



# Positron emission tomography-CT surveillance versus neck dissection in advanced head and neck cancer: time for a paradigm shift in management

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Prior to the introduction of the positron emission tomography-CT (PET-CT), the role of planned neck dissection before or following definitive chemoradiation (CRT) was controversial. Most patients who presented with N3 disease would undergo routine post-CRT neck dissection, and practitioners struggled to determine whether the post-treatment neck with N2a/N2b disease was completely treated (1). This is particularly true when post-treatment neck dissection specimens contained disease, but the viability of the disease remained in question (2). Improvements in both structural and functional imaging have gradually allowed head and neck oncologists to consider radiographic resolution of disease as sufficient for surveillance. Over the past decade there has been an ongoing shift to relying on PET-CT/MRI as an indicator of response to treatment, particularly at academic centers in the United States. PET-CT/PET-MRI provides precise anatomical correlation to the FDG-glucose avidity and is especially useful since the physical exam has limitations after CRT secondary to lymphedema and fibrosis. Until now, however, there has been no level I evidence on the efficacy of PET-CT for post-treatment surveillance when compared to planned neck dissection.

In the UK, patients with advanced nodal disease (N2/N3) still undergo planned neck dissection, either before or following definitive CRT (3). In a recent study, reported in the *New England Journal of Medicine*, Mehanna *et al.* conducted a randomized trial to evaluate whether surveillance with a PET-CT was an acceptable alternative to planned neck dissections (4). This well-designed clinical trial enrolled 564 patients from 57 different hospitals in the UK,

and randomized patients to either a planned neck dissection (before or after CRT) or PET-CT guided surveillance. Of the patients assigned to planned-surgery, 221 (78%) of the patients received a neck dissection, with 54% following CRT and 24% before CRT. In the surveillance group (282 patients), only 54 neck dissections were performed. The results of the study demonstrated non-inferiority with regards to the primary outcome (2 year overall and disease free survival) with a HR of 0.92 (95% CI, 0.65–1.32) when comparing PET/CT surveillance to planned neck-dissection, validating PET-CT as an acceptable surveillance strategy for this particular patient population.

There are a number of notable aspects of this study. First, nearly 85% of the cohort had an oropharyngeal primary with the majority of these tumors (75%) staining positive for p16. This reflects similar demographic changes in HPV-associated oropharyngeal disease seen in the USA and globally. Despite these changes in prevalence, PET-CT surveillance is an acceptable strategy, regardless of p16 status, and results in similar 2-year overall survival. Next, this was a cohort of patients with significantly advanced disease. Nearly 20% had N2c neck disease and 40% of the patients enrolled had locally advanced T3/T4 disease, indicating that advanced-stage disease can be followed for complete treatment responses. Finally the neck dissection, while not without significant complication rates (22% overall rate), had little impact on overall quality of life (QOL). Patients that had a neck dissection were indistinguishable from those that did not receive one at 12 months after treatment.

In many ways, this study validates a protocol head and

neck oncologists have been heading toward over the last decade. This study supports retrospective studies, as well as smaller prospective studies, that evaluate the positive predictive value (PPV) and negative predictive value (NPV) of PET-CT. There are current efforts, within the American College of Radiology, to implement a standardized approach to reporting head and neck radiologic exams based on the success in standardizing mammography reporting. A neck imaging reporting and data system (NI-RADS) has been proposed to better understand the accuracy for predicting tumor recurrence (5). The University of Pittsburgh Medical Center (UPMC) head and neck oncology group, using a similar standardized approach, had reported that the NPV of a normal post-operative PET-CT is 90% and that increases to 98% after a second scan (6). This cohort included patient from multiple subsites (30% oropharynx, 30% oral cavity, 15% larynx, 9% sinonasal) and did not distinguish based on HPV status. In HPV-associated oropharyngeal disease this same group has shown that a negative first post-treatment PET/CT has an improved NPV of 93% (7).

This study did not comment on the pathology in the post-treatment salvage neck dissections. It would be interesting to know, of the patients with equivocal or incomplete responses, how many had viable disease in the neck. In these patients was there more occult disease than just indicated by the PET-CT, and did the imaging provide a sufficient roadmap for salvage surgery? Also, not addressed in this study are the PET-CT characteristics of patients who were going to fail upfront CRT and require salvage surgery. For example patients with N3 disease, a very small number treated in this study, may be more likely to require salvage surgery or benefit from upfront neck dissection. To address that question pre-operative PET-CT should be performed as part of the evaluation. Nevertheless this study places the 12-week PET-CT as an important adjunctive imaging technique in the surveillance of head and neck cancer patients, particularly those with HPV-related oropharyngeal disease.

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