ACR APPROPRIATENESS CRITERIA® IPSILATERAL RADIATION FOR SQUAMOUS CELL CARCINOMA OF THE TONSIL

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Abstract: Background. Controversy exists as to the criteria for selecting patients with carcinoma of the tonsil for treatment with ipsilateral radiotherapy (RT).

Methods. The American College of Radiology (ACR) Appropriateness Criteria are evidence-based guidelines for specific clinical conditions that are reviewed every 2 years by a multidisciplinary expert panel. The guideline development and review include an extensive analysis of current literature from peer reviewed journals and the application of a well-established consensus methodology (modified Delphi) to rate the appropriateness of treatment procedures by the panel. In those instances where evidence is not definitive, expert opinion may be used to recommend treatment.

Results. The ACR Expert Panel on Radiation Oncology – Head and Neck Cancer developed consensus recommendations for selecting patients with tonsillar carcinoma for ipsilateral RT.

Conclusion. Patients that are appropriate for ipsilateral RT have less than 1 cm of tumor invasion into the soft palate or base of tongue, and nodal stage of N0 to 1.

Keywords: appropriateness criteria; ipsilateral radiotherapy; tonsillar cancer; radiation therapy volume; oropharynx cancer

Treatment of early- and intermediate-stage carcinoma of the palatine tonsil with primary radiotherapy (RT) has a high success rate.1 The well-lateralized location of the tonsils means that squamous cell carcinomas (SCCs) arising in this region rarely metastasize to lymph nodes in the contralateral hemi-neck.2 Because of this finding, multiple reports have questioned the need to electively irradiate the clinically negative contralateral hemi-neck in selected patients.3–5 Controversy exists, however, as to the specific criteria for selecting patients for ipsilateral RT (defined as radiation to the primary site and ipsilateral regional nodes only). Important factors in determining appropriateness of ipsilateral radiation are T stage, N stage, and the extent of invasion of the soft palate and base of tongue. Appropriate patient selection is a critical issue, as regional recurrences are rarely successfully salvaged.6,7 The benefit of limiting radiation to the ipsilateral hemi-neck is decreasing the rate of permanent xerostomia, a condition that often results in poor nutrition and accelerated tooth decay, as well as decreased quality of life.8–14 This article specifically discusses the appropriate RT volume without addressing the role of systemic chemotherapy concurrent with radiation.

Results from Surgical Literature. Although there are multiple reports on the outcome of tonsillar carcinoma treated with primary surgery,15–17 only a few specifically address the rate of neck failure in the...
undissected and unirradiated contralateral neck. The Mayo Clinic published its results on 56 patients with stage T1 to 4 N0 to 2b SCC of the tonsil who underwent surgery alone.\textsuperscript{18} Seventy-nine percent of patients were stage T1 to 2, and 88% were stage N0 to 1. All patients underwent resection of the primary tumor, and 75% underwent an ipsilateral neck dissection. No patient had a dissection of the contralateral neck. With a minimum follow-up of 3.5 years, 3 of the 56 patients (5%) failed in the contralateral neck with control at the primary and ipsilateral neck.

Multiple pathologic studies have shown that for tonsillar primaries, the risk of pathologically occult contralateral lymph nodes is about 15% overall, and depends on the extent of the primary tumor and clinical N stage. Patients with T1 to 2 N0 to 1 tonsillar cancers have an extremely low risk of pathologically positive contralateral nodes, supporting the use of ipsilateral RT techniques in these patients.

Lim et al\textsuperscript{19} retrospectively analyzed 43 patients with SCC of the tonsil who underwent elective dissection of the clinically negative contralateral hemi-neck. The rate of pathologically positive contralateral lymph nodes was 16% in the entire patient cohort, with none occurring in the 10 patients that were N0. Six of the 7 patients with pathologically positive contralateral nodes were T3 or T4. No attempt was made to correlate the results with extent of soft palate or base of tongue invasion.

Olzowy et al\textsuperscript{20} reviewed 197 patients with SCC of the tonsil who underwent bilateral neck dissections and showed that 14.7% had pathologically positive contralateral lymph nodes, although the authors did not specify the clinical stage of the contralateral hemi-neck before neck dissection.

A recent report from Korea by Cho et al.\textsuperscript{21} showed that 2 of 21 patients (9.5%) with SCC of the tonsil who underwent an elective contralateral neck dissection in addition to resection of the primary and ipsilateral neck dissection had pathologically positive contralateral nodes. These 2 patients were clinically N+, but the report does not specify the exact N stage. None of the patients that were clinically N0 had pathologically involved contralateral nodes.

**Extent of Soft Palate or Base of Tongue Invasion.**

The extent of invasion of the primary tonsillar tumor into the soft palate and base of tongue has been shown to be an important predictor of contralateral lymph node failure. As the tumor approaches midline in the base of tongue or soft palate, the risk of contralateral nodal involvement increases.

The seminal study on ipsilateral RT for tonsillar carcinoma is a retrospective study from the Princess Margaret Hospital group of O’Sullivan et al\textsuperscript{22} which reported the outcomes of 228 patients with carcinoma of the tonsil treated with ipsilateral RT techniques. All patients had a clinically negative contralateral hemi-neck. The majority of patients were treated to 50 gray (Gy) at 2.5 Gy per fraction using Cobalt 60. Contralateral neck failure occurred in 8 patients (3.5%), although only 3 occurred in patients with control at the primary site. Of the 3 patients who experienced failure in the contralateral neck with the primary controlled, all had significant soft palate involvement (to within 1 cm of midline in 2 cases, and involving the middle third of the palate hemi-structure in the third case). Two of the 3 patients were T3, and 1 patient was T2. All 3 patients were also N1. No patient with T1 or N0 disease failed in the contralateral neck. The authors concluded that <1 cm of extension into the soft palate or base of tongue is associated with a low risk of occult contralateral nodal involvement and is appropriately treated with ipsilateral RT.

A much smaller study showed excellent contralateral neck control when patients with only minimal soft palate or base of tongue extension were selected for ipsilateral radiation. Cerezo et al\textsuperscript{23} reported on 8 patients with tonsillar carcinoma who had <1 cm of tumor extension to the soft palate or base of tongue and were treated with ipsilateral RT to a total dose of 66 to 70 Gy at 2 Gy per fraction to the primary tumor. The nodal stage varied from N0 to 2b. No contralateral neck failures were detected at 5 years.

Other authors have demonstrated that even tumors with more extensive base of tongue or soft palate invasion are successfully treated with ipsilateral radiation. Kagei et al\textsuperscript{24} reported on 32 patients with carcinoma of the tonsil or soft palate treated with ipsilateral RT. The only selection criteria was that the primary tumor did not cross midline. The stage varied from T1 to 4 and N0 to 3. Patients were treated to 65 Gy plus a 15 Gy boost depending on clinical response, delivered at 2.5 Gy per fraction using Cobalt 60. Eight node-positive patients received bilateral lower neck irradiation. Twelve patients received concurrent carboplatin. They found no isolated contralateral neck failures at a median follow-up of 44 months (Variant 1, Variant 2, and Variant 3).

**Nodal Stage.** The extent of ipsilateral nodal disease has also been correlated with the risk of contralateral nodal failure. Patients with lateralized tumors that...
 Variant 2. A 50-year-old man with a T3N0 SCC of the right tonsil, with tumor extending 1 cm onto the soft palate (2 cm from midline). There is no base of tongue involvement. HPV status is negative.

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| Abbreviations: SCC, squamous cell carcinoma; HPV, human papillomavirus.
Rating scale: 1, 2, 3: usually not appropriate; 4, 5, 6: may be appropriate; and 7, 8, 9: usually appropriate.

A prospective study was performed by Rusthoven et al. that specifically addressed the issue of the node-positive patient. Twenty patients with carcinoma of the tonsil with stage T1 to 3 N1 to 2b were treated with ipsilateral RT. Thirteen of 20 patients were stage N2b. Patients with any invasion of the soft palate or base of tongue were excluded. All patients underwent pretreatment scans with CT and positron emission tomography using fluorine-18-2-deoxy-D-glucose tracer to rule out occult contralateral neck lymphadenopathy. Sixteen of the 20 patients were treated with a tonsillectomy with a resultant positive margin, and 14 had undergone ipsilateral neck dissection before ipsilateral RT. Four patients with N2a or large N2b disease were treated with neoadjuvant chemotherapy followed by a planned neck dissection. Nineteen of the 20 patients received chemotherapy, which was concurrent platinum-based chemotherapy in most cases. The total RT dose was 60 to 66 Gy to the primary tumor or tumor bed for patients treated postoperatively, and 66 to 70 Gy for the 4 patients treated with primary RT. At a median follow-up of 19 months, there were no contralateral nodal failures.

 Jackson et al. retrospectively reviewed the medical charts of 178 patients with carcinoma of the tonsil treated with ipsilateral RT. The majority of patients received 60 Gy at 2.4 Gy per fraction. In 155 patients with stage N0 to 1 and control at the primary site, only 4 (2.6%) had isolated contralateral nodal failures. The authors did not analyze the contralateral nodal failures in the small number of patients with N2 to 3 (Variant 4 and Variant 5).

 Variant 4. A 50-year-old man with a T1N1 SCC of the right tonsil, with no soft palate or base of tongue extension. There is a single positive node in right level II. HPV status is negative.

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Role of Human Papillomavirus Status. Human papillomavirus (HPV)-associated SCC of the oropharynx is thought to be a distinct epidemiologic, clinical, and molecular entity from non-HPV-associated tumors. Given these differences, specific attention has recently been given to determining if ipsilateral RT is appropriate in HPV-associated tonsillar tumors.

 Shoushtari et al. reviewed the medical charts of 41 patients with T1 to 2 SCC of the tonsil to assess the rate of radiographically positive contralateral nodes. Patients with any soft palate or base of tongue invasion were excluded. Of the 28 patients with p16þ tumors, 25% presented with contralateral nodal disease. None of the 13 patients with p16- tumors had contralateral nodal disease. The authors conclude that, given the high rate of clinically involved nodes in patients with p16þ tumors, the subclinical rate of contralateral nodal involvement may be sufficiently high to warrant elective irradiation of the contralateral subclinical disease, even in early stage disease with no extension to the base of tongue or soft palate (Variant 6).

 Radiation Technique. Ipsilateral RT can be done with either a 3D-conformal wedge-pair photon beam technique or intensity modulated radiation therapy (IMRT). Both techniques achieve a low mean dose to the contralateral parotid gland, which is the main benefit in using ipsilateral RT. The benefit of using a wedge-pair technique is that the contralateral parotid gland can usually be completely excluded. However, achieving adequate coverage of the primary tumor can be challenging. On the other hand, the benefit of IMRT compared to traditional 3D-conformal RT is the ability to sculpt the dose around the target, sparing the surrounding critical organs as much as possible. Although IMRT is superior to 3D-conformal RT

 Variant 5. A 50-year-old man with a T1N2b SCC of the right tonsil, with no soft palate or base of tongue extension. There are 2 positive nodes located in right level II. HPV status is negative.

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ACR Appropriateness Criteria® on Ipsilateral Radiation
regarding dose conformity and homogeneity. RT delivery time is, however, generally increased, as well as the number of monitor units, resulting in a greater integral body dose.

**Summary.** (1) Regarding the extent of soft palate or base of tongue invasion, we recommend ipsilateral radiation when there is <1 cm of tumor invasion into the soft palate or base of tongue. If there is extension of 1 cm or greater, then we recommend bilateral neck irradiation because of the increased risk of occult contralateral nodal involvement.

(2) For nodal stage of N2b or greater, we recommend bilateral neck irradiation, regardless of the extent of soft palate or base of tongue invasion. For nodal stage N0 to 1, we recommend basing the decision about whether to use ipsilateral or bilateral neck irradiation on the extent of soft palate and base of tongue invasion.

(3) For HPV status, the panel concludes that there are insufficient data at this time to alter treatment decisions based on HPV status. Our recommendation is to treat with ipsilateral neck irradiation if the patient is an appropriate candidate based on the factors listed above, regardless of the patient’s HPV status.

**REFERENCES**
