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Redefining Risk of Contralateral Cervical Nodal Disease in Early-Stage Oropharyngeal Cancer in the Human Papillomavirus Era

Andrew W Smith, Matthew Gallitto, Eric J Lehrer, Isaac Wasserman, Vishal Gupta, Sonam Sharma, Jerry T Liu, Marshall Posner, Krzysztof Misiukiewicz, William H Westra, Eric M Genden, Yarah Haidar, Mike Yao, Marita S Teng, Brett A Miles, Richard L Bakst

From the *Head and Neck*. May 2021.

Background: The optimal extent of surgery and/or radiation to the contralateral lymph node region is unknown in early-stage human papillomavirus (HPV)-related oropharyngeal squamous cell carcinoma (OPSCC).

Methods: To investigate the pathologic incidence of and risk factors for contralateral nodal disease (CND) in cT1-T2 HPV-related OPSCC treated with transoral robotic surgery (TORS) and bilateral neck dissection (BND), the records of 120 patients were reviewed.

Results: Eleven patients displayed pathologic contralateral nodal disease (pCND), including 7.1% of tonsil and 10.9% of base of tongue (BOT) cases. Medial hemistruature involvement and cN2 disease were significantly associated with pCND. Zero cN0 patients had pCND, and on multivariate analysis only cN classification remained significantly associated with pCND. Four percent of BOT patients and 2% of tonsil patients with a well-lateralized primary and cN0/N1 neck demonstrated pCND.

Conclusions: HPV-related OPSCC that are cN0-N1 have exceedingly low rates of pCND. Well-lateralized HPV-related BOT primaries with limited clinical nodal disease may be candidates for ipsilateral only treatment.

Summary statements

- This study retrospectively reports incidence of occult nodal metastatic disease in 120 patients with clinical T classification 1-2 human-papillomavirus related oropharyngeal tumors undergoing transoral robotic surgery with bilateral neck dissection.
- Among patients with clinical N0-1 tonsil tumors that were well-lateralized (n=44), one patient (2%) had pathologic contralateral nodal disease.
- Among patients with clinical N0-1 base of tongue tumors that did not involve the medial hemistruature (n=49), two patients (4%) had pathologic contralateral nodal disease.

Strengths

- Pathologic evaluation of contralateral lymph nodes allows more clear understanding of risk of contralateral disease when compared to studies that report rates of clinical contralateral nodal emergence, which may be impacted by other factors such as adjuvant therapy.
- Study addresses a patient population of great interest and addresses a very timely and relevant clinical question.
- Clear definition of a “well-lateralized” tumor and patient inclusion criteria supports study reproducibility and comparison to other future studies.



Weaknesses

- Relatively small number of patients in cohort of greatest interest (well-lateralized cN0-1 base of tongue tumors, n=49) limits generalizability.
- Median lymph node yield of 17 in contralateral neck dissections may lead to false-negative findings, and in the absence of any reported clinical follow-up it cannot be determined whether any clinical contralateral nodal emergence may have occurred.
- Lack of inclusion of American Joint Committee on Cancer 7th edition nodal classification limits ability to determine impact of ipsilateral nodal burden on risk of contralateral nodal disease, although total clinical node number is evaluated without univariate significance.

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[Salvage Total Laryngectomy Swallowing Outcomes Based on Flap Reconstruction: Onlay vs Incorporated Technique](#)

Andrea Ziegler, Amy Pittman, Eric Thorpe

From the *Otolaryngology Head Neck Surgery*. March 2021.

Background: The benefits of using vascularized, healthy tissue when reconstructing a salvage total laryngectomy defect is well established. The advantages of fasciocutaneous flaps over muscle-containing flaps as they related to swallowing and speech related outcomes is also well documented. However, outcomes related research that directly compares different reconstructive techniques after salvage total laryngectomy is lacking. The authors aimed to compare swallowing outcomes in a cohort of patients reconstructed with either a vascularized onlay flap over a primary closure versus those reconstructed with incorporated flaps.

Methods: Single institutional retrospective review of all patients who underwent salvage total laryngectomy reconstructed with pedicled or free flaps. The study excluded those with partial laryngectomies as well as those whose remnant pharyngeal mucosa that was not amenable to primary closure (cutoff of 3 cm). Incorporated flaps were excluded if the operative report did not include a measurement of remnant pharyngeal mucosa.

Results: A total of 59 patients met the study's inclusion criteria, 19 patients in the onlay cohort and 40 patients in the incorporated flap cohort. No significant differences were found between the cohorts in terms of demographics and comorbidities. Overall incidence of PCF was 23.7%, with no significant difference between the two groups. The onlay cohort had significantly less dysphagia and lower rates of stricture formation. Independence of enteral support was achieved in 74.6% of the total cohort at a median of 4.25 weeks. Subset analysis of the incorporated flap group (fasciocutaneous flaps vs musculocutaneous flaps) demonstrated no significant difference in outcomes between the fasciocutaneous group and the onlay group, however the musculocutaneous incorporated flap cohort had significantly higher rates of patient reported dysphagia and stricture formation when compared to the onlay group.



Conclusions: Upon a single institution's retrospective review, the incidence of pharyngocutaneous fistula formation was not influenced by the type of pharyngeal reconstruction technique chosen, based on the study's inclusion/exclusion criteria. To the authors' surprise, the onlay reconstructive technique demonstrated superior swallowing related outcomes compared to the incorporated reconstructive technique. Contributing factors discussed included the impact of suture lines required by each reconstructive technique (1 vs 2) as well as the impact of the rapid pharyngeal narrowing between the dilated neopharynx compared to the narrower (normal-sized) esophageal introitus. Authors also conclude that the superior outcomes of the onlay technique was not evident upon subset analysis of the incorporated cohort, where fasciocutaneous incorporated flaps were equivocal with the onlay cohort.

Summary Statements:

- Rate of PCF is equivocal between reconstruction with primary closure with onlay flap vs incorporated flaps
- Overall higher incidence of dysphagia and stricture formation in those with incorporated flap reconstruction, specifically musculocutaneous incorporated flaps (fasciocutaneous incorporated flaps did not show difference in swallowing outcomes)
- Type of reconstruction did not influence the ability or time until independence from enteral support.

Strengths:

- Study that directly compares two distinct reconstructive techniques after salvage laryngectomy
- Results and analysis demonstrate need for more research regarding the utilization of onlay vs incorporated flaps after salvage surgery

Weaknesses:

- Retrospective study with small sample size and limited documentation of study design and statistical analysis
- Vague inclusion/exclusion criteria (citing 2 CPT codes + pedicled or free flap reconstruction) without further explanation
- As acknowledged by the authors, it remains unclear if the results were impacted by the ambiguity surrounding the presence or lack of information regarding the remnant pharyngeal mucosa in both cohorts

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[Patients With cT1N0M0 Oral Squamous Cell Carcinoma Benefit From Elective Neck Dissection: A SEER-Based Study](#)

Alimujiang Wushou, Meng Wang, Feiluore Yibulayin, Lei Feng, Meng-Meng Lu, Yuan Luo, Hui Liu, Zhi-Cheng Yang

From the *National Comprehensive Cancer Network JNCCN*, January 2021

Background: Despite reports describing favorable short-term results for thermal ablation of thyroid cancer, there remains a need to evaluate long-term results because of its indolent characteristics. The purpose of this study was to evaluate the long-term efficacy and safety of ultrasound (US)-guided radiofrequency ablation (RFA) for low-risk papillary thyroid microcarcinoma (PTMC) over a follow-up period of more than five years.

Methods: From a cohort of patients under surveillance after US-guided RFA for primary low-risk PTMC, those with a record of follow-up data of more than five years were selected for this study. Before RFA, all patients underwent US and computed tomography to evaluate the PTMC and the presence of neck metastasis. RFA was performed using thyroid-dedicated electrodes. Follow-up US was performed 6 and 12 months after initial RFA, and then every 12 months. The status of ablated tumors was evaluated according to volume reduction, local tumor progression, newly developed cancers, lymph node (LN) or distant metastasis, and delayed surgery during follow-up. Complications during the procedure and follow-up period were evaluated.

Results: A total of 84 nodules from 74 patients were included in this study. All patients tolerated RFA, and the mean follow-up duration was 72 months. After RFA, complete disappearance rates of 98.8% and 100% were achieved at 24 and 60-month follow-up, respectively. Additional ablations were performed in 13 of 84 tumors. The mean number of RFA sessions was 1.2. There were four newly developed cancers in three patients, and these were also treated with RFA and completely disappeared. During the follow-up period, there was no local tumor progression, no LN or distant metastasis, and no patients underwent delayed surgery. The major complication rate was 1.4% (1/74), and there was no delayed complication or procedure-related death.

Conclusions: RFA is effective for treating low-risk PTMC patients, without occurrence of local tumor progression, LN or distant metastasis, delayed complications, procedure-related death, or delayed surgery over more than five years of follow-up.

Summary Statements:

- RFA resulted in complete disappearance of all 84 ablated tumors with no lymph node metastases or distant metastases for the cohort and no patients undergoing delayed surgery.
- RFA was overall safe with only 4 complications (two hematomas, one first-degree skin burn, one temporary voice change)
- RFA may alleviate patient anxiety by treating the primary tumor.

Strengths

- Longest follow-up of any RFA study with all patients with at least 5 years follow-up after RFA and mean follow-up duration of 6 years.
- Complete disappearance of all papillary thyroid microcarcinomas with no LN or distant metastases for the entire cohort.
- No patients underwent delayed surgery which is often not the case with an active surveillance approach (cancer progression, patient anxiety).

Weaknesses

- All RFA procedures performed at single institution by one expert radiologist with greater than 10 years of experience with thyroid RFA using hydrodissection technique limits the applicability to institutions with less experience.
- Median tumor diameter was 0.4 cm with only 32 of 84 tumors ≥ 0.5 cm, therefore the vast majority of these nodules would not meet guidelines for FNA within the United States in the first place.
- Study subject to selection bias due to retrospective study design.

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[Low-Risk Human Papilloma Virus Positive Oropharyngeal Cancer with One Positive Lymph Node: Equivalent Outcomes in Patients Treated with Surgery and Radiation Therapy Versus Surgery Alone](#)

Reilly A Sample, Carey Burton Wood, Angela L Mazul, Thomas F Barrett, Randal C Paniello, Jason T Rich, Stephen Y Kang, Jose Zevallos, Mackenzie D Daly, Wade L Thorstad, Stephanie Y Chen, Patrik Pipkorn, Ryan S Jackson, Sidharth V Puram

From the *Head and Neck*. February 2021.

Background: For human papilloma virus positive (HPV+) oropharyngeal squamous cell carcinoma (OPSCC), management recommendations for patients with a single metastatic lymph node < 6 cm in diameter remain nebulous, leading to treatment heterogeneity in this common subgroup of patients.

Methods: We utilized the National Cancer Database to perform survival and multivariable analyses of patients with HPV+ OPSCC with one positive lymph node < 6 cm and negative surgical margins.

Results: We found that 5-year survival is comparable between patients who receive surgery and adjuvant radiation versus surgery alone. In multivariable analyses, we found no significant difference in the hazard ratio of overall survival after adjusting for various potential confounders.

Conclusions: These data suggest that patients with margin-negative HPV+ OPSCC with a single positive lymph node < 6 cm have comparable survival with or without adjuvant radiation. Future studies exploring outcomes for this specific group in randomized-controlled trials will be critical for further evaluating these initial observations.

Summary statements

- This is a retrospective study conducted between 2010 and 2016. Data are derived from the NCDB. The cohort included 898 patients with low-risk HPV+ OPSCC with only one positive lymph node and were either N1 or N2a according to the 7th edition of the AJCC staging system and with negative margin. All patients were M0.
- Patients were divided into two groups: surgery alone (n= 412) and S + RT (n= 486). Exclusion criteria included patients who received adjuvant chemotherapy, had less than 18 lymph nodes examined and were margin positive. For S + RT group, the authors excluded patients who received less than 50 Gy of radiation. The overall 5-year survival – adjusted for potential confounders via multivariable hazard regression analysis – suggested that adjuvant radiation does not significantly improve overall survival for this subset of patients.
- Study results should be taken cautiously in patients with ENE+ which represents a hostile pathological feature. Adjuvant radiation should be at least considered in ENE+ patients.

Strengths

- Large sample size (898 patients) from 1500 commission on CoC-accredited facilities in the USA using the NCDB over 6 years.
- Strict inclusion criteria involving patients who were treated with curative intent surgery (primary resection plus high-quality neck dissection) +/- adjuvant radiation.
- This study represents the largest series to date describing this unique cohort.

Weaknesses

- The inherent recall bias of the retrospective studies.
- The NCDB records are subjected to coding errors and misclassification. As well, it does not include cause-specific mortality data, data on locoregional recurrence and clinical features associated with more aggressive disease such as perineural invasion, challenging tumor location and complex tumor characteristics.
- Survival rates were relatively high for both groups which might decrease the power of the study.

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Surgical Treatment of the Neck in Patients with Salivary Gland Carcinoma

Marie Westergaard-Nielsen, Christian Godballe, Jesper Grau Eriksen, Stine Rosenkilde Larsen, Katalin Kiss, Tina Agander, Benedicte Parm Ullhøi, Birgitte Wittenborg Charabi, Tejs Ehlers Klug, Henrik Jacobsen, Jørgen Johansen, Claus Andrup Kristensen, Elo Andersen, Maria Andersen, Kristine Bjørndal

From *Head and Neck*. March 2021

Background: Elective neck dissection (END) in patients with salivary gland carcinoma is controversial and there are no universally accepted guidelines.

Methods: Patients were identified from the Danish Head and Neck Cancer Group. Between 2006 and 2015, 259 patients with primary salivary gland carcinoma were treated with END. Variables potentially associated with regional metastases were analyzed using logistic regression. Neck recurrence-free survival was calculated using the Kaplan-Meier method.

Results: Occult metastases were found in 36 of the patients treated with END (14%) and were particularly frequent among patients with T3/T4 tumors and high-grade histology tumors. In multivariate analyses, high-grade histology and vascular invasion were associated with occult metastases.

Conclusion: We recommend END of levels II and III for patients with high-grade or unknown histological grade tumors, and for T3/T4 tumors. Levels I, II, and III should be included in END in patients with submandibular, sublingual, or minor salivary gland carcinomas.

Summary statements

- This is a retrospective study with data derived from The National Danish Head and Neck Cancer Group (DAHANCA) database over a period of 10 years. All patients with salivary gland carcinoma – between 2006 and 2015 – were evaluated. Eventually, 295 patients had previously untreated salivary gland carcinoma and clinically negative lymph nodes (cN0) treated with excision of the primary tumor and elective neck dissection (END).
- The main outcome was the evaluation of neck-recurrence free survival (neck-RFS). The follow up time was calculated from the date of surgery to the date of death or the end of data collection (January 2018).
- Occult metastases were found in 36/259 of patients (14%). Multivariate analysis proved that high-grade histology and vascular invasion were significantly associated with occult metastases.
- Neck-RFS for patients with pN+, pN0 and noND at 5- and 10-year intervals were: 77% and 57%, 98% and 94%, 98% and 96% respectively. Histologic grade and elective neck irradiation did not improve recurrence rates for patients with noND.
- The authors recommend END should include levels II and III in patients with parotid gland carcinoma, and levels I, II and III in patients with submandibular, sublingual, and minor salivary gland carcinoma. If pN+, then levels IV and V should be treated either by surgery or radiotherapy. Frozen section examination of level II may aid decision on whether to proceed with dissection of levels IV and V or not. In patients with T3/T4 tumors, high-



grade histology or unknown grade prior to surgery, END of levels II and III should be recommended.

- Selected patients with T1/T2 with cN0 may be candidates for observation of their neck. The decision should be individualized.

Strengths

- Large study cohort, starting with 730 patients in total and ending with 259 patients who met the inclusion criteria.
- Completeness of the database was verified by cross-referencing with two additional Danish databases: The Danish Cancer Register and The Danish Pathology Register.

Weaknesses

- The possible inherent bias of retrospective studies.
- The heterogeneity of the study population with multiple pathological subtypes involved in the analysis. This limits the generalizability of the results.
- Information on perineural and vascular invasion were missing in many patients.
- The study included patients with noND who might have influenced the true proportion of patients with occult metastases.
- The reasons for having noND group in study were not discussed in detail.
- The value of frozen section examination to determine the extent of resection during ND is not thoroughly studied.
- The radiographic staging was done using various methods including neck US which is operator dependent.
- The extent of ND was variable among the study population limiting the generalizability of the results.

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