Letters to the Editor

Comparison between Organ Preservation Surgery and Radiation in Early Supraglottic Carcinoma Is Limited by Bias

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We read with interest the article by Arshad et al comparing survival for early supraglottic cancer between definitive radiation and organ preservation surgery (OPS) using the Survival, Epidemiology, and End Results (SEER) database. The authors report significantly improved disease-specific survival (DSS) for stage I and II supraglottic cancers treated with OPS + neck dissection (ND) vs radiation, with 5-year DSS for stage II patients of 86% vs 60% (hazard ratio, 0.31; \(P\) < .001), respectively. This result is remarkable and would have great importance for management decisions in early supraglottic cancer, if true.

However, we are concerned that the comparison is made between dissimilar groups of patients in relation to neck metastases and that the subsequent bias is not adequately taken into account in the interpretation of the results. Based on the methods described, the authors excluded from the analysis all patients with node-positive (N+) disease. Since in the SEER database, staging represents a “best stage,” taking all available clinical and pathologic information into account, the primary-radiation group in this study was clinically N–, and the OPS + ND group was pathologically N–. The radiation group would have included patients with occult nodal metastases, but the OPS + ND group would have excluded them. Based on the reported rate for occult metastases for T1 and T2 supraglottic cancer identified by elective neck dissection, we would expect that 30% of the patients in the radiation group had occult nodal metastases. Since the presence of nodal metastases is a powerful negative prognostic factor for survival and signifies a more aggressive behavior of the disease, the exclusion of these patients from the OPS + ND group would be expected to have a significant positive effect on the survival outcome and is a significant source of bias in the study.

We appreciate the role that epidemiologic studies such as this can have in provoking further investigation, but the biased results reported by Arshad et al are unlikely to lead to a useful hypothesis and should not be used to guide clinical decision making.

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References

Response to “Comparison between Organ Preservation Surgery and Radiation in Early Supraglottic Carcinoma Is Limited by Bias”

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We thank Drs Sperry and Pagedar for their interest in our article. We were aware of the issue of how the Survival, Epidemiology, and End Results (SEER) data classify stages and expected this concern from others. For that reason, we specifically addressed this concern in our Discussion section. In it, we remark the following:

One reason for the worse outcomes in the RT-only group and the OPS-only group could be the presence of occult nodal metastases. Because the true involvement of the
lymph nodes was not ultimately ascertained via a histologic specimen, the RT-only group and the OPS-only group may well have included pathologically node-positive patients who were understaged originally.\[1(p243]\]

As Drs Sperry and Pagedar correctly imply, 30\% of the patients in the radiation-only group were likely higher than stage II because of occult nodal metastasis—and this we fully acknowledge. However, this was our point exactly and highlights one of the benefits of primary surgery. One of the advantages of surgery over radiation is that performing a neck dissection helps determine the true nodal status and, thus, the true stage.

We also acknowledged other limitations such as the inherent issues of a retrospective review using SEER data and the unknown effect of expertise on radiotherapy quality. For these reasons, we tempered our conclusion by not proclaiming that surgery is the best option but by saying that surgery should be considered a viable and preferred treatment option. Although the commenters dismiss our conclusions, we feel that the article makes a meaningful contribution to the body of data concerning this very interesting problem.

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We read with interest the systematic review by Khoueir et al\’ on the endoscopic resection of juvenile nasopharyngeal angiofibroma (JNA). They performed a literature review for articles from 1995 to 2012 using the search terms angiofibroma and endoscopic. Only purely endoscopic series of patients were included in the final analysis. The authors, however, do not define the terms open, endoscopic, and endoscopic assisted, and the classification of cases where the resection is performed endoscopically through an open incision is not addressed. In our opinion, the classification of an intraoral incision (anterior transmaxillary approach) as an open approach misses the point. The key point is that endoscopic visualization is being used to perform the tumor dissection. Benefits of endoscopy include superior visualization, less dissection of normal tissues, and the potential for decreased morbidity. Large JNAs that extend lateral to the pterygopalatine space and involve the skull base need the additional access and multiple ports for instruments that a combination of endonasal and transmaxillary approaches provides.

The authors state, "A good staging system should be universal, have a prognostic value, and have a therapeutic correlation."\[1(p354]\] Previously, we proposed a new staging system for JNA that incorporates the residual vascularity of the tumor following embolization as a major prognostic factor.\[2\] Most of the cases analyzed (77\%) were endoscopic resections. In our series of 35 patients, the University of Pittsburgh Medical Center (UPMC) staging system was superior to other staging systems for predicting operative blood loss and the risk of residual/recurrent tumor.

They conclude, "A new staging based on the endoscopic boundaries should also be proposed."\[1(p355]\] The UPMC staging system can be applied to all JNAs regardless of surgical approach. It has been applied to the treatment of giant JNAs with encasement of the internal carotid artery (ICA) and intracranial extension. It differentiates between tumors that erode the skull base medial or lateral to the ICA. In our experience, anatomical boundaries have not been the limiting factor with the surgical management of JNA as long as the principles of team skull base surgery are practiced. Rather, the vascular contribution from the intracranial circulation and the residual vascularity following embolization are most important with surgical management.

We would like to see more centers test the validity of the UPMC staging system in their own patient populations to see if it has wide applicability.

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