

Original Research Article

Role of PETCT in the management of untreated advanced squamous cell carcinoma of the oral cavity, oropharynx and hypopharynx

Angshuman Dutta¹, B. G. Chaithra^{1*}, Harkirat Singh²

¹Department of ENT & Head and Neck Surgery, ²Department of Radionuclear Medicine, Command Hospital Air Force, Bangalore, Karnataka, India

Received: 07 December 2017

Accepted: 01 February 2018

*Correspondence:

Dr. B. G. Chaithra,

E-mail: drchaithrabg@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Advanced stage cancers of the oral cavity, oropharynx and hypopharynx have the worst prognosis owing to higher incidence of regional and distant metastases. PET/CT scan can detect distant metastases and can therefore be done at the initial presentation in advanced stage head and neck cancers to facilitate the chalking out of an appropriate treatment plan.

Methods: The study included 41 patients having stage III & IV of oral cavity, oropharyngeal and hypopharyngeal squamous cancer. The patients underwent clinical examination, an initial imaging with CT/MRI of the disease site and conventional metastatic workup. An initial TNM staging and treatment plan was formulated. The patients then underwent PET/CT. Tumor restaging was done and the treatment plan was altered if required after the PETCT.

Results: There was change in management of 4(9%) owing to upstaging of disease following PETCT.

Conclusions: PETCT scan had a significant impact on the staging of disease affecting change in the treatment protocols.

Keywords: Positron emission tomography, Cancer, Staging

INTRODUCTION

Head and neck cancer comprises about one third of all cancers in India.¹ Of all the head and neck cancers, cancer of oral cavity, oropharynx, hypopharynx have the worst prognosis owing to a large number of distant metastases. According to SEER (Surveillance, epidemiology and end results) database (1974-1999) published, percentage of distant metastases at presentation are oral cavity- 6%, oropharynx-13%, hypopharynx – 19%.

Treatment of advanced head and neck malignancy involves multidisciplinary approach depending upon the stage. The combination includes surgery, radiotherapy and chemotherapy. Intensive treatment in advanced stage is a huge drain to patients and of the system resources hence needs to be justified and existence of nodal and

distant metastasis at the first contact with the health care professional needs to be evaluated. There is no role for local control of disease in the presence of distant spread. Hence it is imperative to diagnose distant metastasis at initial presentation.² Despite the development of multi modality treatment and advanced infrastructure the 5 yr survival rate in advanced cancers is poor.

Detection of distant spread by PETCT at initial presentation helps in chalking out appropriate treatment plan. This study was aimed at assessing the clinical impact of PET CT affecting the initial treatment plan in the evaluation of advanced head and neck squamous cell carcinoma of oral cavity, oropharynx and hypopharynx.

Aim of the study was to assess the change in the course of initial therapeutic management on the basis of detection of distant metastases, second primaries and

nodal metastases in advanced stage III/IV in high risk sites of HNSCC by doing PET/CT.

METHODS

A prospective cohort study was conducted at a tertiary care oncology centre for a period of two years from 2014-2016. The study included 41 patients having histologically confirmed stage 3 and 4 of oral cavity, oropharyngeal and hypopharyngeal squamous cancer. Written informed consent from the patients and Institute Ethical Committee clearance was taken.

Inclusion criteria

Inclusion criteria were histologically confirmed squamous cell cancers; Stage III & IV oral cavity, oropharyngeal and hypopharyngeal cancers.

Exclusion criteria

Exclusion criteria were previous surgery or radiation therapy; concurrent active cancer; symptomatic or radiological evidence of distant metastasis; allergy to contrast material; pregnancy.

Instruments used for assessment

Initially patients performance score (ECOG) was noted. The staging with conventional investigations was done based on clinical examination, endoscopy, initial CECT scan/MRI of the disease site, Xray Chest and USG abdomen, biochemical evaluation renal and hepatic function followed by fine needle aspiration cytology (FNAC) of suspected neck metastases and biopsy of the primary lesion was carried out. An initial TNM staging and treatment plan was formulated according to AJCC 7th edition and NCCN guidelines. The patients then

underwent contrast whole body PET-CT as an initial investigation and the incidence of distant metastases and second primary cancers were noted and the lesions were radiologically and histologically confirmed wherever possible. A restaging of squamous cell cancer was done as per TNM and the treatment plan was altered if required after the PET-CT.

The data obtained was analysed at the end of the study and the rationale of role PET-CT as preliminary investigation in high risk advanced stage HNSCC patients and its impact on the treatment plan was evaluated. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

+ Suggestive significance (p value: 0.05<p<0.10)

* Moderately significant (p value: 0.01<p ≤ 0.05)

** Strongly significant (p value: p≤0.01)

RESULTS

The mean age of the patients is 60.27. The minimum age of patient studied was 38 and the maximum age of the patient is 82. Of all the patients (n=41) enrolled to the study 33 patients (80%) were males and 8 patients were female. Of all the patients included in the study 35 patients (85%) had grade 2 of ECOG performance score.. Of all the patients (n=41), 12 patients (30%) had oral cavity cancer, 13 patients (30%) had oropharynx and 16 patients (60%) had hypopharynx cancer.

After initial evaluation of HNSCC as per CT/MRI patients were distributed according to TNM stage of the disease as stage III (7 patients), stage IVa (29 patients), stage IVb (5 patients).

Table 1: Change in the staging of the disease following PET-CT.

TNM staging	site	Before PET/CT	After PET/CT	Remarks
Oral cavity (n=12)	StageIII	1	-	1pt upstaged to IVa
	StageIVa	11	12	
	StageIVb	-	-	
	StageIVc	-	-	
Oropharynx (n=13)	StageIII	3	1	2 pt upstaged to IVa
	StageIVa	9	10	1pt upstaged to IVc
	StageIVb	1	-	1pt upstaged to IV c
	StageIVc	-	2	
Hypopharynx (n=16)	StageIII	3	1	2pts upstaged to IVa
	StageIVa	9	10	1pt upstaged to IVc
	StageIVb	4	3	1pt upstaged to IVc
	StageIVc	0	2	
Total		41	41	

Table 2: Change in the nodal stage of patients after PET-CT.

Site	Staging	Before PETCT	After PETCT
Oral Cavity	N0	1	0
	N1	3	1
	N2a	2	2
	N2b	4	6
	N3	0	0
Oropharynx	N0	2	1
	N1	2	1
	N2a	3	1
	N2b	3	2
	N2c	2	7
	N3	1	1
Hypopharynx	N0	1	0
	N1	3	2
	N2a	0	1
	N2b	3	0
	N2c	6	10
	N3	3	3

Table 3: Comparison of Initial treatment plan (before PETCT) and final treatment plan.

Treatment plan	Initial	Final	% change
Sugery with adjuvant radiotherapy	20	18	-5
Concurrent chemoradiotherapy	20	18	-5
Palliative chemotherapy	0	4	10
Neo adjuvant surgery+ adjuvant radiotherapy	1	1	0.0
Total	41 (100%)	41 (100%)	-

Table 1 depicts the change in the staging of the disease following PET-CT. PET-CT changed the staging by upstaging the nodal disease and detecting the distant metastasis. There was detection of distant metastasis in 4 patients

Majority of the patients were of stage III and stage IVa and there was no change in the T staging between the MRI/CT and PET-CT.

21 patients had an upstage in nodal staging after PETCT. 3 patient of N0 is upstaged to N1. 4 patients of N1 upstaged to N2a. 3 patients of N1 to N2c. 1 patient of N2a to N2c. 4 patients of N2a upstaged to N2b. 6 patients of N 2b to N2c. After PET-CT there is statistically significant change in the identification of nodal metastasis in N0 group and identification of multiple additional nodes in N2a and N2b group.

Distant metastasis following PETCT:

Among the study population (n=41), distant metastasis was seen in 4 patients (9.75), 2 patient had lung metastasis, 2 patients had liver metastasis.

In 1 patient each of stage IVa and stage IVb oropharynx there was distant metastasis to lung and liver

respectively. Similarly in 1 patient each of Stage IVa and Stage IVb hypopharynx there were distant metastasis to lung and liver.

Change in the treatment plan from curative to palliative was done in 4 patients owing to distant metastasis.

In the oral cavity group all 12 patients were planned for surgery and there was no change in treatment plan in them. In the patients with carcinoma oropharynx out of 13 planned for chemoradiation 2 had a change in treatment plan to palliative chemotherapy owing to distant metastasis. In patients of cancer hypopharynx 7 were planned for surgery and 8 planned for concurrent chemoradiotherapy. 1 patient in each group had change in management to palliative chemotherapy owing to distant metastasis.

Impact of upstaging of nodal staging on surgery

Change in surgical fields

Change in neck dissection from unilateral to bilateral was done in 1 patient of oral cancer owing to change in staging from N2b to N2c. Change in plan of neck dissection from Supraomohyoid Neck Dissection to Modified Neck Dissection was done in one case of oral

ca due to nodal upstaging from N0 to N1. 2pts of Ca hypopharynx the neck dissection levels were changed from Level II to IV to level II to V (primary hypopharynx) owing to upstaging from N0 to N1. There was no change in neck dissection fields in 4 pts of ca oral cavity inspite of nodal upstaging from N1 as they had already been planned for modified neck dissection.

Change in radiation fields

Change in radiation fields of Intensity Modulated Radiotherapy (IMRT) changed in 13 patients (4 of Ca hypopharynx and 9 of ca oropharynx) due to nodal upstaging of disease.

DISCUSSION

The study focuses on the impact of PET-CT in changing the staging of the disease and subsequent change in the management plan of advanced head and neck cancers by detection of nodal and distant metastasis.

Of the patients in the study group, 16 had hypopharyngeal cancer, 13 had oropharyngeal cancer and 12 had oral cavity cancer.

One of the most important applications of PET scan in the initial staging of Head and Neck Squamous cancers is in identifying metastatic disease in cervical nodes. At the time of initial presentation, metastatic disease to cervical nodes is present in a significant number of cases.³ The presence of nodal disease in HNSCC indicates a higher disease load with change in management and prognosis.³ PETCT scan due to its higher sensitivity and specificity is useful in identifying nodal disease leading to change in initial staging, which modifies the overall treatment plan affecting survival rates.³

Of the 41 patients majority of cases studied were T3/T4 and there were no changes in T staging after WB 18F-FDG PET-CT scan.

Change in nodal staging was seen in 21 patients and change in overall staging was seen in 9 patients after WB 18FFDG PETCT which were both found to be statistically significant ($p < 0.5$). In the nodal staging after WB 18FDG PETCT scan, there was a statistically significant change in identification of nodal metastasis in N0 group and also identification of additional multiple/bilateral nodes (N2c).

The change in the nodal staging led to change in the area of surgical dissection from unilateral neck dissection to bilateral neck dissection and also change in levels of neck dissection in 4 patients. It also influenced change in fields of IMRT in 13 patients

As the nodal stage increases so is the incidence of distant metastases. Lindberg et al studied distant metastases in HNSCC and found while it was 10% in N0-N1 stage, it

increased to 30% in N2-N3 stage.⁴ Ellis et al also correlated the increasing incidence of distant metastases as the nodal stage progressed (N1, 11%; N2, 18%; N3, 27%) and they also found a higher incidence of nodal disease in the lower neck.⁵

The presence of distant metastasis from a primary in HNSCC suggests advanced disease with a poor outcome. The treatment modality also in these cases changes from a curative intent to a palliative treatment protocol. Our results showed additional identification of distant metastasis in 4 patients with change in treatment modality. 4 patients had a change in M status with identification of distant metastasis in lungs (2 patients) and in the liver (2 patients). This led to upstaging of disease in 4 patients of the study group. This result is in accordance with other studies.³ There were no second primaries detected.

There was one false positive result where FDG PET-CT showed increased uptake in the right upper lobe of the right lung which was diagnosed as inflammatory lesion following image guided FNAC. Merino et al in a review of 5,060 patients of previously untreated squamous cell carcinoma of upper aerodigestive tract who completed treatment found clinical manifestation of distant metastases in 10.9%.⁶ The most common site of spread was lung (52%), followed by bone (20.3%) in their study.

Other studies in the literature have identified the change in TNM staging after PETCT scan to be in the range of 20-30%.^{7,8} Our results are different from the published literature as our study was a prospective one which included patients of HNSCC of various sites as compared to other studies which evaluated only a specific site. In our study we included different sites like oral cavity, oropharynx and hypopharynx since these sites has higher propensity to metastasize distantly.

Patrick et al carried out a retrospective study of 36 patients evaluated the role of PET- CT fusion in the management of early and advanced stage of primary HNSCC.⁹ The results showed confirmation of the treatment plan in 25 patients (69%) and altered treatment plan 11 patients (31%). 6 of 11 patients in altered treatment group had their tumour upstaged. 4 of 8 patients with early tumour had their treatment plan altered compared with 7 of 28 patients of advanced staged disease. In conclusion this study showed the use of PET- CT has an impact in the initial treatment planning of early stage and advanced stage HNSCC.

Lonneux et al addressed the impact of FDGPET on the initial staging and management of patients with head and neck squamous cell carcinoma.¹⁰ It is a multicentric prospective study including 233 patients with newly diagnosed and untreated HNSCC patients. Overall adding WB FDGPET to the pre therapeutic conventional staging of HNSCC improved the TNM staging of the disease and altered the management in 13.7% of patients.

Literature review have shown that when PET-CT is done at initial presentation in advance stages of head and neck squamous cancers, it can alter the therapeutic management approach in 31% to 56% of patients.¹¹ PET-CT scan may detect distant metastasis at initial presentation in high risk and advanced stage of head and neck squamous cancers and subsequently aid in proper planning of treatment.

Fleming et al in a retrospective study of 268 patients showed that treatment was altered in 30.9% of previously untreated head and neck cancer patients following PETCT.¹² The FDG PET-CT had an impact on upstaging, diagnosing distant and unresectable and detecting second primary malignancies which altered the treatment plan.

Gordin et al did a prospective nonrandomised study of 90 patients to assess the value of FDG- PET-CT in patients with head and neck carcinoma found that PETCT altered management in 56% of patients.¹³ Thus they concluded that PET-CT has high diagnostic performance in the assessment of head and neck cancer and had a high impact in changing the clinical management in these patients.

CONCLUSION

WB FDG PET-CT has high impact in the initial evaluation of HNSCC of high risk sites like oral cavity, oropharynx and hypopharynx. Following WB18FDG PETCT scan, there was significant change in identification of nodal metastasis inN0 group and also identification of additional multiple/bilateral node (N2c). PETCT also helped identify distant metastasis in 4 patients. There was an alteration the treatment in 4 patients from curative to pallative which were both found to be statistically significant (p<0.5). The results seen in this study can be validated by applying to a larger population.

ACKNOWLEDGEMENTS

Department of Nuclear Medicine, Radiology, Laboratory medicine, Radiation Oncology and Medical Oncology, Command Hospital Air Force Bangalore

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Trivedi N, Kekatpure V, Kuriakose M. Head and neck cancer in India: Need to formulate uniform national treatment guideline? Indian J Cancer. 2012;49 (1):6.
2. Gregoire V, Lefebvre J-L, Licitra L, Filip E, On behalf of the EHNS-ESMO-ESTRO Guidelines Working Group. Squamous cell carcinoma of the

- head and neck: EHNS-ESMO-ESTRO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncol. 2010;21(Supplement 5):v184–6.
3. Nair S, Mohan S, Nilakantan A, Gupta A, Malik A, Gupta A. Impact of 18F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography Scan on Initial Evaluation of Head and Neck Squamous Cell Carcinoma: Our Experience at a Tertiary Care Center in India. World J Nucl Med. 2015;14(1):19–24.
4. Lindberg R. Treatment of cervical lymph node metastases from lesions of oropharynx, supraglottis, larynx and hypopharynx. Am J Roentgenol Nucl Med. 1968;102(1):132-7.
5. Ellis ER, Mendenhall WM, Rao PV, Parsons JT, Spangler AE, Million RR. Does node location affect the incidence of distant metastases in head and neck squamous cell carcinoma? International Journal of Radiation Oncology Biology Physics. 1989;17(2):293–7.
6. Merino OR, Lindberg RD, Fletcher GH. An analysis of distant metastases from squamous cell carcinoma of the upper respiratory and digestive tracts. Cancer. 1977;40(1):145–51.
7. Murakami R, Uozumi H, Hirai T, Nishimura R, Shiraishi S, Ota K et al. Impact of FDGPET/CT imaging on nodal staging for head and neck squamous cell carcinoma. Int J Radiat Oncol Biol Phys. 2007;68:377-82.
8. Ha PK, Hdeib A, Goldenberg D, Jacene H, Patel P, Koch W, et al. The role of positron emission tomography and computed tomography fusion in the management of early stage and advanced stage primary head and neck squamous cell carcinoma. Arch Otolaryngol Head Neck Surg. 2006;132:12-6.
9. Patrick KH, Hdeib A, Goldenberg D, Jacene H, Patel P, Koch W, et al. The Role of Positron Emission Tomography and Computrd Tomography Fusion in the Mangement of Early- stage and Advanced – stage primary Head and Neck Carcinoma. Arch Otolaryngol Head Neck Surg. 2006;132:12–6.
10. Lonneux M, Hamoir M, Reychler H, Maingon P, Duvillard C, Calais G, et al. Positron Emission Tomography With [18F] Fluorodeoxyglucose Improves Staging and Patient Management in Patients With Head and Neck Squamous Cell Carcinoma: A Multicenter prospective study J Clin Oncol. 2010;28(7):1190-5.
11. Li X, Di B, Shang Y, Zhou Y, Cheng J, He Z. Clinicopathologic risk factors for distant metastases from head and neck squamous cell carcinomas. European Journal of Surgical Oncology. 2009;35(12):1348–53.
12. Fleming AJ, Smith SP, Paul CM, Hall NC, Daly BT, Agrawal A, et al. Impact of [18F]-2-fluorodeoxyglucose-positron emission tomography/computed tomography on previously untreated head

and neck cancer patients. *Laryngoscope*. 2007;117(7):1173–9.

13. Gordin A, Golz A, Keidar Z, Daitzchman M, Bar-Shalom R, Israel O. The role of FDG-PET/CT imaging in head and neck malignant conditions: impact on diagnostic accuracy and patient care. *Otolaryngol Head Neck Surg*. 2007;137(1):130–7.

Cite this article as: Dutta A, Chaithra BG, Singh H. Role of PETCT in the management of untreated advanced squamous cell carcinoma of the oral cavity, oropharynx and hypopharynx. *Int J Otorhinolaryngol Head Neck Surg* 2018;4:526-31.