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Lessons from a standardized program using PET–CT to avoid neck dissection after primary radiotherapy for N2 squamous cell carcinoma of the oropharynx

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SUMMARY

Objectives: To report the results of a standardized program using positron emission tomography (PET)–computed tomography (CT) approximately 12 weeks after primary radiotherapy to determine the need for a planned neck dissection in patients with radiographic N2 squamous cell carcinoma (SCC) of the oropharynx.
Methods: Fifty consecutive patients with T1–4 and hemineck radiographic stage N2A–B SCC of the oropharynx for whom the only indication for planned neck dissection was a positive PET–CT performed ~12 weeks after completing primary treatment with radiotherapy.
Results: Results of PET–CT to identify residual neck disease were as follows: sensitivity and positive predictive value, 0%; specificity, 89%; negative predictive value, 91%; potential neck recurrence from using this 12-week PET–CT program, 2%. The time between negative PET–CT and detection of neck recurrence was 0.5, 0.6, 1.2, and 2.0 years. The rate of successful (>1 year) salvage of neck recurrence was 25% (1/4).
Conclusions: PET–CT approximately 12 weeks after radiotherapy for oropharyngeal cancer is an excellent way to identify patients who do not need neck dissection. Approximately half of neck recurrences present over 1 year after negative PET–CT and the chance of successful salvage is low.

Introduction

In an effort to improve the accuracy of imaging to determine the need for neck dissection, multiple groups have published encouraging results with post-treatment 18-fluorodeoxyglucose positron emission tomography (PET), usually with CT (PET–CT) [1–4]. The existing literature does an excellent job at defining the basic issues, but most studies are limited by the heterogeneity of the study population and duration of follow-up. Specifically, most studies include patients with N1 neck disease, report a wide range of times between RT and PET–CT, include patients with short follow-up after neck imaging, and/or group patients with various primary sites [1–4].

To contribute to the understanding of this subject, members of the head and neck oncology team at our institution established a prospective program in August 2009 to evaluate the role of PET–CT approximately 12 weeks after primary RT for patients with node-positive squamous cell carcinoma of mucosal sites of the head and neck. The purpose of this paper is to report the results of our program in a relatively uniform study population with neck stages for which the question of better imaging is most applicable and a minimum follow-up interval that is likely to identify the great majority of neck recurrences.

Materials and methods

Standard practice for many years in our program was to obtain a contrast-enhanced neck CT scan approximately 4 weeks after the completion of RT in all node-positive patients for whom RT is the primary treatment modality. The main purpose of the 4-week CT was to determine the need for planned neck dissection. In August of 2010 we changed our policy to use PET–CT approximately 12 weeks after the completion of RT to determine the need for planned neck dissection in patients with squamous cell carcinoma of a mucosal primary site and neck stage N1–3. Since

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starting this program, all eligible patients have been managed with the 12-week PET–CT approach.

The study that is the subject of this paper evaluates a subset of our 12-week PET–CT experience. The University of Florida Institutional Review Board approved this study as part of the Radiation Oncology Outcome Tracking Protocol. The population for this study was comprised of the first 50 patients who met the following inclusion criteria: (1) Managed with the 12-week PET–CT program beginning August 2010 to determine the need for planned neck dissection following primary treatment with RT at our institution. (2) Primary-site squamous cell carcinoma in the oropharynx. (3) Primary site stage T1–4 according to the 7th edition of the American Joint Committee on Cancer (AJCC) system. (4) Neck stage based on evaluation of nodal station levels I–V of N2A-C with a hemineck radiographic stage N2A-B according to the 7th edition of the AJCC system (stage N1 and N3 are not included). (5) Patients with a radiographically positive retropharyngeal node are included. (6) Stage M0 based on chest radiograph, chest CT, or PET–CT within 12 weeks of starting RT. (7) No history of neck surgery before RT that could disrupt the cervical lymphatics. (8) No history of prior RT to the head and neck. (9) No history of other cancers that could confound evaluation of treatment for oropharyngeal cancer. (10) Twelve-week PET–CT at least 1 year before the date of last data collection (December 31, 2014) such that the minimum potential neck follow-up time is 1 year following the 12-week PET–CT.

Table 1 lists the main features of the study population.

Outcome

The prospective plan to monitor the neck after the 12-week PET–CT included a neck CT and clinical examination every 3 months for the first 12 months, every 4 months for the next 12 months, and every 6 months for the third 12-month period.

All PET–CT scans related to this study were performed and interpreted at our institution. A written report describing the PET–CT findings was generated by a board-certified Nuclear Medicine physician. The written interpretation was reviewed by the authors of this paper at our head and neck tumor conference, which included a neuroradiologist specializing in head and neck oncology (A.A.M). In all cases, the tumor conference group agreed with the dictated report in terms of status of the neck on the 12-week PET–CT. Planned neck dissection was performed if the 12-week PET–CT was interpreted as positive or equivocal for residual disease in the neck. If the 12-week PET–CT was positive at the primary site in addition to the neck, we evaluated the primary site further and decided to dissect the neck based on the likelihood of salvaging the patient with surgery to the primary site and neck. There was no case in this series with local and neck persistence on the 12-week PET–CT, so we will not confuse the analysis by mentioning this potential scenario again.

Complications from neck dissection

A potential risk of the 12-week PET–CT program is complications from neck dissection as a result of increased time between the completion of RT and neck surgery. The coauthor of this paper who is also our director of head and neck surgery (J.A.W) graded toxicity from all neck dissections using the Common Terminology Criteria for Adverse Events v4.0 in two categories: (1) surgical procedures and (2) skin and subcutaneous tissue [5].

Harm from the PET–CT program

The most important question to try to answer with this study is whether patients were harmed by our use of a 12-week PET–CT to determine the need for neck dissection. Answering this question related to cancer recurrence requires more than accuracy endpoints for three major reasons: (1) Tumor status at sites that are

Table 1
Study population ($N = 50$ patients).

Characteristics	Value
Oropharynx subsite	
Base of tongue	56% (28 pts)
Tonsil	28% (14 pts)
Glossotonsillar silcus	6% (3 pts)
Anterior tonsillar pillar	6% (3 pts)
Soft palate	4% (2 pts)
p16 or HPV status[a]	
Positive	64% (32 pts)
Negative	14% (7 pts)
Insufficient tissue	22% (11 pts)
Tobacco smoker	
⩽10 pack-years	50% (25 pts)
>10 pack-years	50% (25 pts)
p16/HPV and smoking	
p16/HPV positive and ⩽ 10 pack-years	34% (17 pts)
p16/HPV positive and > 10 pack-years	30% (15 pts)
p16/HPV negative and ⩽ 10 pack-years	6% (3 pts)
p16/HPV negative and > 10 pack-years	8% (4 pts)
Insufficient tissue and ⩽ 10 pack-years	10% (5 pts)
Insufficient tissue and > 10 pack-years	12% (6 pts)
Age at completion of RT	
Median	60 yrs
Range	40–83 yrs
Sex	
Male	92% (46 pts)
Female	8% (4 pts)
Race	
White	98% (49 pts)
Black	2% (1 pts)
N stage, ipsilateral[b]	
N2A	8% (4 pts)
N2B	92% (46 pts)
Retropharyngeal node	
Positive	26% (13 pts)
Negative	74% (37 pts)
T stage	
T1	22% (11 pts)
T2	44% (22 pts)
T3	8% (4 pts)
T4	26% (13 pts)
Node number, ipsilateral	
1 (N2A)	8% (4 pts)
2	12% (6 pts)
3	4% (2 pts)
⩾4[c]	76% (38 pts)
Maximum node diameter	
Median	1.5 cm
Range	1.5–6.0 cm
Main node level	
Level 2A	90% (45 pts)
Level 2B	4% (2 pts)
Level 3	6% (3 pts)
RT technique	
IMRT[4]	96% (48 pts)
3-dimensional conformal[d]	4% (2 pts)
RT dose to the high-risk CTV[d]	
70 Gy at 2 Gy in 30 days[d]	62% (31 pts)
70 Gy at 2 Gy in 35 days[d]	6% (3 pts)
74.4 Gy at 1.2 Gy BID[d]	32% (16 pts)
Chemotherapy (during RT)	
Weekly cisplatin[d] (30 mg/m2)	82% (41 pts)
Weekly cetuximab[d]	8% (4 pts)

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