Clinicopathologic Determinants of PET-CT Positivity

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ABSTRACT

Objective: Although positron emission tomography-computerized tomography (PET CT) has been shown to have diagnostic and staging value for the head and neck carcinoma, it still has deficiencies to give an optimal level of sensitivity and specificity. Standardized uptake value (SUV) has been shown to associate with the stage of the carninoma . This study evaluates the impact of major clinicopathologic factors on SUV at primary site and lymph node metastases.

Design: Retrospective chart review of the case series.

Setting: The Ohio State University Comprehensive Cancer Center- James Cancer Hospital and Solove Research Institute.

Subjects and Methods: Two hundred and forty-three oral cavity (OC) and laryngopharyngeal carcinoma patients who underwent PET CT and neck dissections in the 3 consecutive years were included in the study. Major primary site was OC followed by oropharynx (OP), larynx (Lx) and hypoharynx (HP) and carcinoma of unknown primary (CUP).

Results: Oral cavity and OP were the two major primary sites (70 %, n=173), followed by Lx, CUP, and HP. Correlation of the PET CT SUV value and the clinicopathologic factors like the T stage, size of the largest lymph node, number of positive lymph nodes, extracapsular spread, tumor grade, primary site, size and depth of infiltration of the primary tumor, lymphatic and perineural invasion are all analyzed; correlation was found with the size and depth of infiltration of the tumor, and number of positive lymph node. T stage was directly proportional with the SUV. Presence of perineural invasion (p=0.013), lymphatic invasion (p=0.0093), and extracapsular spread (p<0.0001) were significantly altering the SUV when compared to absent control.

Conclusions: Most of the clinicopathologic features of head and neck carcinoma which are well known to be poor prognostic factors have significant impact on SUV.

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INTRODUCTION

The use of PET CT as a non-invasive diagnostic method has the advantage of combining functional imaging with anatomical localization. Although it has higher sensitivity, specificity and accuracy than CT, MRI or PET alone, false negative and positive results still constitute a major problem for detecting and staging nodal metastases in head and neck carcinoma.. Threshold of SUV to propose a malignancy is 2.5.

Specificity, sensitivity and accuracy of PET CT for detection of primary and metastatic disease have been widely studied. However, impact of clinicopathological factors on SUV at head and neck tumors have not been emphasized in the literature yet. It is traditionally well-known that factors such as higher tumor stage, perineural and extracapsular lymphatic invasion in metastatic nodes and poor differentiation are related to poor prognosis. Also, higher SUV is proposed as a poor prognostic factor for head and neck cancer in the literature.[1-4] Pathological and biological mechanisms underlying close correlation between SUVmax and these clinicopathological factors has not yet been adequately examined. Therefore we aimed to evaluate whether SUV is correlated with clinicopathological features of head and neck tumors which were shown to be associated with survival of head and neck cancer patients.

MATERIALS AND METHODS

After the Ohio State University Institutional Review Board approval, 243 previously untreated head and neck cancer patients who underwent PET CT evaluation and either diagnostic or therapeutic neck dissections with the diagnosis of oral cavity, and laryngopharyngeal carcinoma and CUP excluding the nasopharynx between January 1, 2005 and December 12, 2007 at the Department of Otolaryngology – Head and Neck Surgery at the James Cancer Hospital and Solove Research Institute of the Ohio State University Medical Center were identified and included in the study. Electronic medical records of each of these patients including the detailed clinical, pathological, and operative reports were retrospectively reviewed and analyzed.

All patients except for the patients having carcinoma of unknown primary were treated by surgical resection of the primary site with bilateral or unilateral neck dissection by three senior surgeons and the histopathologically examined by three senior pathologists. Histopathologic analysis was including the tumor stage, tumor grade, size and depth of infiltration of the primary tumor, size of the largest lymph node, number of positive lymph nodes, extracapsular spread, lymphatic and perineural invasion. Correlation of the PET CT SUV with the above mentioned clinicopathological factors were examined. Effect of primary tumor location on SUV was also examined.

RESULTS

Eighty nine of 243 patients were OC primary (36.6%) followed by OP (33.7%), Lx (18.5%), carcinoma of unknown primary (CUP) (7.4%), and HP (3.7%) (Figure 1).

Pathological T stage and their corresponding mean SUV distributions are presented in figure 2. T stage was found to have a significant effect on SUV. Mean SUV of T1 was significantly lower than SUV of T2, T3 and T4 (table 1). Mean SUV of T2 was also significantly lower than mean of SUV of T3 or T4 (p<0.001).

The depth of infiltration of primary tumor has also significant impact on SUV (Figure 3). Distribution of mean SUVs according to the depth of infiltration is seen in table 2. The depth of infiltration of 1 mm or lower has much less SUVs than the deeper infiltrating tumors.

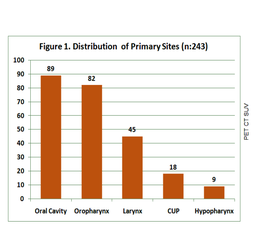
In addition, the size of largest metastatic lymph node (Figure 4), number of positive nodes (Figure 5), and extracapsular invasion (Figure 6) have also showed significant impact on SUV (p<0.0001). Perineural (p=0.013) and lymphatic invasion (p=0.0093) was altering the SUVs either. But SUV was found to be not affected by the tumor grade.

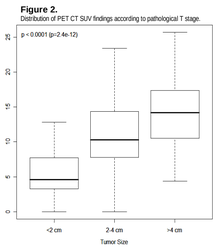
Table 1: Distrubution of PET CT SUV findings according to pathological T stage.

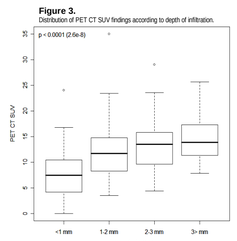
	SUVmax		P<0.001
	Mean	SD	
T 1 (n=36)	6,22	3,94	
T 2 (n=78)	10,08	4,89	
T 3 (n=59)	13,71	6,22	
T 4 (n=52)	11,90	5,09	

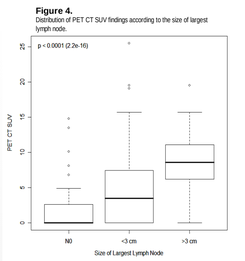
Table 2: Distrubution of PET CT SUV findings according to depth of infiltration.

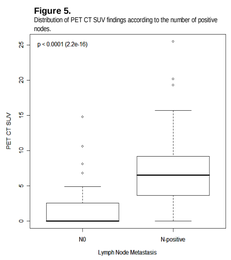
	SUVmax		P<0.001
	Mean	range	
< 1 mm	7.81	0-24	
1-2 mm	12.32	3.5-35	
2-3 mm	13.41	4.4-29	
3-4 mm	14.72	7.8-25.7	

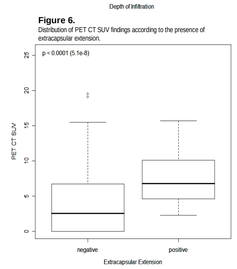












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DISCUSSION

Malignant tumors are characterized by increased glucose metabolism compared with healthy cells.[5] Besides head and neck tumors , SUVmax clinically predicts the prognosis of patients with various primary tumors.[6-9] Association of increased SUV with poor prognosis may be due to cellular and clinicomorphological features of the tumor. FDG uptake was shown to correlate with cell viability and and proliferating activity.[10,11] FDG uptake is higher in fast growing tumors than in slow growing tumors.[12]

Clinicopathological features of a primary tumor; tumor size and depth of invasion was found to correlate with SUV. As tumor size and depth of invasion are the components which determine the T stage; presumption is that the T stage is expected to correlate with SUV. T stage was found to correlate with SUV in conformity with this proposition in this study. This result is consistent with the conclusion of studies in which primary tumor size and depth of invasion were reported to have a correlation with SUV at esophageal carcinoma[13] , and oral cavity carcinoma.[14] The results of these studies point out that that SUVmax of a cancer is closely correlated with both tumor size and depth of invasion, and in other words, tumors with high SUVmax expresses greater tumor mass and invasiveness. Intratumoral lymphatic invasion of the tumor was found to alter SUV significantly. This may be related with the above mentioned feature, that is, a tumor with an aggressive biological cellular characteristics tends to display higher SUV. Higashi et al.[15] reported that the incidence of lymphatic vessel invasion and lymph node metastasis in non-small cell lung cancer depended on 18F-FDG uptake and concluded that 18F-FDG by the primary tumor is a strong predictor of lymphatic vessel invasion and lymph node metastasis.

Number of metastatic nodes was found to correlate well with SUV in this study. This relation was also demonstrated by several studies at different locations other than head and neck such as lung[16-17] cervix[18] and esophagus[13] It is already very well-known that the tumors with higher T stages are more prone to develop lymphatic metastases. This, indirectly, reflects to poor prognosis. However, SUV was found no different among patients having different nodal status but same T stage. Average SUV was similar in the patients having the same T stage with and without nodal metastases.

We did not find any correlation of histologic grade of the tumor with SUV. Histologic grade could be expected to correlate with SUV since poorly differentiated tumors are predisposed **to low glycolytic activity. Similar to the present** study, Suzuki et al [19] reported that neither histological grading nor mitotic/apoptotic status is correlated with SUV in the patients with head and neck carcinoma. Feng et al.[13] reported that the poorly differentiated tumors had exhibited higher SUV than well differentiated tumors in patients with esophageal carcinoma. But, this study has an important drawback against our study due to its relatively small sample size of 68 patients.

CONCLUSION

Results of this study strengthen the allegation that affirms the increased SUV as a poor prognostic sign by displaying the impact of various clinicopathological factors on SUV. Most of the adverse features of the current pathologic staging system are shown to have significant impact on the PET CT SUV findings.