

Oncologic Outcomes of Extended Neck Dissections in HPV-related Oropharyngeal Squamous Cell Carcinoma

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Abstract

Objective: To evaluate the oncologic outcomes of patients with HPV-related oropharyngeal squamous cell carcinoma (OPSCC) in cases where resection of extralymphatic structures (RELS) is necessary due to nodal invasion. Study Design: Retrospective cohort

Methods: Patients with HPV-related OPSCC undergoing neck dissections requiring RELS were compared to those receiving standard SND without RELS. Patients who had RELS were identified from a database including two academic institutions from 1998 to 2013. This group was matched by pathological T-stage, pathological node number, and comorbidity to a group of patients undergoing standard SND.

Results: Seventy-two patients were included in each group. There were no significant baseline differences between treatment groups. RELS included the spinal accessory nerve (51%), internal jugular vein (82%), and sternocleidomastoid muscle (57%). In a Kaplan-Meier survival analysis, patients undergoing RELS had decreased disease-specific survival compared with those receiving a standard SND (log-rank 0.03). Regional recurrence, however, was similar between groups (4%). Distant recurrence occurred in 17% of patients undergoing RELS and 7% of those who received a standard SND, although the difference did not reach statistical significance (p>0.05). Initial gastrostomy tube placement was significantly higher in the RELS group (58% vs 22%, difference 36%, 95%CI 18% to 54%), however, this difference was no longer significant at 2 years (10% vs 4%, p>0.05).

Conclusions: Patients with invasive nodal disease from HPV-related OPSCC can be managed with RELS as indicated without increased regional recurrence. The need for RELS appears to be an associated with decreased survival.

Introduction

The incidence of HPV-associated oropharyngeal squamous cell carcinoma (OPSCC) continues to rise in the United States. Given the overall excellent prognosis of patients with HPV-related disease, there has been significant effort devoted to identifying appropriate patient groups for de-escalation.¹ However, understanding which risk factors necessitate intensification of therapy is equally important. The size and extent of nodal metastases have consistently been associated with the risk of recurrence for non-surgical therapy including N3 staging² and radiographically matted nodes.^{3,4} The surgical treatment of such patients with infiltrative nodal disease, who require extensive dissections including removal of major muscular or neurovascular structures, has not been well studied, particularly for HPV-related OPSCC. The objective of this report is to compare the oncologic and functional outcomes of patients with HPV-related OPSCC requiring **resection of extralymphatic structures (RELS)** during neck dissection to an otherwise similar group of patients undergoing **standard selective neck dissections (SND)**.

Methods and Materials

- Retrospective review 1998 to 2013 Washington University and Mayo Clinic
- Surgically managed patients with HPV-related OPSCC
- Patients who had RELS (resection of major muscular or neurovascular tissue) case-matched with patients who had standard SND.
- Matched for pathological T-stage, pathologically positive node number, and severity of comorbidity.
- Exclusion criteria: distant metastatic disease on presentation, previous treatment for an upper aerodigestive tract cancer, or not treated with curative intent.
- Standard SND included levels 2-4, and was extended to levels 1 or 5 as indicated. For patients who underwent RELS, extent of dissection was determined intraoperatively based on nodal invasion. Adjuvant therapy was determined in multidisciplinary fashion.
- The primary endpoint was regional recurrence. Secondary endpoints included overall (OS), disease-specific (DSS), and disease-free survival (DFS), as well as complications of the neck dissection and gastrostomy tube rates. Statistical analysis was performed using SPSS (SPSS v22, IBM, Chicago, IL). Univariable analysis was performed with a McNemar Test for categorical variables and a paired sample T-Test or Wilcoxon Signed Ranks Test for continuous data, depending on data normality.

Results

72 patients with HPV-related OPSCC (20%) underwent RELS and were matched to 72 similar patients who underwent standard SND. Median follow up was 48.6 months (range 0.9 to 211.7 months). All patients were treated with upfront transoral resection of their primary tumor along with ipsilateral or bilateral neck dissection as determined by disease extent. Demographic, tumor, and treatment characteristics for both standard SND and RELS are shown in Table 1. Treatment details for the patients undergoing RELS including type of neck dissection and extralymphatic structures resected are shown in Table 2. Oncologic and functional outcomes are shown in Table 3 and Kaplan-Meier survival outcomes are shown in Figure 1. **Regional recurrences were the same (4%) while distant recurrences were higher in the RELS group** although this did not reach statistical significance (17% vs 7%, p>0.05). **Disease-free survival was significantly worse in patients undergoing RELS.** Overall complications of the neck dissection, similarly, were higher in the RELS group but did not reach statistical significance (14% vs 4%, p>0.05). Placement of a gastrostomy tube at any point during treatment was significantly higher in the RELS group (58% vs 22%, difference 36%, 95%CI 18% to 54%, p=0.001). Presence of a gastrostomy tube in survivors at 2 years was also higher in the RELS group but did not reach significance (10% vs 4%, difference 6%, -12% to 24%).

Discussion

This study shows that even for invasive nodal disease requiring RELS, primary surgical management does not result in increased regional recurrence when compared to a set of matched controls undergoing standard SND. The regional recurrence rate of 4% for both groups in this study is similar to other recent large surgically managed cohorts of HPV-related OPSCC.⁵⁻⁷ These studies, however, do not discuss in detail the need for resection of extralymphatic structures and do not include extent of dissection in multivariable models when determining risk factors for recurrence and survival. Although in the current series regional control was excellent **in patients undergoing RELS, disease-specific survival was significantly worse than matched controls undergoing standard SND. This may be at least partly explained by the increased rate of distant failure in the RELS group (17% vs 7%).** Similar increases in distant metastases have been reported in both surgical and non-surgical studies examining outcomes of patients with invasive nodal disease.⁸ Development of new systemic agents and clinical trials for HPV-related OPSCC should have a focus on this group of patients with infiltrative nodal disease.

Major limitations of this study include the lack of non-surgical comparison and the absence of quality of life data. Initial gastrostomy tube rates were significantly higher in patients requiring RELS (58% vs 22%). Major cranial nerves were resected in over 50% of patients in this group. Although the long-term gastrostomy tube rate decreased to 10% in the RELS group, without data from validated dysphagia indices, swallowing-related quality of life remains uncertain.

Conclusions

In patients with HPV-related OPSCC requiring RELS due to invasive nodal disease, up front surgical management with adjuvant therapy results in excellent long-term regional control. Despite this, the need for RELS appears to be an independent risk factor for decreased disease-specific survival and increased distant failure. In addition, RELS may come with increased treatment-related morbidity including increased early gastrostomy tube rates and the need for resection of major cranial nerves. In patients who may require RELS to clear invasive nodal disease, the value of excellent regional control must be weighed against the surgical morbidity and risk of distant metastasis.

	RELS (n=72)	Standard SND (n=72)	Difference (95% CI)
pT0-2	56 (78%)	56 (78%)	0%
pT3-4a	16 (22%)	16 (22%)	
pN0-2a	11 (15%)	11 (15%)	0%
pN2b-3	61 (85%)	61 (85%)	
0-4 pos nodes	49 (68%)	49 (68%)	0%
5+ pos nodes	23 (32%)	23 (32%)	
ACE-27 0-1	58 (84%)	60 (85%)	1% (-100% to 100%)
ACE-27 2-3	11 (15%)	11 (15%)	
cT0-2	56 (78%)	62 (86%)	6% (-2% to 14%)
cT3-4a	16 (22%)	10 (14%)	
cN1-2a	11 (15%)	11 (15%)	0%
cN2b-3	61 (85%)	61 (85%)	
Male	67 (93%)	66 (92%)	1% (-100% to 100%)
Female	5 (7%)	6 (8%)	
Mean age	57.6	55.1	2.5 (-0.9 to 5.9)
Smoking <10 py	28 (42%)	39 (53%)	11% (-6% to 28%)
Smoking 10+ py	39 (58%)	34 (47%)	
Bilateral ND	26 (36%)	18 (25%)	11% (-6% to 28%)
ECE	66 (96%)	60 (84%)	12% (0% to 24%)
Adjuvant RT	23 (32%)	22 (31%)	1% (-100% to 100%)
Adjuvant CRT	44 (61%)	44 (61%)	0%

Table 1. Demographics, tumor, and treatment characteristics.

	n=72
ND type	
• SND	0
• MRND	4 (6%)
• RND	5 (7%)
• Extended SND	56 (77%)
• Extended MRND	2 (3%)
• Extended RND	5 (7%)
Structures resected	
• XI	37 (51%)
• IJV	59 (82%)
• SCM	41 (57%)
• Other*	18 (25%)
• Multiple structures	45 (63%)

Table 2. Treatment details for patients who underwent resection of extra-lymphatic structures. *Other structures include deep neck musculature, superficial parotidectomy, thyroid, external carotid artery, sympathetic chain, and the vagus and hypoglossal nerves.

	RELS (n=72)	Standard SND (n=72)
Recurrence		
• Local	1 (1%)	0
• Regional	4 (6%)	4 (6%)
• Distant	12 (17%)	5 (7%)
5-year K-M survival (95% CI)		
• Overall survival	78% (68% to 88%)	89% (81% to 97%)
• Disease-specific survival	82% (72% to 92%)	95% (89% to 100%)
• Disease-free survival	68% (54% to 80%)	79% (69% to 89%)
Complications		
• Overall complications	10 (14%)	3 (4%)
• Surgical site infection	5 (7%)	0
• Fistula	3 (4%)	0
• Neck hematoma	2 (3%)	1 (1%)
• Cranial nerve injury	1 (1%)	1 (1%)
• Chyle leak	0	1 (1%)
Gastrostomy tube		
• Ever	42 (58%)	16 (22%)
• Present at 2 years	7 (10%)	3 (4%)

Table 3. Outcomes

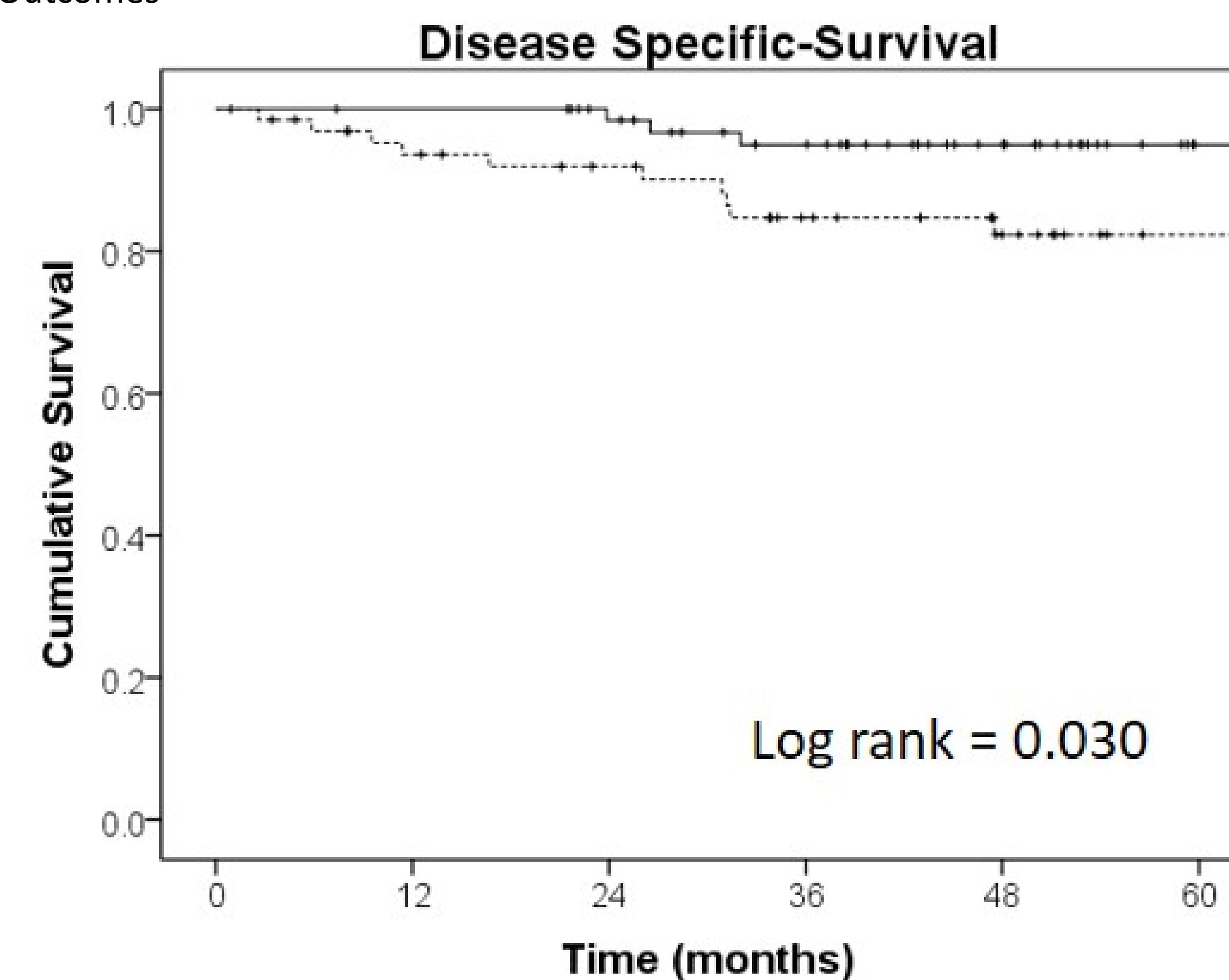


Figure 1. Disease-specific survival of for patients undergoing standard SND (solid line) and neck dissection with RELS (dotted line).

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