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Routine surveillance scanning in HNSCC: Lung screening CT scans have value but head and neck scans do not

Austin J. Iovoli, BSc^a, Alexis J. Platek, MS^a, Luke Degraaff, BSc^a, Chong Wang, MA^b, William D. Duncan, MS, PhD^b, Kimberly E. Wooten, MD^c, Hassan Arshad, MD^c, Vishal Gupta, MD^c, Moni A. Kuriakose, MD^c, Wesley L. Hicks Jr, MD^c, Mary E. Platek, PhD^{d,e}, Anurag K. Singh, MD^e

^aJacobs School of Medicine, 955 Main St, Buffalo, NY 14203, United States

^bDepartment of Biostatistics and Bioinformatics, Roswell Park Comprehensive Cancer Center, 665 Elm St, Buffalo, NY 14203, United States

^cDepartment of Head and Neck/Plastic and Reconstructive Surgery, Roswell Park Comprehensive Cancer Center, 665 Elm St, Buffalo, NY 14203, United States

^dDepartment of Health, Nutrition & Dietetics, Buffalo State College, 1300 Elmwood Ave, Buffalo, NY 14222, United States

^eDepartment of Radiation Medicine, Roswell Park Comprehensive Cancer Center, 665 Elm St, Buffalo, NY 14203, United States

Abstract

Objectives: To examine the utility of computed tomography (CT) imaging during routine surveillance for the detection of recurrent head and neck squamous cell carcinoma (HNSCC).

Materials/Methods: Clinical characteristics of HNSCC patients treated between 2008-2017 with radiation therapy or concurrent chemoradiation were abstracted from medical records. In patients who achieved a complete response to treatment by positron emission tomography scan, surveillance CT scans were conducted to the maxillofacial area, neck, and chest every 3 months in year 1, every 6 months in year 2, and every 12 months in years 3 and beyond.

Results: Within the entire cohort (n = 534), complete response was achieved in 446 patients (83.5%); of these, 84 (15.7%) patients had a recurrence. Among the 84 patients with disease recurrence, 25 (30%) patients remained alive, of which 15 (18%) underwent successful salvage treatment and became free of disease. Lung screening CT scans detected failure in 8 of these successfully salvaged patients. Among the 8 patients successfully salvaged for locoregional recurrence, 3 failures were asymptomatic at onset and detected by laryngoscope or dental exam.

Corresponding Author Anurag K. Singh MD, Professor of Medicine, University at Buffalo School of Medicine, Professor of Oncology, Director of Medicine Research, Roswell Park Comprehensive Cancer Center, Elm and Carlton Streets, Buffalo NY 14263, Phone: 716-845-1180, Fax: 716-845-7616, Anurag.Singh@Roswellpark.org.

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The remaining 5 failures were symptomatic and detected upon work up prompted by symptoms. Maxillofacial and neck surveillance CT imaging failed to detect any successfully salvaged patients.

Conclusions: Routine surveillance for HNSCC patients with lung CT imaging had value but routine head and neck CT scans failed to identify any successfully salvaged patients. Given this finding, routine CT imaging surveillance in HNSCC patients should be restricted to annual lung screening with low-dose chest CT.

Keywords

Head and Neck neoplasms; Tomography; X-Ray Computed; Carcinoma; Squamous Cell; Neoplasm recurrence; Salvage therapy

INTRODUCTION

Surveillance for recurrence or metastasis of head and neck squamous cell carcinoma (HNSCC) is a critical component of follow-up care after completion of treatment. The goal of surveillance is to catch localized disease failure early enough to be amenable to salvage treatment. The effectiveness of routine surveillance imaging in asymptomatic HNSCC survivors is dubious. A study done by Spector et al. demonstrated that detecting a greater number of distant metastases in HNSCC patients with PET scans does not improve life expectancy versus those who were diagnosed through other imaging modalities [1]. Another study found no survival differences between HNSCC patients with PET/CT-detected or clinically detected recurrences [2]. Despite these data, a survey among 502 physicians responsible for the surveillance of HNSCC patients found that 79% endorsed ever using positron emission tomography (PET)/computed tomography (CT) scans for routine surveillance imaging and 39% were high imaging users who used PET/CT scans on more than half of their asymptomatic patients [3].

As opposed to PET/CT, the role of routine CT surveillance in the detection of HNSCC recurrence remains relatively less explored though both the National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) guidelines agree there is no benefit to routine surveillance imaging for most cancers, including HNSCC [4,5]. Since 2007, our institute used the surveillance imaging schedule used in Radiation Therapy Oncology Group (RTOG) protocol 0522 for all HNSCC patients who successfully completed treatment with CT scans of the maxillofacial area, neck, and chest as a part of routine surveillance that decreased in frequency with increasing follow-up duration [6]. This study assessed the utility of such CT imaging as a routine surveillance tool for HNSCC patients.

MATERIALS AND METHODS

Our Institutional Review Board approved this retrospective study of HNSCC patients diagnosed and treated with radiation therapy (RT) or concurrent chemoradiation (CCRT) between 2008 and 2016.

Eligibility

To be included in this study the primary tumor had to be: (1) an invasive squamous cell carcinoma limited to the head and neck, (2) treated with curative RT or CCRT, (3) successfully completed treatment, and (4) have no prior history of malignancy. Our complete patient selection criteria are shown in Figure 1. Overall, 835 HNSCC patients were diagnosed or treated between 2008 and 2016. Of these, 534 (70%) patients met the selection criteria and had complete follow up data. Patients with 6 months of follow up data or greater were included based on studies that demonstrate this is when survival events begin to occur for this patient population [7,8].

Data Collection, Treatment, & Follow-up

Demographic and clinical characteristics of study subjects, including age, gender, social habits, and previous cancer history, were collected by a detailed medical chart review. Clinical information regarding the HNSCC such as stage, grade, anatomical subsite, treatment modality, cancer recurrence, survival status, survival duration, and cause of death were also collected. The cisplatin based chemotherapy (weekly or every three weeks) and intensity modulated radiation therapy regimens (70 Gy to the primary tumor and 56 Gy to the elective lymph nodes in 35 fractions) applied in this cohort have been previously described in detail [9,10].

PET/CT was performed on all patients who underwent CCRT at 13 weeks to assess for complete response (CR) to treatment. In patients who achieved a CR to treatment, surveillance CT scans were conducted to the maxillofacial area, neck, and chest every 3 months in year 1, every 6 months in year 2, and every 12 months in years 3 and beyond. Treatment failure was defined as clinical or pathological evidence of local, regional, or distant recurrence in a patient who previously achieved a CR to treatment. Patients with HNSCC recurrence were categorized as symptomatic or asymptomatic at the time of failure based on the history noted on their clinical record at diagnosis. Asymptomatic patients were further subdivided based on the screening method used to detect recurrence, which included laryngoscopy and dental exam.

Statistical Analyses

Summary statistical analyses are provided for the demographic features of the patients included in this study. The differences of the outcomes between study groups are compared by T-Test (continuous variables) and Fisher's / Chi-Square Test (categorical variables). SAS version 9.4 (SAS Institute, Cary, NC) was used for statistical analyses. All tests are two-sided and performed at a nominal significance level of 0.05.

RESULTS

Table 1 contains descriptive characteristics for the entire HNSCC cohort. The mean age of this predominantly male cohort was 60.9 years old (SD = 10.34). Among the 534 HNSCC patients evaluated, 26% of patients (n = 140) were current smokers, 54% (n = 286) were former smokers, and 20% (n = 108) were never smokers. Within the cohort, 49% (n = 263) patients met NCCN criteria for high-risk smoking history warranting annual low-dose

thoracic CT screening. Median follow-up duration for the entire cohort was 30.9 months (range = 6-88 months). Table 2 compares characteristics of patients who achieved a complete response to treatment (n = 446) without disease recurrence (n = 362) and patients with disease recurrence (n = 84). The mean age of patients who failed treatment was 61.1 years old (SD = 9.98). Median follow-up duration for the cohort who failed was 45.0 months (range = 6-88 months). There were no statistically significant differences between the two groups for all the characteristics including age, smoking status and TNM stage.

As shown in Figure 2, of the 534 HNSCC evaluated patients, 446 (83.5%) had a complete response to radiation or chemoradiation treatment. Among these 446 patients, 84 (15.7%) patients had a local, regional, or distant failure.

Of the 84 HNSCC patients who failed after achieving a complete response to treatment, 25 (30%) patients remained alive and 59 (70%) patients were deceased (Figure 3). There are 15 (18%) patients who had successful salvage treatment and no evidence of disease. Lung screening CT scans detected failure in 8 of these successfully salvaged patients. Among the 8 patients successfully salvaged for locoregional recurrence, 3 failures were asymptomatic at onset and detected by laryngoscope or dental exam. The remaining 5 failures were symptomatic and detected upon work up. One patient was successfully salvaged for both local and distant failure. Maxillofacial and neck CT imaging screening failed to detect any successfully salvaged patients.

Figure 4 describes the pathology results for patients who received lung surgery following a positive lung finding on a chest CT scan. Of the 40 patients who received a wedge resection or lobectomy following a positive lung finding, 34 (85%) patients had malignant pathology while 6 (15%) patients had benign pathology.

DISCUSSION

This analysis shows that lung screening CT detected failure in 8 successfully salvaged patients but head and neck CT scans failed to detect recurrence in any successfully salvaged patients. In this cohort, routine surveillance with lung CT imaging had value for HNSCC survivors while head and neck CT imaging did not.

A previous study by Ho et al. found no survival benefit to post-treatment PET/CT surveillance at 12 and 24 months in HNSCC patients when compared to clinically detected recurrences [2]. Another study found PET/CT surveillance is effective at detecting asymptomatic disease in HNSCC patients but mortality remains high despite early detection [11]. PET/CT may be limited in detecting salvageable recurrence, however studies demonstrated post-treatment PET/CT at 13 weeks has utility in assessing response to CCRT due to its excellent NPV [12]. While combined PET/CT surveillance has been examined, no studies have looked at the utility of CT surveillance in this population to detect local and regional failure. We found no long term survivors were discovered by routine H&N CT imaging.

These findings generally reinforce the guidelines for set forth by the NCCN and ASCO that suggest there is no benefit to routine surveillance imaging for most cancer patients [4,5].

However, though little discussed in the context of head and neck cancer surveillance, the NCCN does have a guideline for screening lung CTs. These guidelines suggest that any patient over the age of 50 with a greater than 20 pack-year smoking history and prior history of cancer (one of several additional risk factors) as appropriate for annual low-dose thoracic CT for screening. By these criteria, 49% (n = 263) of our patients were high risk. Based on our expanded screening criteria, a much larger pool of patients were screened. While nearly half of our patients are captured in the high risk population, our 8 successfully salvaged patients included 2 with no smoking history.

The NCCN guidelines are not clear with regards to patients who have a prior history of aerodigestive tract cancers without the smoking history. Several other follow up guidelines for lung CT screening have been suggested in the literature. Hsu et al. advocates lung CT every 6 months during the first two years of follow up for HNSCC patients after finding that 44.2% of their follow up scans were abnormal [11]. In a systematic review of HNSCC follow up, another study found a personalized approach by an interdisciplinary team to be most effective and suggested annual lung CT imaging during the first 3 years of follow up [13]. Our study found that lung CT screening can provide a survival benefit to HNSCC survivors and supports these guidelines recommending their use.

Despite the benefit of lung CT screening, there are risks associated with screening that must be discussed with the patient. Adverse events from the actual screening exam occur rarely but have the potential to cause complications. Cancer screening also runs the risk of overdiagnosis, where the diagnosis of a cancer would otherwise not go on to cause symptoms or death [14]. Another risk is the incidence of false positive results, which can lead to unnecessary procedures. In our study, among the 40 patients who underwent lung resection, 34 (85%) had positive pathology and 6 (15%) were found to have benign pathology. These results indicate caution must be taken when considering a patient with suspected recurrence for lung resection. When feasible, clinicians should consider obtaining a biopsy before proceeding with surgery. While lung screening has its risks, within the National Lung Screening Trial (NLST) screening with low-dose chest CT reduced mortality from lung cancer by 20% in high risk patients [15]. Since half the patients in our study do not meet the criteria of the NLST, it remains unclear whether there is a mortality benefit in our cohort and this would need to be explored in a randomized setting.

This study is limited by several factors. First, although the median follow-up was 30.9 months, the minimum follow-up was 6 months. Second, while the size of the patient cohort was large, the number of HNSCC recurrences was small at 84 and the number of successfully salvaged patients was smaller at 16. Nonetheless, our data suggests routine surveillance with lung CT imaging had value but head and neck CT scans failed to identify any successfully salvaged patients.

Promising early trials of novel immunotherapy agents such as pembrolizumab and nivolumab have demonstrated clinically meaningful antitumor activity in recurrent or metastatic HNSCC [16-19]. These or future agents may eventually allow for more aggressive surveillance of HNSCC survivors to catch failures early and treat with

immunotherapy. Until then, we recommend only annual low-dose screening CT for HNSCC survivors.

CONCLUSION

Routine surveillance for HNSCC patients with lung CT imaging had value but head and neck CT scans failed to identify any successfully salvaged patients. Given this finding, routine CT imaging surveillance in HNSCC patients should be restricted to annual lung screening with low-dose chest CT. In successfully treated HNSCC patients we recommend follow up with PET/CT at 13 weeks, CT neck/maxillofacial/chest at 6 months, and low-dose chest CT annually. Surveillance head and neck CT imaging is not recommended until better salvage treatment is available to treat locoregional recurrence.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Surveillance for head and neck cancer with lung CT imaging had value
- CT scans of the head and neck failed to identify any successfully salvaged patients
- Imaging surveillance should be restricted to annual low-dose chest CT

Figure 1:
CONSORT diagram for patient selection criteria.

Figure 2:
Response to treatment and failure rate of the overall cohort.

Figure 3:

Outcomes for patients with a complete response to treatment who subsequently failed.

Patients with recurrence were categorized as symptomatic or asymptomatic at the time of failure. Asymptomatic patients were further subdivided based on the screening method used to detect recurrence. One patient was successfully salvaged for both local and distant failure.

Figure 4:
Pathology results for patients who received lung surgery following a positive lung finding on a chest CT scan.

Table 1:

Characteristics of the overall cohort (n = 534).

Characteristic	Mean (SD) Frequency (%)
Age at diagnosis (years)	60.91 (10.34)
Gender	
Male	442 (82.77)
Female	92 (17.23)
Race	
White	458 (85.77)
Other	76 (14.23)
Tobacco Status	
Never	108 (20.22)
Former	286 (53.56)
Current	140 (26.22)
T-Stage	
TX/T0/Tis	38 (7.12)
T1	77 (14.42)
T2	160 (29.96)
T3	158 (29.59)
T4	101 (18.91)
N-Stage	
NX/N0	161 (30.15)
N1	67 (12.55)
N2	264 (49.44)
N3	42 (7.87)
M-stage	
MX/M0	524 (98.13)
M1	10 (1.87)
Disease Site	
Lip and Oral Cavity	81 (15.17)
Pharynx	269 (50.37)
Larynx	139 (26.03)
Anterior/Lateral Neck	34 (6.37)
Other	11 (2.06)
Treatment Type	
RT only	46 (8.61)
CCRT	303 (56.74)
Surgery + CCRT	98 (18.35)
Surgery + RT/ICT + CCRT	79 (14.79)
Other treatment combination	8 (1.50)
Response to Treatment	

Characteristic	Mean (SD) Frequency (%)
Complete (patient free of cancer)	446 (83.52)
Not Complete	88 (16.48)

Abbreviations: RT (radiation therapy), CCRT (concurrent chemoradiation therapy), ICT (induction chemotherapy)

Table 2:

Characteristics of patients with complete response (n = 446) who failed (n = 84) and did not fail (n = 362) treatment.

Characteristic	Non-Failures (n=362) Mean (SD) Frequency (%)	Failures (n=84) Mean (SD) Frequency (%)	p-value ^a
Age at diagnosis (years)	60.64 (9.97)	61.12 (9.98)	0.70
Gender			
Male	295 (81.49)	76 (90.48)	0.05
Female	67 (18.51)	8 (9.52)	
Race			
White	314 (86.74)	77 (91.67)	0.22
Other	48 (13.26)	7 (8.33)	
Tobacco Status			
Never	83 (22.93)	17 (20.24)	0.08
Former	197 (54.42)	38 (45.24)	
Current	82 (22.65)	29 (34.52)	
T-Stage			
TX/T0/Tis	29 (8.01)	6 (7.14)	0.07
T1	63 (17.40)	8 (9.52)	
T2	119 (32.87)	23 (27.38)	
T3	100 (27.62)	26 (30.95)	
T4	51 (14.09)	21 (25.00)	
N-Stage			
NX/N0	114 (31.49)	28 (33.33)	0.17
N1	48 (13.26)	6 (7.14)	
N2	180 (49.72)	41 (48.81)	
N3	20 (5.52)	9 (10.71)	
M-stage			
MX/M0	356 (99.17)	84 (100)	1.00
M1	3 (0.83)	0 (0)	
Disease Site			
Lip and Oral Cavity	45 (12.43)	14 (16.67)	0.07
Pharynx	199 (54.97)	36 (42.86)	
Larynx	83 (22.93)	29 (34.52)	
Anterior/Lateral Neck	26 (7.18)	5 (5.95)	
Other	9 (2.49)	0 (0)	
Treatment Type			
RT only	28 (7.73)	9 (10.71)	0.48
CCRT	215 (59.39)	42 (50.00)	
Surgery + CCRT	70 (19.34)	17 (20.24)	
Surgery + RT/ICT + CCRT	44 (12.15)	15 (17.86)	

Characteristic	Non-Failures (n=362) Mean (SD) Frequency (%)	Failures (n=84) Mean (SD) Frequency (%)	p-value ^a
Other treatment combination	5 (1.38)	1 (1.19)	

Abbreviations: RT (radiation therapy), CCRT (concurrent chemoradiation therapy), ICT (induction chemotherapy)

^a Age was compared by T-test; all other variables were compared by Fisher's Exact/Chi Square test.