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Patterns of distant metastasis in head and neck cancer at presentation: Implications for initial evaluation☆

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ABSTRACT

Importance: Evaluation of distant metastasis (DM) is part of every new cancer evaluation. Understanding DM presentation patterns may impact the imaging workup of Head and Neck Squamous Cell Carcinoma (HNSCC).
Objective: Examine the frequency and location of DM at presentation in HNSCC. We hypothesize that DM are rare, and the lung is the most common site for DM. Secondary evaluation includes identifying patient and tumor factors predictive of DM, and the implications for selection of workup imaging.
Design: Data from the National Cancer Data Base (NCDB) from 2010 to 2015 were analyzed. Subsites evaluated included oral cavity, oropharynx, larynx, hypopharynx, and nasopharynx. Sites of distant metastasis were evaluated in available cases and analyzed.
Setting: Population based database study.
Results: 151,730 cases were available for analysis. Nasopharynx had the highest percentage of M1 disease (9.1%) followed by hypopharynx (7.3%). Excluding the nasopharynx (NP), 3.1% of cases were reported as M1. Advanced T-stage, positive N-stage, and N3 status were all predictors of M1 status on univariate and multivariate analysis for all subsites ($P < 0.05$). Where site of metastasis was available, most (53.1%) DM cases presented with at least lung involvement. In nasopharynx cancers, only 32.8% of DM included the lung.
Conclusions and relevance: Distant metastasis in HNSCC are rare events. PET/CT offers many advantages, but for routine distant metastasis evaluation in HNSCC, CT scan of the chest may be more cost-effective.

Introduction

While multiple studies have evaluated risk factors for the development of distant metastasis (DM) after treatment of head and neck squamous cell carcinoma (HNSCC), there are limited reports on evaluation and frequency of distant metastasis at presentation [1–6]. The National Cancer Comprehensive Network (NCCN) guidelines recommend workup for distant metastatic disease "as clinically indicated" for head and neck cancers [7]. The guidelines do not recommend specific studies to complete this evaluation. Prior to the dissemination of cross sectional imaging, chest xray and laboratory studies of the bone and liver were utilized in the metastatic work of HNSCC [8]. Additional studies at that time also included evaluation with radionuclide liver and bone scans [9,10]. Subsequently, computed tomography (CT) scans replaced the chest xray and became the common evaluation of both the primary and evaluation of distant disease [11]. More recently, PET/CT has become routinely used in the initial evaluation of head and neck cancers [12,13]. Most PET/CT scans evaluate from skull base to thigh, thereby covering a larger area than the traditional chest CT. Another advantage of PET/CT is having metabolic functional data to aid in the evaluation of any masses. However, Chest CT may have a higher resolution then PET/CT.

Although the cost of a PET/CT scan continues to decrease, it still remains approximately 4.4× the cost of a Chest CT with contrast [14]. In this study, we set to examine the frequency and location of DM at initial presentation in HNSCC, and examine the implications for workup

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Table 1
Patient demographics.

	Oral cavity N (%)	Oropharynx N (%)	Larynx N (%)	Hypopharynx N (%)	Nasopharynx N (%)
Total patients	*38,367*	*57,889*	*44,637*	*8247*	*2590*
Age at diagnosis	64.1 ± 13.4	60.8 ± 10.2	64.5 ± 11.0	64.1 ± 10.7	57.2 ± 13.0
≤55	9947 (25.9)	18,336 (31.7)	9715 (21.8)	1824 (22.1)	1140 (44.0)
56–70	16,082 (41.9)	29,907 (51.7)	21,786 (48.8)	4129 (50.1)	1060 (40.9)
> 70	12,338 (32.2)	96.5 (16.7)	13,136 (29.4)	2,294 (27.8)	390 (15.1)
Race					
White	32,565 (84.9)	49,657 (85.8)	35,342 (79.2)	6303 (76.4)	1647 (63.6)
Black	2432 (6.3)	4929 (8.5)	6,238 (14.0)	1292 (15.7)	373 (14.4)
Hispanic	1502 (3.9)	1931 (3.3)	1861 (4.2)	343 (4.2)	152 (5.9)
Asian/pacific islander	1228 (3.2)	636 (1.1)	523 (1.2)	171 (2.1)	371 (14.3)
Other/unknown	640 (1.7)	736 (1.3)	673 (1.5)	138 (1.7)	47 (1.8)
Gender					
Female	15,561 (40.6)	10,809 (18.7)	9802 (22.0)	1660 (20.1)	720 (72.2)
Male	22,806 (59.4)	47,080 (81.3)	34,835 (78.0)	6587 (79.9)	1870 (72.2)
High-risk HPV status					
Negative	8900 (23.2)	11,131 (19.2)	8649 (19.4)	2130 (25.8)	488 (18.8)
Positive	1554 (4.1)	21,809 (37.7)	1597 (3.6)	519 (6.3)	271 (10.5)
Unknown	27,913 (72.8)	24,949 (43.1)	34,391 (77.1)	5598 (67.9)	1831 (70.7)
Tumor grade					
Well-differentiated	26,099 (68.0)	39,448 (68.1)	28,878 (64.7)	5846 (70.9)	1724 (66.6)
Moderately, poorly or undifferentiated	8557 (22.3)	2356 (4.1)	5555 (12.4)	374 (4.5)	75 (2.9)
Unknown	3711 (9.7)	16,085 (27.8)	10,204 (22.9)	2027 (24.6)	791 (30.5)
T stage					
T1	14,819 (38.6)	14,554 (25.1)	15,728 (35.2)	1238 (15.0)	732 (28.3)
T2	11,358 (29.6)	22,948 (39.6)	11,604 (26.0)	2783 (33.8)	576 (22.2)
T3	3,471 (9.1)	11,094 (19.2)	11,171 (25.0)	2216 (26.9)	528 (20.4)
T4	8719 (22.7)	9293 (16.1)	6134 (13.7)	2010 (24.4)	754 (29.1)
N stage					
N0	26,578 (69.3)	11,986 (20.7)	31,014 (69.5)	2618 (31.7)	657 (25.4)
N1	4263 (11.1)	9585 (16.6)	4069 (9.1)	1365 (16.6)	695 (26.8)
N2 (any)	7236 (18.9)	33,600 (58.0)	8960 (20.1)	3781 (45.9)	941 (36.3)
N3	290 (0.8)	2718 (4.7)	594 (1.3)	483 (5.9)	297 (11.5)
M stage					
M0	37,690 (98.2)	55,816 (96.4)	43,441 (97.3)	7642 (92.7)	2355 (90.9)
M1	677 (1.8)	2073 (3.6)	1196 (2.7)	605 (7.3)	235 (9.1)
Stage					
I	13,566 (35.4)	3747 (6.5)	14,638 (32.8)	574 (7.0)	204 (7.9)
II	7787 (20.3)	5130 (8.9)	7679 (17.2)	961 (11.7)	447 (17.3)
III	4445 (11.6)	11,036 (19.1)	9179 (20.6)	1710 (20.7)	817 (31.5)
IVA/B	11,958 (31.2)	36,066 (62.3)	12,028 (27.0)	4432 (53.7)	908 (35.1)

Table 2
Reported sites of distant metastasis.

	Oral cavity N (%)	Oropharynx N (%)	Larynx N (%)	Hypopharynx N (%)	Nasopharynx N (%)
Total patients	38,367	57,889	44,637	8247	2590
Any distant metastasis	677 (1.8)	2073 (3.6)	1196 (2.7)	605 (7.3)	235 (9.1)
Bone metastasis	203 (30.0)	528 (25.5)	195 (16.3)	131 (21.7)	118 (50.2)
Brain metastasis	17 (2.5)	48 (2.3)	20 (1.7)	11 (1.8)	16 (6.8)
Liver metastasis	73 (10.8)	267 (12.9)	126 (10.5)	74 (12.2)	53 (22.6)
Lung metastasis	366 (54.1)	1,033 (49.8)	734 (61.4)	331 (54.7)	77 (32.8)
Other metastasis	143 (21.1)	525 (25.3)	268 (22.4)	151 (25.0)	41 (17.5)

imaging. We hypothesized that given an infrequent rate of DM and the lungs as the most common site of DM, staging CT scans of the chest may be more cost effective than PET/CT. Secondarily, we examined patient and tumor factors predictive of DM at presentation.

Methods

Data source

The NCDB (National Cancer Database) [15] is a nationwide, facility-based, comprehensive clinical surveillance resource oncology data set. It is a joint project of the American Cancer Society and the Commission on Cancer (CoC) of the American College of Surgeons. It captures approximately 70% of all newly diagnosed cancers in the United States, including more than 80% of head and neck cancers, from approximately 1500 CoC-accredited facilities from around the country. Data used in this study came from the NCDB's participant user files for the tongue, floor of mouth, gum and other mouth, tonsil, oropharynx, hypopharynx, other oral cavity and pharynx, and larynx. Institutional Review Board approval was not necessary, as all data in the NCDB is de-

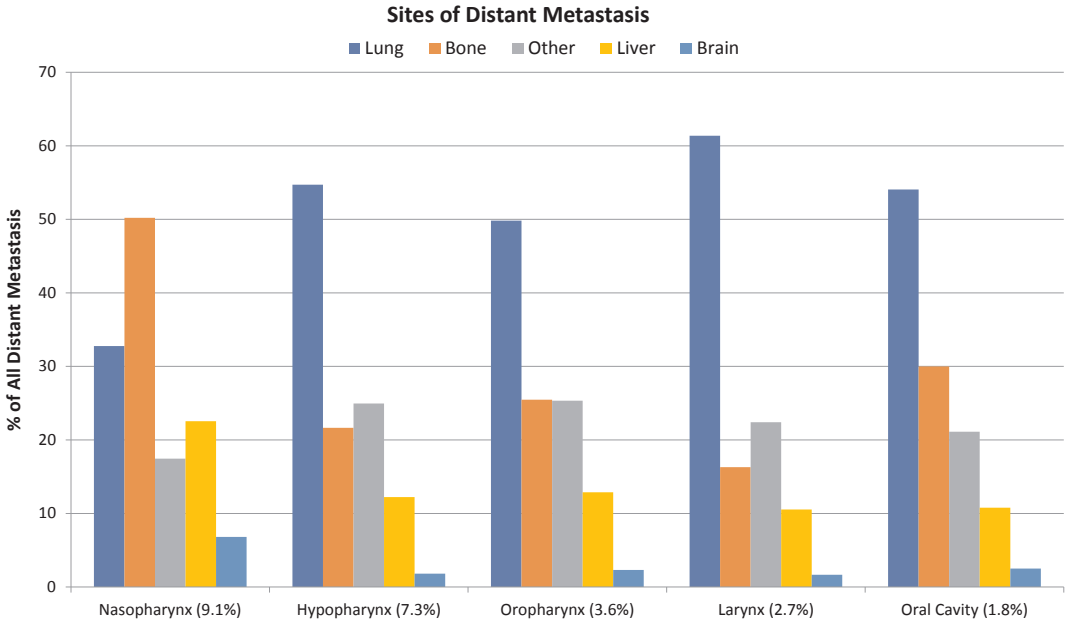

Fig. 1. Sites of distant metastasis by subsite.

identified.

Study population

We identified patients diagnosed with invasive HNSCC using histology codes 8070–8074 and International Classification of Diseases for Oncology Third Edition (ICD-O-3) topographical codes as follows: Oral Cavity – (C020, C021, C022, C023, C028, C029, C030, C031, C039, C040, C041, C048, C049, C050, C060, C061, C062, C068, C069). Oropharynx (C019, C024, C051, C052, C090, C091, C098, C099, C100, C102, C103, C108, C109) Larynx – (C101, C320, C321, C322, C323, C328, C329) and Hypopharynx (C129, C130, C131, C132, C138, C139). Nasopharynx (C110, C111, C112, C113, C118, C119). Cases with missing TNM staging data were excluded. T0 and Tis T-stage patients were also excluded. To allow for uniform analysis, all T-stages were collapsed into T1, T2, T3, and T4 – for example in larynx cancer T1a and T1b glottic cancers were collapsed to T1. Similarly, all N-stages were collapsed into N0, N1, N2, and N3. Clinical, not pathological, TNM stage was used to allow examination of all patients. The NCDB began reporting sites of distant metastasis starting in 2010, thus, our time period for analysis was 2010–2015. Sites of DM are reported only at four sites: Bone, Brain, Lung, Liver, and other sites, not specified. Analysis of sites of distant metastasis included only this subset of cases.

For HPV tumor status, tumors were collapsed into two variables: either high-risk HPV was present or absent. If HPV was present without any further information, this was labeled as high-risk present.

Demographics including age, race, gender, tumor grade, TNM stage, and subsite were evaluated. Descriptive statistics are presented as mean with standard deviation or frequency and percentage. The independent *t*-test and chi-square test were used to compare patient demographics between patients who did and did not have DM at presentation. Multivariable logistic regression was used to identify patient and clinical factors associated with DM at presentation. Statistical analysis was performed with SAS 9.3 (SAS Institute, Cary, NC) and a level of significance set at $p < 0.05$.

Results

A total of 151,730 case records were available and grouped into five major subsites: oral cavity, oropharynx, larynx, hypopharynx, and nasopharynx (NP). Table 1 shows the demographics of the examined cohort. Patients presenting as M1 were rare, overall representing only 3.0% of non-nasopharynx (non-NP) sites. Within the non-NP subsites, hypopharynx cases had the highest frequency of M1 disease at 7.3% and oral cavity having the lowest frequency at 1.8%. In contrast, 9.1% of nasopharynx cases presented with M1 disease.

We further evaluated the site of distant metastasis by subsite to determine the most common sites of distant metastasis. 2464 (54.1%) patients presented with and 2087 (45.9%) patients presented without a lung distant metastasis, with metastasis to the bones being the most common site non-lung site (Table 2). At non-NP sites, cases with a distant metastasis usually included at least a lung metastasis (50–61%). Nasopharynx cancers had a distinctly different metastatic pattern. The majority of nasopharyngeal DM cases excluded the lung (32.8%), with the most common site of metastasis being bone (50.2%). (Table 2) The breakdown of sites of metastasis is shown in Fig. 1.

Tumor variables predictive for M1 status were evaluated. On univariable analysis, age at diagnosis, race, HPV status, tumor grade, as well as T and N stage were associated with DM. Results of multivariable analysis are shown in Table 3. On multivariate analysis, nodal status and specifically N3 status was strongly predictive of DM across all subsites. Advanced T stage was also predictive of M1 disease, but less so than N3 status. Older age and black race were associated with DM for oral cavity, oropharynx, and larynx subsites, while Hispanic race was associated with DM in oral cavity and hypopharynx subsites. Well differentiated oral cavity and larynx tumors were less likely to develop DM than more poorly differentiated tumors. Lastly, high-risk HPV status was associated with a lower chance of DM.

While oral cavity, oropharynx, and larynx, and hypopharynx are often grouped as “head and neck cancer” in the literature, we evaluated whether subsite was an independent predictor of DM on multivariate analysis controlling for age, race, HPV status, tumor grade, and T and N stage. Using oral cavity cancers as a reference, having the lowest DM incidence, all 4 other subsites were predictive of M1 disease (Table 4). Nasopharynx (OR 3.01, 95% CI 2.55–3.55, $p < 0.0001$) and hypopharynx (OR 2.27, 95% CI 2.02–2.56, $p < 0.0001$) were most strongly associated with DM.

An evaluation of oropharynx cancers with available HPV status was also performed. A total of 20,180 cases with HPV status were available for analysis. Of these cases, 64% were reported to have high risk HPV present. The rate of distant metastasis was noted to be higher in the HPV negative cohort (4.0% vs. 2.1%, $p < 0.05$). In a multivariate

Table 3
Multivariable analysis of factors associated with distant metastasis, by subsite.

	Oral cavity		Oropharynx		Larynx		Hypopharynx		Nasopharynx	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Age at diagnosis										
56–70 vs. ≤55	1.17 (0.97–1.42)	0.1099	1.26 (1.14–1.41)	< **0.0001**	1.40 (1.20–1.63)	< **0.0001**	1.14 (0.92–1.41)	0.2174	1.38 (1.03–1.86)	**0.0333**
> 70 vs. ≤55	1.29 (1.04–1.60)	**0.0181**	1.79 (1.57–2.04)	< **0.0001**	2.17 (1.82–2.58)	< **0.0001**	1.25 (0.98–1.60)	0.0699	1.18 (0.77–1.83)	0.4477
Race										
Black vs. White	1.76 (1.42–2.19)	< **0.0001**	1.33 (1.17–1.52)	< **0.0001**	1.29 (1.11–1.50)	**0.0009**	1.21 (0.97–1.51)	0.0858	1.16 (0.79–1.70)	0.4388
Hispanic vs. White	1.59 (1.16–2.18)	**0.0039**	1.16 (0.92–1.45)	0.2060	1.06 (0.80–1.41)	0.6837	1.93 (1.39–2.69)	< **0.0001**	1.08 (0.61–1.93)	0.7946
API vs. White	0.54 (0.29–1.00)	0.0508	0.95 (0.62–1.46)	0.8147	1.05 (0.61–1.81)	0.8564	1.09 (0.61–1.94)	0.7637	1.14 (0.76–1.69)	0.5277
Other/Unknown vs. White	0.69 (0.33–1.43)	0.3178	1.11 (0.77–1.62)	0.5741	1.36 (0.88–2.11)	0.1650	1.40 (0.79–2.46)	0.2462	1.27 (0.50–3.18)	0.6147
High-risk HPV status										
Positive vs. Negative	1.19 (0.82–1.72)	0.3691	0.56 (0.49–0.64)	< **0.0001**	0.90 (0.64–1.25)	0.5206	0.88 (0.59–1.33)	0.5447	0.90 (0.52–1.58)	0.7212
Unknown vs. Negative	1.09 (0.90–1.32)	0.3638	1.07 (0.96–1.20)	0.2257	1.08 (0.93–1.26)	0.3026	1.11 (0.91–1.36)	0.2958	1.11 (0.77–1.60)	0.5644
Tumor grade										
Well vs. Mod/Poor/Undiff	0.70 (0.54–0.90)	**0.0060**	0.91 (0.7–1.17)	0.4548	0.61 (0.45–0.81)	**0.0007**	0.93 (0.58–1.49)	0.7497	0.85 (0.35–2.10)	0.7312
Unknown vs. Well vs. Mod/Poor/Undiff	1.85 (1.51–2.27)	< **0.0001**	1.18 (1.07–1.30)	**0.0006**	1.25 (1.09–1.43)	**0.0014**	1.34 (1.12–1.61)	**0.0016**	1.17 (0.87–1.56)	0.2941
T stage										
T2 vs. T1	2.18 (1.55–3.07)	< **0.0001**	1.43 (1.23–1.67)	< **0.0001**	1.61 (1.28–2.03)	< **0.0001**	1.20 (0.87–1.65)	0.2566	0.90 (0.57–1.42)	0.6493
T3 vs. T1	3.29 (2.26–4.77)	< **0.0001**	2.23 (1.90–2.62)	< **0.0001**	1.85 (1.47–2.32)	< **0.0001**	1.36 (0.99–1.88)	0.0614	1.52 (1.00–2.31)	**0.0476**
T4 vs. T1	6.00 (4.34–8.28)	< **0.0001**	4.28 (3.68–4.99)	< **0.0001**	3.71 (2.95–4.65)	< **0.0001**	2.21 (1.62–3.01)	< **0.0001**	2.39 (1.66–3.44)	< **0.0001**
N stage										
N1 vs. N0	2.76 (2.12–3.59)	< **0.0001**	1.87 (1.52–2.30)	< **0.0001**	4.55 (3.71–5.58)	< **0.0001**	2.59 (1.85–3.63)	< **0.0001**	1.85 (1.20–2.85)	**0.0051**
N2 (any) vs. N0	4.94 (4.00–6.09)	< **0.0001**	3.33 (2.81–3.94)	< **0.0001**	7.45 (6.32–8.77)	< **0.0001**	4.14 (3.13–5.47)	< **0.0001**	2.01 (1.33–3.02)	**0.0009**
N3 vs. N0	15.7 (10.86–22.68)	< **0.0001**	8.22 (6.72–10.07)	< **0.0001**	23.2 (18.03–29.85)	< **0.0001**	7.13 (4.99–10.18)	< **0.0001**	3.56 (2.22–5.71)	< **0.0001**

API = Asia Pacific Islander.

Table 4
Combined Multivariable Analysis of Factors Associated with Distant Metastasis.

	All Sites	
	OR (95% CI)	p-value
Subsite		
Oropharynx vs. Oral Cavity	1.34 (1.22–1.48)	< **0.0001**
Larynx vs. Oral Cavity	1.55 (1.40–1.71)	< **0.0001**
Hypopharynx vs. Oral Cavity	2.27 (2.02–2.56)	< **0.0001**
Nasopharynx vs. Oral Cavity	3.01 (2.55–3.55)	< **0.0001**
Age at diagnosis		
56–70 vs. ≤55	1.28 (1.19–1.37)	< **0.0001**
> 70 vs. ≤55	1.69 (1.55–1.84)	< **0.0001**
Race		
Black vs. White	1.35 (1.25–1.47)	< **0.0001**
Hispanic vs. White	1.28 (1.12–1.46)	**0.0004**
Asian/Pacific Islander vs. White	0.93 (0.74–1.15)	0.4843
Other/Unknown vs. White	1.14 (0.90–1.44)	0.2780
High-risk HPV status		
Positive vs. Negative	0.61 (0.55–0.68)	< **0.0001**
Unknown vs. Negative	1.07 (0.99–1.15)	0.0712
Tumor grade		
Well vs. Moderately/poorly/ undifferentiated	0.71 (0.61–0.82)	< **0.0001**
Unknown vs. Moderately/poorly/ undifferentiated	1.26 (1.18–1.35)	< **0.0001**
T stage		
T2 vs. T1	1.53 (1.37–1.71)	< **0.0001**
T3 vs. T1	2.14 (1.92–2.39)	< **0.0001**
T4 vs. T1	4.08 (3.68–4.53)	< **0.0001**
N stage		
N1 vs. N0	3.11 (2.77–3.48)	< **0.0001**
N2 (any) vs. N0	5.14 (4.68–5.64)	< **0.0001**
N3 vs. N0	12.28 (10.82–13.94)	< **0.0001**

analysis controlling for nodal status, advanced T stage, and gender, the presence of high risk HPV was independently associated with a lower risk of distant metastasis. (OR 0.5 (0.46–0.64)) HPV status was not significant at any other subsites.

Discussion

Evaluation for distant metastases remains an important part of the HNSCC patient workup. With its growing availability, PET/CT has largely replaced the CT scan of the chest in the evaluation of the head and neck cancer patient. We set out to examine rates and patterns of distant metastasis to better understand implications for imaging selection in DM workup. This analysis of the NCDB shows that distant metastasis at presentation in head and neck cancers are rare. While M1 disease from non-NP subsites are rare, on average present in only 3% of head and neck cancer patients, in contradistinction nasopharynx tumors present much more often with DM, approximately 9% of available cases. As expected, clinical parameters like node positivity, N3 status, and advanced T status were all predictors of distant metastasis at presentation.

Historical studies from the 1980–90s suggested DM rates at presentation were high, reported as high as 10–17% [8,11,16]. More recent studies, including studies using the Surveillance Epidemiology and End Reporting (SEER) database, report rates closer to 3% [17,18]. The reason for this reported difference is unclear. This analysis, utilizing the NCDB, mirrors the SEER data with a non-NP DM rate of 3.0%. Prior studies have also found that tumor factors, including Tstage, primary tumor subsite, the number of lymph nodes involved by cancer, and inferior neck metastatic lymph nodes were predictive of DM [11,17]. Our study reports similar findings, with advanced T stage, subsite, and nodal status- especially N3 status, as predictive of distant metastasis.

Previous literature reports the lung as the most common site of DM, and we found this to be true in the NCDB as well [17]. At Non-NP sites, approximately 50–60% of DM will present with at least a lung metastasis. Distant metastasis that did not include lung involvement represented only 0.73% of all non-NP cases.

Our analysis shows that subsite also matters in the pattern of distant metastasis. Cancers of the nasopharynx are almost three times as likely to present with a DM than non-NP sites (9.3% vs. 3.1%). The hypopharynx also has a high distant metastatic rate (7%). Whether this is due to tumor biology or later presentation is not clear. In our cohort, approximately 75% of hypopharynx cancers were AJCC Stage III/IV. In contrast to the hypopharynx, while 80% of oropharynx cancers were advanced cases the rate of distant metastasis is much lower (3.6%), suggesting that tumor biology may play a role.

When examining non-NP cases (oral cavity, oropharynx, larynx, hypopharynx), only 0.73% of these cases present with a non-lung distant metastasis, which is very rare. If every head and neck cancer patient, regardless of stage, underwent a PET/CT for distant metastasis workup, approximately 137 PET/CT scans would be needed to identify a distant metastasis that otherwise would be detected by a CT Chest. The reimbursement of a 2 view chest xray (CPT 71020), CT scan of the chest with contrast (CPT 71260), and a PET/CT scan from skull base to mid-thigh (CPT 78812) is $73.08, $316.44 and $1402.90 respectively [14]. This is professional fees only and excludes other facility fees. A PET/CT is approximately 4.4× more expensive than a CT scan of Chest with contrast. Every PET/CT performed over a CT chest is approximately $1000 of additional cost.

In our analysis, the only reported DM sites available for evaluation in NCDB were lung, bone, liver, and brain. Also, as cervical imaging with a CT neck is routinely performed during HNSCC evaluation, the combination with a CT of the chest would likely capture metastases to the cervical or thoracic spine, and imaged part of the liver – potentially making the CT evaluation of the neck and thorax of further benefit over PET/CT alone for distant metastasis.

Therefore, given the rarity of distant metastasis and distant metastasis that do not include the lung, we conclude that routine PET/CT scanning for distant metastasis evaluation for HNSCC is not justified, as a CT scan of the Lung would be an effective cheaper study for the workup of distant metastasis at presentation. PET/CT would be most effective in cases with a higher risk of distant metastasis, such as advanced T and N stage cases and hypopharynx cases. In addition, a PET/CT scan would be more useful in nasopharynx cancers, where the site of DM usually does not involve the lung. Published data shows that PET/CT is highly effective at identifying distant metastasis, especially extrapulmonary metastasis, compared to CT of the Chest [19,20]. However, FDG avid lesions.

It is important to note that pretreatment PET/CT has many other advantages over CT scans that increases its value. The functional data from PET/CT can be additionally helpful for the evaluation of borderline sized suspicious lymph nodes or evaluation for contralateral neck lymph node metastasis. Functional data can be helpful for radiation planning. PET/CT is more helpful than CT to evaluate any incidental lung nodules or chest adenopathy, because low SUV lesions are unlikely to be metastatic disease. In addition, PET/CT is useful for identification of the primary site during unknown primary evaluation. Our findings reflect the value of PET/CT for workup of distant metastasis only in HNSCC.

Finally, there are some other limitations as this study utilizes the NCDB as a data source. As a large retrospective dataset, the database occasionally has missing data, inconsistent data, and inaccurate data. While the NCDB is an excellent resource, it is not a true cross section of cancer cases in the United States.

Conclusions

Distant metastasis at presentation is rare in head and neck cancer, presenting in approximately 3% of oral cavity, oropharynx, larynx, and

hypopharynx sites. When distant metastasis are present, the lung is most common location. Therefore, for the routine evaluation of distant metastasis, a CT scan of the chest appears is an effective study for initial evaluation. PET/CT offers many other benefits but its role in evaluating distant metastasis is most effective in advanced head and neck disease, the nasopharynx, and hypopharynx where the risk of distant metastasis is elevated. Further study with attention to cost analysis could help clarify patients who would benefit most from PET/CT in the workup of distant metastasis.

Conflict of interest

None declared.

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