

## RESEARCH ARTICLE

# Pre-Treatment Performance Status and Stage at Diagnosis in Patients with Head and Neck Cancers

Manigreeva Krishnatreya<sup>1\*</sup>, Tashnin Rahman<sup>2</sup>, Amal Chandra Kataki<sup>1</sup>, Jagannath Dev Sharma<sup>1</sup>, Pintu Nandy<sup>1</sup>, Nizara Baishya<sup>2</sup>

### Abstract

Performance status (PS) is a key factor in the selection of treatment in head and neck cancer patients (HNC). There is a probability in the development of an unfavorable PS with HNC advancing stages. This retrospective study was done on data of patients registered during the period from January 2010 to December 2012 at a cancer registry in the North Eastern India. PS was recorded according to the WHO scale. Multinomial logistic regression analysis was conducted to assess the probability of poor performance status with advancing stage. Out of 3,593 patients, there were 78.9% (2,836) males and 21.1% (757) females. Average PS0 was seen in 57.4% of all HNCs, less than 1% of all cases in HNCs with poor PS3-4 except in cases with thyroid, parotid and nose and PNS cancers, 0.7% stage IV ( $\pm$ M1) HNC with PS4, favorable PS0-1 was seen in 84% to 100% of cases, RR=57.1 (CI=21.2-154.1) in M1 for PS4 and with advancing stages the probability of worsening of PS0 to PS4 was 3 times (P=0.021, 95% CI= 1.187-8.474). In HNC, the majority of patients presents with a favorable PS0-1 with different odds of worsening of PS with advancing stages and the presence of metastasis in stage IV is significantly associated with a poor PS.

**Keywords:** Head and neck cancer - performance status - pre treatment - stage at diagnosis

*Asian Pac J Cancer Prev*, 15 (19), 8479-8482

### Introduction

Head and neck cancers (HNC) are common in our population and it constitutes around 30-40% of all cancers. The true burden of HNC in our population may not be reflected by the current literature and what appears is only the tip of the ice berg (Mishra and Mehrotra, 2014). The HNC are the cancers of the lip, oral cavity, tongue, tonsil, oropharynx, hypopharynx, nasopharynx, nose and para nasal sinus (PNS), larynx, parotids and the thyroid. In India, the proportion of head and neck cancers diagnosed at an early stage (stage I and II) is less and a vast majority are diagnosed at an advanced stage (stage IV) (Pandey et al., 2014). Performance status (PS) assessment is an observer dependent measurement of the patient's level of function and their ability of self care. Performance status is a key factor in the selection of treatment in head and neck cancer patients, given the high impact of tumor on nutritional status and the potential treatment-induced toxicities. PS has been determined as an important prognostic factor for advanced stomach cancers (Shitara et al., 2009). There are several techniques for assessment of PS, like Karnofsky's Scale and European Cooperative Oncology Group (ECOG) scale or World Health Organization (WHO) scale of PS. WHO scale of PS is used

both in the pre treatment and post treatment assessment in cancer registries under the National Cancer Registry Programme of the Indian Council of Medical Research. The differences of WHO scale of PS and Karnofsky's scale PS is outlined by Peus et al (2013). West (2013) has shown that outcome of treatment in patients with poor pre treatment PS is also poor. Not much is known about the association of pre treatment PS and different stages at diagnosis in patients with HNCs in our population. In this analysis, we did a comparative study on the different pre treatment WHO scale of PS and stages at diagnosis in patients with HNCs. The objectives were to see the probability in the development of an unfavorable PS with advancing stages in patients with HNC and estimate the relative risk of poor performance status with distant metastasis in stage IV HNC.

### Materials and Methods

This retrospective study was done on data of HNC patients of a hospital cancer registry in the North Eastern India. Strict confidentiality of patient information was maintained while handling the data set. The data set consisted of patient information of HNC that were registered during the period from January 2010 to

<sup>1</sup>Department of Cancer Registry, Epidemiology and Biostatistics, <sup>2</sup>Department of Head and Neck Oncology, Dr.B Borooah Cancer Institute, Guwahati, India \*For correspondence: mani\_greeva@yahoo.co.in

December 2012. A total of 6099 HNC were identified. Out of which, the complete information on stage and PS were seen in 3593 patients. So, the final data set for the present analysis was on 3593 (58.9%) patients. Cases of HNC sites were identified by International Statistical Classification for Diseases, 10<sup>th</sup> revision (ICD-10) coding. The ICD-10 coding for HNC sites are C00 (lip), C01-02 (tongue), C03-06 (oral cavity), C07 (parotid), C09 (tonsil), C10 (oropharynx), C11 (nasopharynx), C12-14 (hypopharynx), C30-31 (nose and PNS), C32 (larynx) and C73 (thyroid glands). The staging of HNC was according to the American Joint Committee on Cancer Classification (AJCC) (Edge et al., 2010). In our data set, the PS was recorded according to the WHO classification (Table 1). The pre treatment PS was considered as a dependent variable and all the stage at diagnosis was taken as covariates.

*Statistical analysis*

Descriptive statistics up to single decimal place was used to tabulate the results. The test of independence was done by Chi square test. Multinomial logistic regression analysis was done to see the probability of poor performance status with advancing stages. The test was conducted at 95% confidence interval and p<0.05 was considered as statistically significant. The present analysis was done by Statistical Package for Social Sciences (SPSS) and Epi Info 3.5.1.

**Results**

Out of 3593 patients, there were 78.9% (2836/3593) males and 21.1% (757/3593) female patients. The mean age of all patients was 56.3 years (standard deviation [SD] =12.6). The characteristics of stage at diagnosis and PS for each anatomic site of HNCs are shown in Table 2. In HNC patients, in stage I disease the following PS was seen, PS0 was seen in 73.1% (71/97), PS1 in 24.7% (24/97), PS2 in 2.0% (2/97) patients. In stage II diseases, PS0 was seen in 67.5% (306/453), PS1 in 28.9% (131/453), PS2 in 2.8% (13/453), PS3 in 0.4% (2/453), and PS4 in 0.2% (1/453) patients. For stage III HNCs, PS0 was seen in 61.1% (751/1229), PS1 in 33.4% (411/1229), PS2 in 3.7% (46/1229), PS3 in 1.5% (19/1229), and PS4 in 0.1% (2/1229) patients. In stage IV diseases, PS0 was seen in 51.5% (936/1814), PS1 in 40.5% (736/1814), PS2 in 5.3% (97/1814), PS3 in 1.7% (32/1814), and PS4 in 0.7% (13/1814) patients. PS0 for all HNC ranged from 34.5% in nose and PNS to as high as 65.7% of nasopharyngeal cancers with an average presenting with PS0 in 57.4%. A poor PS4 for HNCs for most of the anatomic sites ranged from 0% to 0.9%. However, PS4 for thyroid was 3.3%, nose and PNS was 3.4% and for parotid it was highest at 4% in comparison to PS of other sites (Table 2).

*Influence of distant metastatic disease with poor PS in HNC*

Out of all stage IV diseases of HNC, 97% (1760/1814)

**Table 1. Performance Status According to the World Health Organization**

Grade	Explanation of activity
0	Fully active, able to carry on all pre-disease performance without restriction.
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work.
2	Ambulatory and capable of all self care but unable to carry out any work activities. Up and about more than 50% of waking hours.
3	Capable of only limited self care, confined to bed or chair more than 50% of waking hours.
4	Completely disabled. Cannot carry on any self care. Totally confined to bed or chair.

**Table 2. Base Line Characteristics of Stage at Diagnosis and PS in All the Anatomic Sites of HNCs**

HNC Sites	F (%)	Stages				PS				
		Stage-I (%)	Stage-II (%)	Stage-III (%)	Stage-IV (%)	PS0 (%)	PS1 (%)	PS2(%)	PS3(%)	PS4(%)
Lip	35	7	11	4	13	23	11	1	0	0
	1.0	20.0	31.4	11.4	37.1	65.7	31.4	2.9	0.0	0.0
Tongue	623	11	76	209	327	359	235	20	5	4
	17.3	1.8	12.2	33.5	52.5	57.6	37.7	3.2	0.8	0.6
Oral Cavity	724	32	101	153	438	472	220	25	6	1
	20.2	4.4	14.0	21.1	60.5	65.2	30.4	3.5	0.8	0.1
Parotid	25	0	4	3	18	13	8	1	2	1
	0.7	0.0	16.0	12.0	72.0	52.0	32.0	4.0	8.0	4.0
Tonsil	413	5	48	133	227	232	160	13	7	1
	11.5	1.2	11.6	32.2	55.0	56.2	38.7	3.1	1.7	0.2
Oropharynx	229	6	47	96	80	122	86	12	8	1
	6.4	2.6	20.5	41.9	34.9	53.3	37.6	5.2	3.5	0.4
Nasopharynx	67	0	9	17	41	44	23	0	0	0
	1.9	0.0	13.4	25.4	61.2	65.7	34.3	0.0	0.0	0.0
Hypopharynx	944	12	78	425	429	545	340	46	12	1
	26.3	1.3	8.3	45.0	45.4	57.7	36.0	4.9	1.3	0.1
Nose, PNS	29	0	1	2	26	10	15	2	1	1
	0.8	0.0	3.4	6.9	89.7	34.5	51.7	6.9	3.4	3.4
Larynx	444	19	62	181	182	221	176	34	9	4
	12.4	4.3	14.0	40.8	41.0	49.8	39.6	7.7	2.0	0.9
Thyroid	60	5	16	6	33	23	28	4	3	2
	1.7	8.3	26.7	10.0	55.0	38.3	46.7	6.7	5.0	3.3

\*F= Frequency, PS= Performance status

**Table 3. Relation of Stage IV with Performance Status 0 and 4**

Stage IV	PS4	PS0	Total
M1	7	12	19
M0	6	925	931
Total	13	937	950

\*PS= Performance status, M=Metastasis

**Table 4. Odds of Worsening of Performance Status from 0 to 4 with Advancing Stages**

PS	OR	P	95% Confidence Interval for OR	
			Lower Bound	Upper Bound
0 (Ref)	1	-	-	-
1	1.364	0	1.246	1.494
2	1.591	0	1.261	2.007
3	1.817	0.005	1.197	2.757
4	3.171	0.021	1.187	8.474

\*PS=Performance status, OR=odds ratio

were M0 and in 3% (54/1814) it was M1 disease. In only 12.9% patients (7/54) with M1 disease had PS4. The stage IV with M0 and M1 vis-a-vis PS are shown in Table 3. The relative risk (RR) of PS4 with M1 disease in comparison with M0 stage IV is 57.17 (CI=21.21-154.05).

#### Poor performance status with advancing stage

Multinomial logistic regression showed the chances of being able to carry out all normal activity without restriction (PS0) versus the chance of being completely disabled (PS4) increases from 1 to 3.17 as the stages of HNC increases (P=0.021, 95% CI= 1.187-8.474). PS0 to PS1 is 1.364 (P=0.00, 95% CI= 1.246-1.494), PS0 to PS2 is 1.591 (P=0.00, 95% CI=1.261-2.007), and PS0 to PS3 is 1.817 (P=0.005, 95% CI=1.197-2.757) as shown in Table 4.

## Discussion

The common HNC sites in males and females of our population are hypopharynx and tongue respectively (National Cancer Registry Programme 2013). In our analysis, the relative proportion of tongue and hypopharynx constituted 43.6% of all HNCs. The pre treatment PS is important to determine the treatment protocol for cancers, as it is a simple and costless patient evaluation tool. Majority of patients with HNC in our population presented with locally advanced or advanced staged (stage III and stage IV) so, aggressive form of treatment by surgery followed by external beam radiotherapy was imperative. As, most of the surgical procedures in HNC results in a functional dysfunction, the importance of assessing pre treatment quality of life index (QOL) by assessing performance status is further important. The importance of neo adjuvant or concomitant chemotherapy is established for disease control, survival, and QOL through the preservation of function (Dimery et al., 1990; Vokes et al., 1990; Vokes et al., 1993). Joshi et al (2013) has advocated induction chemotherapy in T4b oral cancers followed by resection to improve the survival. This assumes significance because in our retrospective analysis 60.5% of oral cavity cancer patients presented

with stage IV ( $\pm$ M1) disease and a poor performance status (PS4) was seen in only 0.1% of such patients. So, in T4b oral cancer cases induction chemotherapy can be offered with lesser risk of systemic intolerance due to a favorable pre treatment PS. In HNCs favorable PS0-1 ranged from 84% (lowest in parotid) to 100% (highest in nasopharynx) of cases and marginal zone set of PS2 ranged from 0% (lowest in nasopharynx) to 7.7% (highest in larynx). Moreover, in this analysis patients with a combined PS3 and PS4 (poor favorable sets) were seen in less than 1% of cases with HNCs except for cases with thyroid, parotids and nose and PNS cancers, which were more likely HNC sites for presenting with pre treatment PS4. This could be due to the involvement of the base of skull and/or intra cranial involvement (T4) in stage IV cancers of the nose and PNS, and parotid with worsening PS at presentation. However, in thyroid cancers, locally advanced disease (Patel and Shaha, 2005) or a distant metastasis (M1) is responsible for poor PS at presentation. Interesting to note was that, in most (100%) of HNC patients with nasopharyngeal cancers presented with a favorable performance status (PS0-1). This could have been due to the regional or nodal presentation in nasopharyngeal cancers rather than locally advanced primary disease at the time of diagnosis. The common sites for metastasis in squamous carcinoma of the head and neck region are the lungs, followed by bone, liver, skin and mediastinum (Ferlito et al., 2001). In this analysis distant metastasis was seen in 3% of all stage IV HNCs and, irrespective of the site of metastasis (lungs, bones etc), in HNC with a stage IV disease patients were at significantly high risk of presenting with PS4 in comparison to patients without distant metastasis. Furthermore, our analysis has revealed that, in HNCs when the stage at diagnosis increases, the odds of presenting in pre treatment PS4 becomes 3 times from PS0. This assumes significance in limited resources setting where the waiting time for cancer directed treatment with external beam radiotherapy (EBRT) or surgery is long in most instances. Prior to surgical resection or EBRT, neo adjuvant chemotherapy in early staged HNC with good PS can be considered to prevent the upstaging due to tumor progression (Eisenhauer et al., 2009). Upstaging of HNC is associated with a statistically significant probability for worsening of PS from the favorable sub sets of PS0, as shown in our analysis. This may have bearing on the treatment compliance as well because; patients with poor pre treatment PS are more likely to drop out during the course of treatment. In low resources settings stage at diagnosis for cancers of the oral cavity, oropharynx, hypopharynx and larynx were significantly associated factor for patient survival (Albano et al., 2013). Furthermore, it has been shown that the stage and treatment are strong prognostic factors for 5-year overall survival in these patients (Pruegsanusak et al., 2012).

There are obvious limitations of this study. The foremost being, it has not taken into account the presence of co-morbid conditions which could have influenced the pre treatment performance status of HNC patients. Also, HNC consists of heterogeneous primary tumors with different clinical behaviors.

In conclusion, Majority of patients with HNC presents with a PS in the favorable sub set of PS0-1. The anatomic sites of HNC which presents with a relatively poor PS in comparison are thyroids, nose and PNS, and parotids. In HNCs there was seemingly no direct association of pre treatment PS with stages at presentation but, advancing stages increases the probability of worsening of PS. In stage IV disease the presence of metastasis is significantly associated with a poor PS.

## Acknowledgements

The National Centre for Disease Informatics and Research under Indian Council of Medical Research.

## References

- Albano PM, Salvador CL, Orosa J, et al (2013). Overall survival of Filipino patients with squamous cell carcinoma of the head and neck: a single-institution experience. *Asian Pac J Cancer Prev*, **14**, 4769-74.
- Dimery IW, Hong WK (1993). Overview of combined modality therapies for head and neck cancer. *J Natl Cancer Inst*, **85**, 95-111.
- Edge S, Byrd DR, Compton CC, et al (2010). *AJCC Cancer Staging Manual*. 7<sup>th</sup> ed. Bangalore: Springer-Verlag.
- Eisenhauer EA, Therasse P, Bogaerts J, et al (2009). New response evaluation criteria in solid tumours: Revised RECIST guideline (version 1.1). *Eur J Cancer*, **45**, 228-47.
- Ferlito A, Shaha AR, Silver CE, Rinaldo A, Mondin V (2001). Incidence and sites of distant metastases from head and neck cancer. *ORL J Otorhinolaryngol Relat Spec*, **63**, 202-7.
- Joshi A, Patil V M, Noronha V, et al (2013). Is there a role of induction chemotherapy followed by resection in T4b oral cavity cancers? *Indian J Cancer*, **50**, 349-55.
- Mishra A, Meherotra R (2014). Head and neck cancer: global burden and regional trends in India. *Asian Pac J Cancer Prev*, **15**, 537-50.
- National Cancer Registry Programme (2013). Consolidated report of Population Based Cancer Registries of India. 2009-2011, ICMR: NCDIR, Bangalore.
- Pandey KC, Revannasiddaiah S, Pant NK, Bhatt HC (2014). Stage-wise presentation of non-metastatic head and neck cancer: an analysis of patients from the Kumaon hills of India. *Asian Pac J Cancer Prev*, **15**, 4957-61.
- Patel KN, Shaha AR (2005). Locally advanced thyroid cancer. *Curr Opin Otolaryngol Head Neck Surg*, **13**, 112-6.
- Peus D, Newcomb N, Hofer S (2013). Appraisal of the Karnofsky performance Status and proposal of a simple algorithmic system for its evaluation. *BMC Med Inform Decis Mak*, **13**, 72.
- Pruegsanusak K, Peeravut S, Leelamanit V et al, (2012). Survival and prognostic factors of different sites of head and neck cancer: an analysis from Thailand. *Asian Pac J Cancer Prev*, **13**, 885-90.
- Shitara K, Muro K, Matsuo K, et al (2009). Chemotherapy for patients with advanced gastric cancer with performance status 2. *Gastrointest Cancer Res*, **3**, 220-4.
- Vokes EE, Weichselbaum RR (1990). Concomitant chemoradiotherapy: Rationale and clinical experience in patients with solid tumors. *J Clin Oncol*, **8**, 911-934.
- Vokes EE, Weichselbaum RR, Lippman SM, Hong WK (1993). Head and neck cancer. *N Engl J Med*, **328**, 184-194.
- West HJ (2013). Patients with advanced non-small-cell lung cancer and marginal performance status: Walking the tight rope towards improved survival. *J Clin Oncol*, **31**, 2841-3.