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Research Article

Is suicide a significant contributor to mortality in head and neck cancer - A surveillance, epidemiology, and end results database study

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ABSTRACT

Introduction: Patients with oral and orofacial cancers have been suggested at increased risk for suicide, but only a few studies have described the survival characteristics. The purpose of this study was to describe survival (5-years), mortality, and suicide among patients with mid-facial head and neck cancer (HNC) and to identify the patient and disease characteristics associated with higher suicide rates.

Methods: Patients in the study were residents of geographic areas served by the Surveillance, Epidemiology, and End Results (SEER) program who were diagnosed with cancer from 1973 to 2014. This was a retrospective cohort study of survival (classified into 5 groups), mortality with a focus on suicide in persons with HNC. All relevant details were collected and analyzed. $P \leq 0.05$ was considered significant.

Results: There were 218,048 cases of HNC of who 774 committed suicide, 63,262 succumbed to HNC, 44,113 died due to other causes, and 81,779 are alive. Tongue was the most common site and most common type was squamous cell carcinomas. The overall mean 5-year survival period did not remarkably change since 1974. The mean survival period significantly varied between the outcome groups. Mean 5-year survival in cases of suicide was progressively decreasing with time frame while death due to other causes occurred at a relatively less time in 2003–08 as compared to 1973–78. Of interest is the nearly stable survival, by volume in death due to HNC in the entire span of time 1973–2008 but different in percentage level.

Conclusion: It has been documented that patients with HNC in the SEER database have a higher incidence of suicides influenced by oral sites, stages, and number of tumors. These points to the need for psychological evaluation of patients with HNC and the relationship of tumor stage with survival characteristics. The study also highlights the burden of oral cancer and mental health issues that are largely neglected.

Keywords: Head and neck cancer, 5-year survival, Depression, SEER database, Suicide, Tumor grades, Tumor numbers.

INTRODUCTION

A diagnosis of cancer is a major stressor event for the patient and family, uncontrolled pain and physical symptoms may lead to suicidal thoughts. The psychological distress, feeling of lack of autonomy, independence/hope, feeling of helplessness, impending morbidity associated with cancer and its treatment, associated economic crisis, familial outlook, decreased quality of life, and depression (psychosocial factors) are factors that play a crucial role in such suicide ideation and completion. Age, gender, treatment type, and stage of cancers (individual factors) may also play a predominant role in determining the suicidal risk. Cumulatively, these factors increase the risk of suicide among People Living With Cancer (PLWC) as compared to the general population.[1] It has been reported that about 17.7% of American PLWC harbor suicidal ideation. Affective illness, alcoholism, and depression are some of the important determinants of suicide even in the physically healthy population.[2,3] Apart from cancer-specific morbidities, psychosocial and psychosomatic effects of cancer, organic mental syndromes, and/or exacerbation of pre-existing psychopathologic abnormalities are also reported to predispose to suicides or suicidal tendencies.[2-4]

There are reports of higher incidence of suicide among mid-facial, head and neck cancers (HNC, including laryngeal and thyroid tumors), as compared to the general population and PLWC.[5-11] Suicide incidence is noted to be very high for larynx and to some extent thyroid cancers and the prevalence influenced by the treatment and staging. The concepts of treatment/staging are constantly evolving with time and repeatedly undergo periodic changes. Irrespective of the evolving concepts of treatment and staging, HNC suicides are reported to be increasing in North America.[5,7] The influence of grade of HNC at diagnosis on survival outcome also has not been studied. Furthermore, there are very few reports addressing suicides in non-laryngeal, non-thyroidal HNC in the recent literature.[5,7] Reports of survival patterns between grades of tumors, number of malignant tumors of non-laryngeal, and non-thyroidal HNC are very few.

There is a recent report of depressive factors influencing survival among patients with HNC.[12] Tongue cancer is emerging as a cause of concern among Indians, and there is no reliable data on the extent of suicides and depression among this subset of patients.[13,14] Lessons from existing large scale data would help Indian oral cancer and mental health-care personnel to address the issue of oral, HNC survival, and suicides effectively. Hence, using a large, publicly available American database, an attempt is made to address the lacunae and describe the survival pattern in non-laryngeal, non-thyroidal HNC with emphasis on suicide.

MATERIALS AND METHODS

Patient Population

This is a secondary data analysis of existing, depersonalized data, available in open web domain (www.seer.cancer.gov); appropriate permission for access was obtained from authorities. The Surveillance, Epidemiology, and End Results (SEER) program was used to identify patients with cancers. The SEER database, covering about 28% of all US citizens has all pertinent patient demographics that allow further analyses of the survival data. For the purpose of this study, all cancers of the head and neck region (nasal cavity, nasal sinuses, nasopharynx, oral cavity, oropharynx, salivary glands, hypopharynx, and abbreviated together as HNC) were collected. The present study did not involve interaction with human participants or the use of any personal identifying information. Hence, Institutional Review Board approval was not required.

Patient Selection Criteria

The patient study population used in this cohort was obtained from the SEER-18 registry, of USA.[15] The time period was from 1973 to 2014. Details of all HNC patients were collected using case listing procedure using SEER*Stat program of SEER (Surveillance Research Program, National Cancer Institute SEER*Stat software (www.seer.cancer.gov/seerstat) version 8.3.4, 2017). Further details about the program remain accessible at https://seer.cancer.gov/resources/.

From this 18 registries all patients with HNC region as described below were included. Sites of cancer were classified as hypopharynx (pyriform sinus, posterior cricoid region, aryepiglottic fold, and hypopharynx), nasopharynx (nasopharynx and walls), oral cavity and oropharynx (external lip, mucosa of lip, commissure of lip, lip, tongue, lingual tonsil, gum, floor of mouth, hard palate, soft palate, palate, uvula, cheek mucosa, vestibule of mouth, retromolar area, tonsillar fossa, vallecula, epiglottis, pharynx, and oropharynx), salivary glands (parotid gland, submandibular gland, and sublingual gland), and nasal cavity and sinuses (accessory sinus, sphenoid sinus, ethmoid sinus, frontal sinus, and maxillary sinus). Larynx and thyroid gland were not included in this study.

Patient Characteristics

Using the case-listing option of SEER*Stat software, all HNC patient data for sex, age, race, marital status, year of diagnosis, primary site of cancer, cause of death, survival time, cancer staging, and status at follow-up were collected. Patients were considered to have committed suicide only if the cause of death on record was entered as "suicide and self-inflicted injury." Based on their last follow-up status, patient's survival outcome was broadly classified as alive, dead due to any HNC, dead due to any other cause, death due to cancer (but not sure of primary - N/A not first tumor) and those committed suicide. The survival months as per the SEER database and the number of tumors (malignant/*in situ*) at the time of initial presentation were also collected.

Based on age (in years), the study population was stratified as 0–14, 15–30, 31–44, 45–60, 61–74, and 75 and above. Race

was broadly classified as Caucasians, Afro-Americans, natives (Alaska and native Indians), and others. Marital status at the time of diagnosis was classified as married, never married, divorced, separated, unmarried, widowed, and unknown. Gender was marked as male or female. The grade of tumor at diagnosis was marked as well differentiated (Grade I), moderately differentiated (Grade II), poorly differentiated (Grade III), and undifferentiated or anaplastic (Grade IV) and unknown. Time periods were 1973–1978, 1979–1984, 1985–1990, 1991–1996, 1997–2002, 2003–2008, and 2009–2014. The side of involvement was reported as a bilateral, single primary, left - origin of primary, not a paired site, only one side - side unspecified, paired site, but no information concerning laterality and right - origin of primary. Based on insurance coverage (where data was available), the study population was divided as those with any Medicaid, insured, insured - no specifics, uninsured and insurance status - unknown. For each of the patient, 5-year survival was calculated, classified as survived or succumbed to any of the cause, as described earlier. As for the time period between 2009 and 2014, 5-year survival could not be calculated; they were excluded from 5-year survival analysis.

All data were acquired in November 2017, and statistical analysis was performed using the Statistical Package for the Social Services (Version-23, IBM, IL, USA). Descriptive statistics were presented for all the variables in the 5 types of outcome groups. Chi-square test was used to identify the difference between them. Using appropriate statistical tools, the difference in mean survival months and the number of malignant/*in situ* tumors were studied. A Kaplan–Meier analysis of survival was carried out to see the survival characteristics in grades of tumors, with death/alive being the event and stratified by the type of outcome. Multiple regression analysis was employed to assess the impact of the demographics parameters studied on the 5-year survival period for the entire study population in the time period 1974–2008. The 2009–2014 was omitted as 5-year survivals for a majority of the patients were not computable. $P \leq 0.05$ was taken as significant.

RESULTS

Individual depersonalized data collected from the SEER-18 registry from 1973 to 2014 as of November-2016 and released in April-2017 (inclusive of adjustments due to Hurricane Katrina) and linked to all states and counties were repeatedly run to collect maximum data. The entire study population with HNC, as defined in the material and method section was classified as that is alive, committed suicide, dead (not first tumor), dead due to HNC, and dead due to other conditions.

In all, data of 218,048 USA residents in the SEER database with HNC (having substantial details) were collated. Of these, 774 people committed suicide during 1973–2014, 81779 (37.5%) were alive, 63262 (29%) dead due to HNC, 28120 (12.9%) dead in not first tumor category, and 44113 (20.2%) dead due to other causes. The average survival period was 62.83 ± 73.87 (95% Confidence interval = 62.52–63.14) months, median of 34 months and the range was 0–503 months, with an interquartile range of 79 (11–90) months. Of all HNC cases, tongue was the most common site (25.6%, n = 55878) followed by gum and other mouth (14.7%, n = 32086). Majority of the cases were squamous cell carcinoma (SCC, 83%, n = 181000).

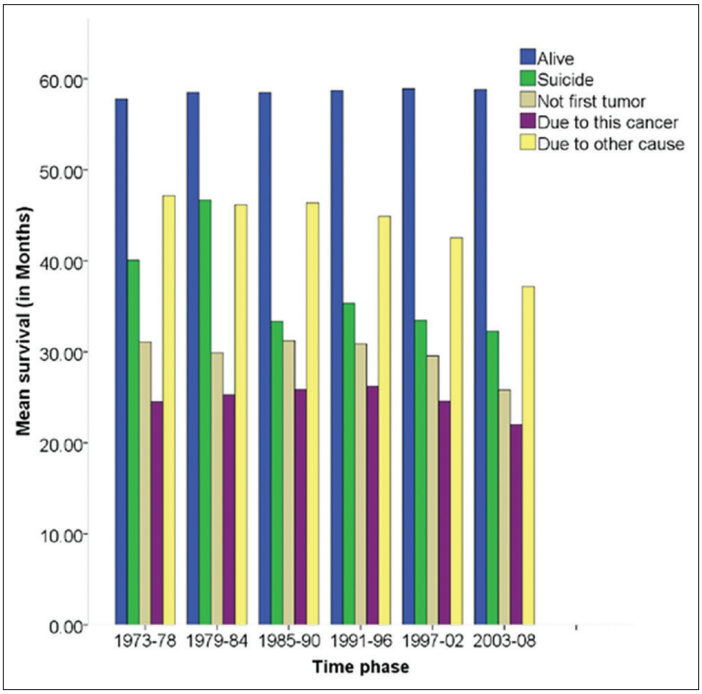

Figure 1: Mean 5-year survival in head and neck cancer patients in different time phases.

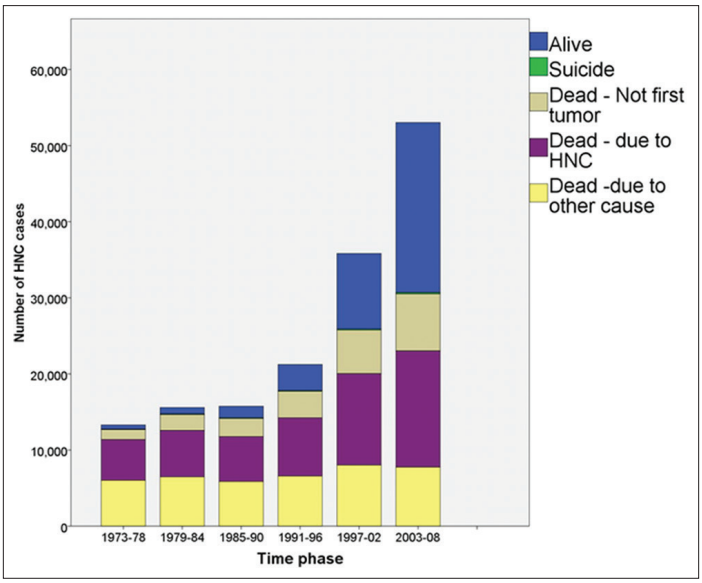

Figure 2: Number of head and neck cancer and 5-year survival in different time phases.

Table 1: The outcome of HNC in SEER database 1973–2014.

Parameters	Alive	Dead			
		Suicide	Not first tumor	HNC	Other causes
Age (years)					
≤14	515 (0.6)	-	3 (0.0)	91 (0.1)	10 (0.0)
15–29	2457 (3)	7 (0.9)	39 (0.1)	497 (0.8)	127 (0.3)
30–44	9843 (12)	60 (7.8)	469 (1.7)	3918 (6.2)	1432 (3.2)
45–59	33,181 (40.6)	261 (33.7)	4866 (17.3)	21,286 (33.6)	11007 (25)
60–74	27,285 (33.4)	321 (41.5)	12155 (43.2)	24,479 (38.7)	19182 (43.5)
>75	8498 (10.4)	125 (16.1)	10588 (37.3)	12,991 (20.5)	12,355 (28)
Sex					
Male	55,483 (67.8)	710 (91.7)	18,486 (65.7)	44,488 (70.3)	30713 (69.6)
Female	26,296 (32.2)	64 (8.3)	9634 (34.3)	18,774 (29.7)	13,400 (30.4)
Race					
Caucasians	97,909 (83)	720 (93)	24,304 (86.04)	49,800 (78.7)	38,204 (86.6)
Afro-Americans	5684 (7)	21 (2.7)	2649 (9.4)	8859 (14)	3647 (8.3)
Natives	466 (0.6)	2 (0.3)	115 (0.4)	371 (0.6)	173 (0.4)
Asian/pacific islanders	64 38 (7.9)	26 (3.4)	1039 (3.7)	4057 (6.4)	1901 (4.3)
Unknown	1281 (1.6)	5 (0.6)	13 (0)	175 (0.3)	188 (0.4)
Marital status					
Married	47,590 (58.2)	426 (55)	14,277 (50.8)	29,614 (46.8)	22,973 (52.1)
Never married	13,903 (17)	111 (14.3)	3098 (11)	11,476 (18.1)	5344 (12.1)
Divorced	7561 (9.2)	105 (13.6)	3003 (10.7)	8163 (12.9)	4371 (9.9)
Separated	780 (1)	4 (0.5)	388 (1.4)	1310 (2.1)	741 (1.7)
Unmarried	115 (0.1)	0	7 (5)	14 (0)	5 (0)
Widowed	4696 (5.7)	71 (9.2)	5431 (19.3)	9287 (14.7)	7309 (16.6)
Unknown	7134 (8.7)	57 (7.4)	1916 (6.8)	3398 (5.4)	3370 (7.6)
Tumor grade					
Well Differentiated	12,389 (15.1)	117 (15.1)	3905 (13.9)	6339 (10)	8327 (18.9)
Moderately	26,595 (32.5)	273 (35.3)	10,274 (36.5)	21,226 (33.6)	13779 (31.2)
Poorly	19,212 (23.5)	177 (22.9)	6145 (21.9)	16,471 (26)	8032 (18.2)
Undifferentiated	3013 (3.7)	22 ((2.8)	732 (2.6)	2426 (3.8)	1175 (2.7)
Unknown	20,570 (25.2)	185 (23.9)	7064 (25.1)	16,800 (26.6)	8327 (18.9)
Site					
Floor of mouth	3452 (4.3)	68 (8.8)	2376 (8.4)	5124 (8.1)	4381 (9.9)
Gum and other mouth	10,116 (12.4)	90 (11.6)	5448 (19.4)	9473 (15)	6959 (15.8)
Hypopharynx	2386 (2.9)	76 (9.8)	2876 (10.2)	7235 (11.4)	3013 (6.8)
Lip	7527 (9.2)	84 (10.9)	1980 (7)	1280 (2)	8337 (18.9)
Nasopharynx	5170 (6.3)	52 (6.7)	925 (3.3)	4977 (7.9)	1863 (4.2)
Oropharynx	1981 (2.4)	31 (4)	1075 (3.8)	2898 (4.6)	1165 (2.6)
Other oral cavity and pharynx	1078 (1.3)	24 (3.1)	1035 (3.7)	2493 (3.9)	969 (2.2)
Salivary gland	11,273 (13.8)	65 (8.4)	2554 (9.1)	5153 (8.1)	4040 (9.2)
Tongue	23,232 (28.4)	191 (24.7)	7075 (25.2)	16,584 (26.1)	8846 (20.1)
Tonsil	15,474 (18.9)	93 (12)	2776 (9.9)	8095 (12.8)	4540 (10.3)
Laterality					
Bilateral, single primary	119 (0.1)	-	38 (0.1)	108 (0.2)	35 (0.1)
Left - origin of primary	16,496 (20.2)	87 (11.2)	3336 (11.9)	7663 (12.1)	4789 (10.9)
Not a paired site	47,727 (58.4)	587 (75.8)	21,312 (75.8)	47,130 (74.5)	34,129 (77.4)
Only one side - side unspecified	60 (0.1)	0	18 (0.1)	89 (0.1)	48 (0.1)
Paired site, but no information concerning laterality	254 (0.3)	0	114 (0.4)	504 (0.8)	171 (0.4)
Right - origin of primary	17,123 (20.9)	100 (12.9)	3302(11.7)	7768 (12.3)	4941 (11.2)
Extent					
Distant	5597 (8.6)	69 (9.1)	3320 (12)	12,843 (20.9)	3252 (7.4)
Localized	32,735 (41.9)	290 (38.2)	10,309 (37.2)	9980 (16.2)	18,924 (43.3)
Regional	35,295 (45.1)	351 (46.2)	11,577 (41.8)	33,215 (54)	18,017 (41.2)
Unstaged	3482 (4.5)	50 (6.6)	2483 (9)	5507 (8.9)	3485 (8)
Time phase (diagnosis)					
1973–78	536 (0.7)	79 (10.2)	1295 (4.6)	5371 (8.5)	6012 (13.6)
1979–84	838 (1)	87 (11.2)	2079 (7.4)	6114 (9.7)	6469 (14.7)

(Contd...)

Table 1: *(Continued)*

Parameters	Alive	Dead			
		Suicide	Not first tumor	HNC	Other causes
1985–90	1505 (1.8)	102 (13.2)	2374 (8.4)	5919 (9.4)	5852 (13.3)
1991–96	3430 (4.2)	80 (10.3)	3496 (12.4)	7659 (12.1)	6575 (14.9)
1997–02	9940 (12.2)	134 (17.3)	5710 (20.3)	12038 (19)	8008 (18.2)
2003–08	22341 (27.3)	179 (23.1)	7494 (26.7)	15279 (24.2)	7748 (17.6)
2009–14	43189 (52.8)	113 (14.6)	5672 (20.2)	10882 (17.2)	3449 (7.8)

All factors had a Chi-square test P=0.001. HNC: Head and Neck Cancer

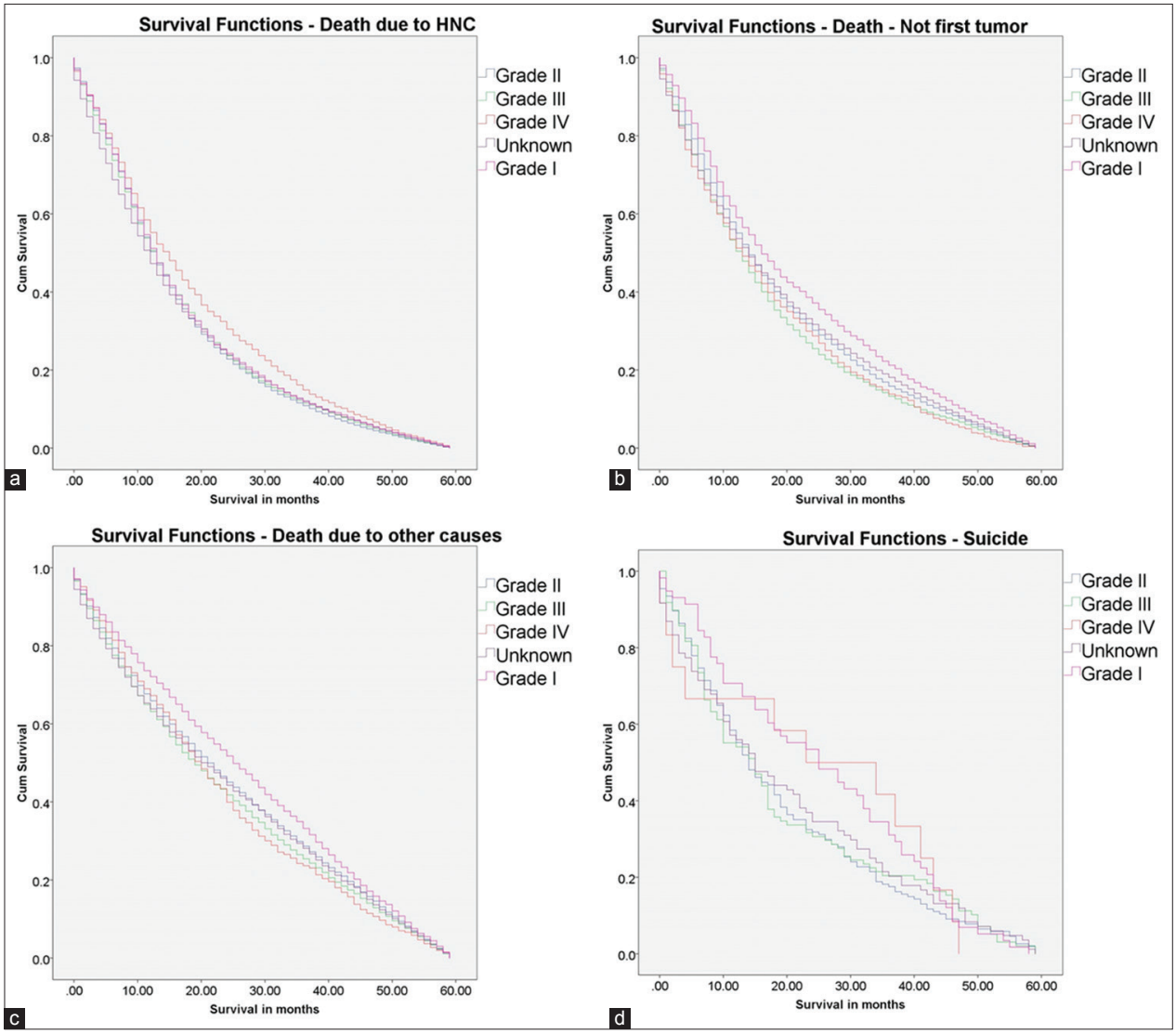

Figure 3: Kaplan–Meier curve for 5-year survival outcome of head and neck cancer as compared by the grades of tumor in the study group. (a) Death due to head and neck cancer (b) Death due to - not first tumor (c) death due to other causes (d) death due to suicides.

The demographics of age group, gender race, insurance subscription, site of HNC, grade of HNC, year of occurrence, and marital state at the time of diagnosis were compared with the present status of the patients. The distribution of the same is given in Table 1. All the parameters considered were statistically significant differences between the patient survival outcomes (P = 0.000).

Table 2: 5-year survival outcome of HNC patients in 1973–2008.

Parameters	Vital status		
	Status at 5 year		
	Alive	Currently Dead	
	Alive	Alive	Dead
	Count (%)	Count (%)	Count (%)
Sex			
Female	26,296 (38.82)	12086 (17.84)	29,351 (43.33)
Male	55,483 (37.2)	24,368 (16.34)	69,300 (46.46)
Site			
Floor of mouth	3542 (22.89)	3821 (24.69)	8110 (52.41)
Gum and other mouth	10,116 (31.74)	6054 (18.99)	15704 (49.27)
Hypopharynx	2386 (15.34)	2071 (13.32)	11094 (71.34)
Lip	7527 (39.26)	6755 (35.23)	4890 (25.51)
Nasopharynx	5170 (40.03)	1918 (14.85)	5827 (45.12)
Oropharynx	1981 (28.02)	737 (10.43)	4351 (61.55)
Other oral cavity and pharynx	1078 (20.56)	621 (11.84)	3544 (67.59)
Salivary gland	11,273 (49.08)	3483 (15.17)	8211 (35.75)
Tongue	23,232 (41.72)	7301 (13.11)	25,158 (45.17)
Tonsil	15,474 (50.03)	3693 (11.94)	11,762 (38.03)
Age group			
<14 years	515 (83.2)	16 (2.58)	88 (14.22)
15–29 years	2457 (78.7)	201 (6.44)	464 (14.86)
30–44 years	9843 (62.67)	1892 (12.05)	3971 (25.28)
45–59 years	33,181 (47.12)	10970 (15.58)	26,270 (37.3)
60–74 years	27,285 (32.84)	16342 (19.67)	39454 (47.49)
75 years	8498 (19.34)	7033 (16.01)	28404 (64.65)
Marital status			
Divorced	7561 (32.87)	3344 (14.54)	12098 (52.59)
Married (including common law)	47,590 (41.55)	21,441 (18.72)	45,509 (39.73)
Separated	780 (24.53)	528 (16.6)	1872 (58.87)
Single (never married)	13,903 (41.16)	3848 (11.39)	16031 (47.45)
Unknown	7134 (45.09)	2540 (16.05)	6149 (38.86)
Unmarried or domestic partner	115 (81.56)	0 (0)	26 (18.44)
Widowed	4696 (17.78)	4753 (17.99)	16966 (64.23)
Race			
American indian/Alaska native	466 (41.57)	139 (12.4)	516 (46.03)
Asian or pacific islander	6438 (48.020	1865 (13.91)	5104 (38.07)
Afro-American	5684 (27.43)	2594 (12.52)	12446 (60.06)
Unknown	1282 (77.89)	112 (6.8)	252 (15.31)
Caucasians	67,909 (37.73)	31,744 (17.64)	80,333 (44.63)
Grade			
Well differentiated; Grade I	12,389 (39.88)	7352 (23.67)	11325 (36.45)
Moderately differentiated; Grade II	26,595 (36.87)	11218 (15.55)	34,324 (47.58)
Poorly differentiated; Grade III	19,212 (38.41)	6210 (12.41)	24,601 (49.18)
Undifferentiated; anaplastic; Grade IV	3013 (40.9)	1011 (13.72)	3343 (45.38)
Unknown	20570 (36.54)	10663 (18.94)	25058 (44.52)
Laterality			
Bilateral, single primary	119 (39.67)	24 (8)	157 (52.33)
Left - origin of primary	16,496 (50.98)	3945 (12.19)	11917 (36.83)
Not a paired site	47,727 (31.82)	28,371 (18.92)	73,881 (49.26)
Only one side - side unspecified	60 (28.71)	40 (19.14)	109 (52.15)
Paired site, but no information concerning laterality	254 (31.24)	95 (11.69)	464 (57.07)
Right - origin of primary	17,123 (51.54)	3979 (11.98)	12,123 (36.49)
Spread- SEER			
Distant	6697 (25.6)	1794 (6.86)	17,671 (67.54)
Localized	32,735 (45.33)	17,542 (24.29)	21,942 (30.38)

(Contd...)

Table 2: *(Continued)*

Parameters	Vital status		
	Status at 5 year		
	Alive	Currently Dead	
	Alive	Alive	Dead
	Count (%)	Count (%)	Count (%)
Regional	35,295 (35.86)	14304 (14.53)	48836 (49.61)
Unstaged	3482 (24.97)	2545 (18.25)	7915 (56.77)
Outcome			
Alive	81,779 (100)	0 (0)	0 (0)
Suicide	0 (0)	248 (32.33)	519 (67.67)
Dead not first tumor	0 (0)	5445 (19.43)	22580 (80.57)
Dead due to HNC	0 (0)	8679 (13.91)	53720 (80.09)
Dead due to other cause	0 (0)	22082 (50.28)	21832 (49.72)
Time phase			
1973–78	536 (4.06)	5228 (39.56)	7452 (56.39)
1979–84	838 (5.4)	5850 (37.69)	8832 (56.91)
1985–90	1505 (9.6)	5520 (35.23)	8645 (55.17)
1991–96	3430 (16.2) 3	6398 (30.28)	11301 (53.49)
1997–02	9940 (27.89)	7622 (21.39)	18079 (50.73)
2003–08	22,341 (42.36)	5676 (10.76)	24720 (46.87)
2009–14	43,189 (68.59)	160 (0.25)	19622 (31.16)
Insurance			
Any medicaid	5368 (51.08)	215 (2.05)	4927 (46.88)
Insurance status unknown	2860 (61.47)	99 (2.13)	1694 (36.41)
Insured	34,579 (68.59)	1195 (2.37)	14643 (29.04)
Insured/No specifics	7584 (58.99)	324 (2.52)	4948 (38.49)
Uninsured	1890 (57.71)	45 (1.37)	1340 (40.92)

Table 3: Mean survival months in the pooled and 5-year period and number of tumors in the study population.

Parameters	Outcome	Mean±SDa*Kruskal-Wallis test; ^One-way ANOVA (in months)	95% CI for mean		Min	Max	*P*-Value
			Lower	Upper			
Overall survival period (1973–2014)*	Alive	146.73±79.81	145.93	147.53	0	503	0.000
	Suicide	62.70±69.55	57.36	68.04	0	397	
	Dead- Not first tumor	41.81±50.43	41.15	42.47	0	478	
	Dead- due to HNC	34.11±48.42	33.69	34.52	0	476	
	Dead - due to other cause	90.26±83.93	89.44	91.08	0	496	
5-year survival period (1973–2008)*	Alive	58.83±7.47	58.75	58.90	0	60	0.0000
	Suicide	35.89±23.28	34.11	37.66	0	60	
	Dead- Not first tumor	28.82±22.34	28.52	29.11	0	60	
	Dead- due to HNC	24.30±20.89	24.13	24.48	0	60	
	Dead - due to other cause	43.71±21.47	43.50	43.92	0	60	
Number of tumors^	Alive	1.31±0.67	1.30	1.31	1	12	0.0000
	Suicide	1.45±0.79	1.39	1.51	1	11	
	Dead- not first tumor	2.55±0.93	2.54	2.56	2	13	
	Dead- due to HNC	1.15±0.46	1.15	1.16	1	11	
	Dead - due to other cause	1.39±0.63	1.38	1.39	1	8	

*Kruskal–Wallis test; ^One-way ANOVA

An attempt was made to compare the survival period in terms of the patient outcome. After excluding the 2009–14 periods for reasons mentioned earlier, it was observed that 154,743 HNC patients formed the study group, out of which survival details of 830 patients were not available. Of the remaining 153,913 HNC patients, 79,514 died within 5 years. It included 416 (0.5%) suicides, 17,092 (21.5%) death (not first tumor), 43,299 (54.5%) death due to HNC, and 18,707 (23.5%) death due to other causes. The difference in other predictors is shown in Table 2.

Table 4: Mean and median differences for Kaplan–Meier's 5-year survival for HNC patients 1973–2008.

Outcome	Mean				Median			
	Estimate	Std. Error	95% Confidence interval		Estimate	Std. Error	95% Confidence interval	
			Lower	Upper			Lower	Upper
Alive								
Grade I	59.448	0.045	59.360	59.535	60.000	0.000		
Grade II	59.423	0.034	59.356	59.491	60.000	0.000		
Grade III	59.420	0.044	59.334	59.506	60.000	0.000		
Grade IV	59.298	0.106	59.090	59.505	60.000	0.000		
Unknown	59.329	0.040	59.251	59.406	60.000	0.000		
Suicide								
Grade I	25.448	2.159	21.216	29.680	25.000	5.074	15.055	34.945
Grade II	19.468	1.311	16.898	22.037	14.000	1.550	10.962	17.038
Grade III	19.724	1.742	16.309	23.140	15.000	2.695	9.718	20.282
Grade IV	24.667	5.472	13.941	35.392	23.000	13.856	0.000	50.159
Unknown	20.440	1.922	16.673	24.208	15.000	2.746	9.617	20.383
Not first tumor								
Grade I	21.373	0.357	20.674	22.072	16.000	0.511	14.998	17.002
Grade II	18.904	0.195	18.521	19.287	14.000	0.233	13.543	14.457
Grade III	17.192	0.237	16.726	17.657	13.000	0.268	12.475	13.525
Grade IV	17.395	0.679	16.065	18.725	13.000	0.880	11.275	14.725
Unknown	18.983	0.253	18.488	19.478	14.000	0.347	13.319	14.681
Due to this cancer								
Grade I	17.073	0.217	16.648	17.498	13.000	0.216	12.576	13.424
Grade II	16.550	0.112	16.330	16.771	13.000	0.120	12.765	13.235
Grade III	16.749	0.129	16.496	17.002	13.000	0.141	12.723	13.277
Grade IV	18.881	0.362	18.173	19.590	15.000	0.491	14.037	15.963
Unknown	16.195	0.141	15.918	16.472	12.000	0.145	11.717	12.283
Due to other cause								
Grade I	26.638	0.319	26.013	27.263	25.000	0.576	23.870	26.130
Grade II	24.297	0.225	23.855	24.738	21.000	0.392	20.231	21.769
Grade III	22.944	0.285	22.385	23.503	19.000	0.468	18.083	19.917
Grade IV	22.859	0.726	21.437	24.281	20.000	1.014	18.013	21.987
Unknown	23.602	0.255	23.103	24.102	21.000	0.468	20.083	21.917

Table 5: Multiple regression analysis of 5-year survival of HNC patients in 1973–2008.

Parameters	Unstandardized coefficients		Standardized coefficients beta	95% CI for B		Sig.
	B	Standard error		Lower	Upper	
Constant	106.187	3.513		99.302	113.072	0.000
Sex	−2.712	0.356	−0.055	−3.410	−2.014	0.000
State	−0.046	0.043	−0.007	−0.131	0.039	0.287
Site	0.309	0.051	0.044	0.209	0.410	0.000
Grade	0.909	0.107	0.060	0.700	1.118	0.000
Laterality	0.490	0.135	0.026	0.224	0.755	0.000
Staging–SEER	1.060	0.205	0.036	0.657	1.462	0.000
Race	1.789	0.185	0.068	1.426	2.152	0.000
Marital status	−1.396	0.094	−0.109	−1.580	−1.212	0.000
Age group	−5.705	0.177	−0.232	−6.053	−5.357	0.000
Time phase	−8.489	0.542	−0.110	−9.551	−7.427	0.000
Insurance subscription	1.766	0.173	0.071	1.426	2.106	0.000

The mean survival period in the 5-year (60 months, 1974–2008) period did not change over the time phases since 1974. [Figure 1] Mean 5-year survival in cases of suicide, was progressively decreasing with time frame while death due to other causes occurred at a relatively less time in 2003–08 as compared to 1973–78. Of interest is the nearly stable survival, by volume

in death due to HNC in the entire span of time 1973–2008 but presented with a difference when expressed as a percentage in 5-year survival [Figure 2].

Kruskal–Wallis test revealed that pooled (overall) and 5-year survival period differed between the 5-outcome groups. The survival period varied significantly between the 5-groups (P = 0.000). Death due to HNC occurred at a relatively lower mean months in pooled and 5-year survival analysis. This was closely followed by death in not first tumor group trailed by suicide and death due to other causes. The difference was statistically significant (P = 0.000). ANOVA test showed that death due to "not first oral tumor" had highest mean number of tumors (2.55 ± 0.93) followed by patients who committed suicide had a mean (1.45 ± 0.79) of malignant tumors while those who were alive had 1.31 ± 0.67 tumors, dead due to HNC had 1.31 ± 0.67, and those dead due to other causes 1.39 ± 0.63. The difference was statistically significant (P = 0.000) [Table 3].

Kaplan–Meier survival statistics were performed to estimate the 5-year (60 months) survival characteristics of the study population in the time frame of 1973–2008. The endpoint was demise due to any cause which was stratified based on survival outcome, as described earlier. A log-rank test was run to determine if there were differences in the survival distribution for the different outcomes in death (suicide, death due to HNC, death due to other causes, and not primary tumor) as strata and grade of tumors as a factor. The survival distribution was statistically significant difference, $\chi^2(2) = 99.192$, $P < 0.0005$. [Figure 3]. The characteristics are given in Table 4. In the case of suicides, it was observed that about 550% of cases succumbed before the 30 months. Anaplastic group (Group IV) had a rapid drop in the slope in the graph as compared to other grades of HNC. In death due to HNC and not a first tumor, there was no remarkable difference between the grades of the tumor while the slope of the graph was uniform for all tumor grades in the group of patients that succumbed due to other causes.

Multiple regression analysis was done to predict 5-year survival (in months) of all HNC in 1973–2008, both years inclusive from race, side laterality, tumor grade, marital status at diagnosis, age group, gender, and site among all HNC patient. There was linearity as assessed by partial regression plots and a plot of studentized residuals against the predicted values. Independence of residuals was seen with Durbin Watson statistics (0.1590). There was homoscedasticity, as assessed by visual inspection of a plot of studentized residuals versus unstandardized predicted values. There was no evidence of multicollinearity, as assessed by tolerance values >0.1. There were no studentized deleted residuals ≥±3 standard deviations, no leverage values ≥0.2, and values for Cook's distance >1. The assumption of normality was met (Q-Q Plot). The multiple regression model statistically significant predicted survival, F (11, 18424) = 203.818, $P < 0.0005$, adjusted R^2 = 0.12. All variables added statistically significant to the reduction, $P \leq 0.05$. Regression coefficients and standard errors can be found in Table 5.

DISCUSSION

The purpose of this study was to describe the suicidal and survival characteristics of HNC patients. Previously, such an attempt was made using data till 2011.[5] Knowledge and insight would help policy framers to formulate guidelines for maxillofacial oncology team to sensitize, educate, and identify the PLWC who might have suicidal ideation. Suicide among Indian PLWC is poorly documented, and there has been a report of increasing trends of tongue cancer, especially in non-habit, elderly women.[13,14] Hence, knowledge from this would help Indians to frame better suicide screening among PLWC.

An attempt was made to decipher the influence of grade of HNC at diagnosis on survival outcome of non-laryngeal, non-thyroidal HNC. An attempt was also made to correlate the grades of tumors, number of malignant tumors of non-laryngeal, and non-thyroidal HNC with survival outcomes as defined earlier.

Relatively more percentage of Caucasians (93% of all suicides) committed suicide as compared to 78.7% due to HNC, 7% of Afro-Americans committed suicide, and 14% succumbed to HNC. Males (91.7%) were more likely to commit suicide. This is consistent with other studies and trends too.[5,7] Proportionally, more suicide was associated with moderately differentiated HNC (31.2–36.5%). About 80% of the study population lay in between 45 and 84 years of age. It was observed that a significant number of suicides in HNC occurs in the initial 6 months of diagnosis. Nearly 55% of all HNC suicides occurred within the first 3 years of diagnosis. Tongue and tonsil are the most common sites involved in HNC suicide while the site is often an unpaired HNCs (75.9%). SCC is the most predominant HNC type. All the findings are consistent with earlier reported literature from several parts of the world.[2,5,10]

Suicides represents a small proportion of HNC patient deaths in this sample (0.4%). It has been reported up to 17.7% of all patients with cancer have suicidal ideation. The 0.4% suicide is only a reflection of completion of suicide and is not a measure of suicide ideation or attempts. Persistence of risk of suicide, even after 60 months of initial diagnosis highlights the need for continuous monitoring in this vulnerable population.[2-4] As seen in Figure 1, the mean 5-year survival outcome has not changed during the time phase studied. The "death due to other causes" was progressively decreasing while other outcomes were nearly stable. The number of HNC being diagnosed is increasing over the time phases. As observed in Figure 2, the number of

PLWC being alive at 5-year period was increasing while the "death due to other causes" was significantly decreasing while death due to cancer is nearly stable. The advances in medical care for non-cancer related ailments could be the suggested reason, and further factors behind this phenomenon need to be explored.

The survival period, especially the Inter Quartile Range denotes that at least 25% of the suicide category had lived only 11 months after diagnosis while 75% of them live up to 7.5 years after the diagnosis. Similarly, 75% of those who are alive live up to 10 years. 75% of the people who are dead due to HNC live only up to 2 years 9 months since diagnosis. Survival is also influenced by the grade of tumor at presentation [Table 3, Figures 1-4]. The survival trend difference between the grades of the tumor ($P = 0.000$) and warrants further investigation.

The number of tumors at initial presentation is also significant. As observed in the Table 2, the number of tumors indicates that those HNC who had committed suicide had relatively higher mean number of tumors. To the best of our knowledge, there is pertinent literature to support or refute this claim. The relationship between 5-year survival and grade of tumor (at presentation), as seen in Figure 3, indicates that the grade of the tumor has a definite role to play in 5-year survival, especially with suicides.

Observations of increased prevalence of depression in several types of cancers including HNCs, in higher frequency than general populations, have been reported.[16,17] Depression is a known to be associated with high risk of suicide, even in normal population. Role of neurotransmitter, particularly of serotonin and noradrenaline in depression and suicide have been documented.[18-20] Conventional history and mental health assessment interviews are the current methods to prevent the suicide in HNCs.[21,22] Often the HNCs team, especially from the first contact, surgeons, often feel not sufficiently trained to screen for suicidal tendency and by reflex, they often refer it to the mental health team. Non-compliance to such referrals is not uncommon and may compound to the magnification of the issue.[23]

The statistical outcome of the multiple regression analysis points out several factors, the adjusted R^2 being 0.12 (for all HNCs) and indicates that sum of all considered independent variables into this regression model (race, side laterality, tumor grade, marital status at diagnosis, insurance status, age group, gender, and site) explained only up to 12% of the variability of the considered dependent variables. Therefore, many other factors such as morbidity associated with treatment/HNC, concomitant substance abuse, treatment approach, and pre-existing mental illness besides numerous other factors may contribute to the occurrence of suicides in patients with HNCs.

The study also suffers from certain limitations inherent to observational data of SEER. Missing data, reproducibility, reproducibility of data collected from database, representative sampling, etc., pose methodological issues.[24,25] Data collected is based on queries posed in the software, and even alteration of one criterion could change the number of cases in the net result. The relying on the cause of death classification and chance of misclassification of death, including inability to differentiate between treatment-related mortality and death from underlying comorbid conditions or missing out of secondary tumors. In addition, important covariates such as comorbidity, pre-existing mental illness, and substance abuse including but not limiting to tobacco and alcohol, HPV, education, and socioeconomic factors were not factored in this study. Limitation of not including TNM staging parameters, treatment factors, and duration of therapy could have a direct bearing on the results. In the present study, the results of Kaplan–Meier statistics and multiple regression analysis have to be interpreted with caution.[26]

Clinical Implication: Globally studies indicate that non-communicable diseases (NCDs) such as mental illness, substance abuse, and cancer are one of the major causes of mortality and morbidity. Oral diseases have emerged as the single most common NCD, which needs to be addressed.[27-29] Impact of mental illness, substance abuse with respect to oral diseases, including HNC has not been adequately studied. This is in spite of the fact that oral diseases, is a part of NCD and has a major impact on quality of life. The results of this study indicate that there should be a multi-disciplinary approach to provide much-needed relief to, especially, when the patients with oral diseases harbor suicidal ideation.

Key points to be taken

Mental health and oral health remains largely out of the universal medical coverage. This manuscript highlights the one of the commonly neglected medical arenas that needs focused work in future to improve the quality of life. With increasing non-communicable diseases, vulnerability to oral and mental diseases is bound to increase. This manuscript adds strength to the call for integrating mental and oral health issues to mainstream health agenda.

CONCLUSION

The number of HNC tumors has an influence on 5-year survival rate. The 5-year survival characteristics of HNC in patients in the SEER database for the period 1974–2008 is presented. It is observed that suicide risk in PLWC HNC is higher and the grade has a bearing on the 5-year survival. The risk of suicide is high in the initial period of diagnosis and persists even after 10–30 years of diagnosis. Hence, PLWC should be screened

by competent mental health professionals, when some signs of negative approach or feelings are expressed by patients. With newer classifications of HNC being proposed based on treatment, importance to mental well-being also should be considered. With increasing survivorship after HNC cancer, there is a need for more structured and evidence-based mental health care that has been already called for.

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Conflicts of interest

There are no conflicts of interest.

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