular spread.

TABLE 2

Correlation between clinical T classification and pathologic T classification.

Clinical T classification	No. of patients by pathologic T classification			
	pT1	pT2	pT3	pT4
cT1	15	3	–	–
cT2	10	17	–	1
cT3	3	17	5	1
cT4	–	1	–	15

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TABLE 3

Factors predictive of overall, disease-specific, and recurrence-free survival.

Variables	OS			DSS			RFS		
	Univariate analysis	Multivariate analysis		Univariate analysis	Multivariate analysis		Univariate analysis	Multivariate analysis	
	5-y OS (%)	RR (95) CI	p value	5-y DSS (%)	RR (95) CI	p value	5-y RFS (%)	RR (95) CI	p value
Age, y									
<60	76	Referent		88			85		
>60	39	1.8 (0.8–3.8)	.15	60	.056		67		.07
Sex									
Male	72			86			71		
Female	49		.04	69	.065		83		.52
Smoking									
Never	69			83			83		
Ever	65		.73	84	.25		82		.63
Alcohol									
Never	88			100			100		
Ever	58		.15	77	.12		75		.15
Clinical T classification									
cT1	76			100			100		
cT2	78			83			83		
cT3	59			75			68		
cT4	38		.02	58	.108		66		.05
Clinical N classification									
cN0	61			77			78		
cN1	60			75			72		
cN2	70			87			85		
cN3	0		.54	100	.62		100		.78
Pathologic T classification									
pT1	81	Referent		92			88		

Variables	OS			DSS			RFS		
	Univariate analysis		Multivariate analysis	Univariate analysis		Multivariate analysis	Univariate analysis		Multivariate analysis
	5-y OS (%)	p value	RR (95) CI	5-y DSS (%)	p value	RR (95) CI	5-y RFS (%)	p value	RR (95) CI
pT2	70	.4	1.5 (0.6–3.5)	78			79		
pT3	40	.09	3.2 (0.8–12.9)	50			50		
pT4	37	.006	2.5 (0.9–6.8)	69	.36	–	75		.13
Pathologic N classification									
pN0	60			80			75		
pN1	73			82			81		
pN2	66	.93	–	83	.822	–	81	.8	–
Grade									
Well differentiated	67			100			100		
Moderately differentiated	57			81			79		
Poorly differentiated	74	.88	–	84	.46	–	82	.86	–
Margin status									
Negative	78		Referent	89			83		
Close/positive	52	.01	1.5 (0.7–3.2)	72	.07	–	74	.32	–
Necrosis									
Present	62			72			75		
Absent	66	.76	–	83	.42	–	81	.08	–
LVI									
Present	23		2.4 (1–5.4)	43	.04	6.9 (1.9–25.3)	37		5.5 (1.9–16.1)
Absent	73	.0001	Referent	89	.0001	Referent	88	.0001	Referent
PNI									
Present	50			71			83		1.5 (0.5–4.7)
Absent	68	.22	–	83	.25	–	83	.07	Referent
ECS (n= 68)									
Positive	51			69		2.7 (0.7–11.2)	71		.16
Negative	79	.2	–	93	.03	Referent	90	.15	–
ECS, all									

Variables	OS			DSS			RFS		
	Univariate analysis		Multivariate analysis	Univariate analysis		Multivariate analysis	Univariate analysis		Multivariate analysis
	5-y OS (%)	<i>p</i> value	RR (95) CI	5-y DSS (%)	<i>p</i> value	RR (95) CI	5-y RFS (%)	<i>p</i> value	RR (95) CI
Positive	51			89			71		
Negative	72	.3	–	88	.05	–	85	.28	–
p16 status									
Positive	74			89			87		
Negative	47	.04	–	66	.08		73	.48	

Abbreviations: OS, overall survival; DSS, disease-specific survival; RFS, recurrence-free survival; RR, risk ratio; CI, confidence interval; LVI, lymphovascular invasion; PNI, perineural invasion; ECS, extracapsular spread.

The figures in bold indicate statistical significance.

TABLE 4

Tracheostomy and percutaneous endoscopic gastrostomy tube dependence.

Tracheostomy tube dependence			PEG dependence		
Duration	No. of patients	%	Duration	No. of patients	%
2 wk	30	50.8	4 mo	7	25.9
2–6 wk	23	39.1	4 mo – 1 y	8	29.6
6 wk – 4 mo	3	5.1	1–2 y	3	11.1
4 mo – 1 y	1	1.7	2–5 y	3	11.1
>1 y	1	1.7	>5 y	5	18.5
Unknown	1	1.7	Unknown	1	3.7
Total	59	100	Total	27	100

Abbreviation: PEG, percutaneous endoscopic gastrostomy.

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TABLE 5

Tonsil and oropharyngeal squamous cell carcinoma survival outcomes and prognostic factors.

Author	Year	Treatment	No. of patients	Site	5-y OS %	5-y DSS %	5-y RFS %	Nodal status	LVI	HPV
Current study	2012	Surgery	88	Tonsil	66	82	80	NS	S	S
Moore ²⁶	2009	Surgery	102	Tonsil	85	94	-	-	-	-
Yildirim ²⁷	2010	Surgery	120	Tonsil	86	-	92	-	-	-
Chuang ²⁸	2011	Surgery	86	Tonsil	-	-	-	S for DSS	NS	NS
Hicks ⁷	1998	Surgery vs nonsurgical	90	Tonsil	-	61/37	-	-	-	-
Perez ³¹	1998	Surgery vs nonsurgical	384	Tonsil	NS	-	-	S for DFS	-	-
Poulsen ⁹	2007	Surgery vs nonsurgical	146	Tonsil	65/41	75/56 (NS)	-	NS	-	-
Shirazi ³²	2006	Surgery vs nonsurgical	74	Tonsil	71/48 (NS)	-	-	S	-	-
Jaber ⁸	2009	Surgery vs nonsurgical	141	Tonsil	45/23	67/30	-	NR	-	-
Mendenhall ²⁹	2000	RT	400	Tonsil	49	70	-	NS	-	-
Setton ¹⁰	2012	CRT	221	OP	86	-	-	S for OS	-	-
Denis ³⁰	2004	RT vs CRT	226	OP	22	27	-	NR	-	-
Mendenhall ²⁹	2010	RT	130	OP	76	85	-	NR	-	-
Fein ³³	1996	RT	490	OP	44	77	-	NR	-	-
Moncrieff ³⁴	2009	Surgery	92	OP	-	83	-	NS	-	-
Haughey ¹⁶	2011	Surgery	204	OP	78	84	74	NS	-	S
Haughey ¹⁷	2012	Surgery	171	OP	91	94	-	NS	S	S

Abbreviations: OS, overall survival; DSS, disease-specific survival; RFS, recurrence-free survival; LVI, lymphovascular invasion; HPV, human papillomavirus; NS, not significant; S, significant; DFS, disease-free survival; NR, not reported; RT, radiotherapy; CRT, chemoradiation; OP, oropharynx.