RESEARCH ARTICLE

Overall Survival of Filipino Patients with Squamous Cell Carcinoma of the Head and Neck: A Single-Institution Experience

Pia Marie Albano[1,2,3]*, Christianne Lumang-Salvador[4], Jose Orosa, III[4], Sheryl Racelis[5], Modesty Leano[5], Lara Mae Angeles[3,6], John Donnie Ramos[1,3,7]

Abstract

This paper is the first to present the incidence and overall survival of patients with squamous cell carcinoma of the head and neck (SCCHN) from the extreme northern part of the Philippines. We retrospectively retrieved the records of patients with histologically-confirmed squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx and larynx at the Mariano Marcos Memorial Hospital and Medical Center, Ilocos Norte, Philippines, from 2003 to 2012 and analysed prognostic factors associated with survival. Of the 150 cases, only 80 (53.3%) were still living when the study was terminated. Median age at initial diagnosis was 61.5 years and the male to female ratio was 7:3. The majority of the cases had tumours in the oral cavity (50.7%), followed by the larynx (36.7%). Sex (log rank=1.94, p value/α=0.16), tumor site (log rank=0.02, p value/α=0.90), tumor grade (log rank=1.74, p value/α=0.42), and node stage (log rank=0.07, p value/α=0.80) were not shown to be associated with the survival of our cases. Only 45 (30.0%) had no regional lymph node involvement (N0) at presentation and 12 (8.0%) had already developed distant metastases. Among the 150 patients, 71 (47.3%) were not able to receive treatment of any kind. Oddly, treatment (log rank=1.65, p value/α=0.20) was also shown to be not associated with survival. The survival rate of those who underwent surgery, radiotherapy, or both was not statistically different from those who did not receive any treatment. Only the tumor stage (log rank=4.51, p value/α=0.03) was associated with patient survival. The overall mean survival was 49.3 months, with survival rate diminishing from 88.3% during the 1st year to 1.80% by end of the study. This relatively low survival rate of our cases only reflects their poor access to quality diagnostic and treatment facilities.

Keywords: Squamous cell carcinoma of the head and neck - survival - treatment - tumor stage - Philippines

Asian Pac J Cancer Prev, **14 (8)**, 4769-4774

Introduction

Squamous cell carcinoma of the head and neck (SCCHN), a neoplasm that primarily develops in the nasal cavity, sinuses, lips, oral cavity, pharynx or larynx (Chaudhary et al., 2009), is the sixth most common cancer and the eighth leading cause of cancer death worldwide (Warnakulasuriya, 2009). An estimated 644,000 new cases of SCCHN are diagnosed annually around the globe, with two-thirds occurring in developing countries (Dobrossy, 2005; Kim et al., 2010).

Over the past decades, a steady increase in the incidence of oropharyngeal cancer especially in young males has been observed in Europe, United States, and Australia (Rosenquist, 2005; Reddy et al., 2010; Chaturvedi et al., 2011; Hocking et al., 2011; Brown et al., 2012; de Souza DL et al., 2012; Hertrampf et al., 2012). In contrast, the number of laryngeal carcinoma cases has dramatically decreased, probably as a result of reduced prevalence of cigarette and alcohol use (Sturgis and Cinciripini, 2007; Kim et al., 2010; Zhang and Marugame, 2010).

In the Philippines, a strong decrease in the incidence of oral cavity cancer among residents from the National Capital Region (NCR) or more commonly known as Metro Manila and the nearby Rizal province was observed during the period 1980-2002 (Laudico et al., 2010). Meanwhile, the incidence of head and neck cancer remained high among residents from Ilocos Norte, which is also popular for being the top tobacco-growing region of the country. The hospital-based cancer registry (unpublished) of the Mariano Marcos Memorial Hospital and Medical Center (MMMH-MC), a government-run hospital that caters to the health needs of patients predominantly from Ilocos Norte, has identified head and neck cancer as the second (23.71%) most common malignancy among its 1147 cases from January 2007 to February 2013.

*[1]Research Center for the Natural and Applied Sciences, [2]Department of Natural Sciences, College of Nursing, [3]Graduate School, [7]Department of Biological Sciences, College of Science, University of Santo Tomas, [6]Department of Clinical Pathology, University of Santo Tomas Hospital, Manila, [4]Department of ENT Head and Neck Surgery, [5]Department of Pathology, Mariano Marcos Memorial Hospital and Medical Center, Ilocos Norte, Philippines *For correspondence: pmalbano@yahoo.com, p.albano2013@gmail.com*

To our knowledge, this paper is the first to present the incidence and overall survival of SCCHN patients from Ilocos Norte, Philippines. It aims to associate the survival of said patients with epidemiologic and clinical factors such as age, gender, tumor site, TNM stage, and treatment received. It also discusses how the religious, socio-economic, and socio-cultural beliefs affect patient decision in the diagnosis, treatment and management of their SCCHN.

Materials and Methods

Records of 150 patients with histologically-confirmed squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx, and larynx at the MMMH-MC between January 2003 and April 2012 were retrospectively reviewed. The design, sampling, questionnaires, and other pertinent documents were approved by the research ethics review committee of MMMH-MC.

Retrieved information on patient demographics, tumor site, tumor grade, lymph node and distant metastasis, TNM (tumor, node, and metastatic) stage, treatment received, and vital status (whether living or dead at time of analysis, age at death, and date of death) were analysed. An independent pathologist performed a blinded review of the H and E slides to prevent inter-observer bias in tumor grading. TNM staging was based on the National Comprehensive Cancer Network Guidelines™ Version 2.2011. Treatment received was classified into surgery, radiotherapy, chemotherapy, a combination of 2 or more, or none at all. The Civil Registration Department of the National Statistics Office of the Philippines validated the vital status (as of October 31, 2012) of the cases. It is important to mention that since MMMH-MC currently has no cancer treatment facilities, patients were endorsed to other institutions, depending on their financial capabilities. Only patients who returned to MMMH for follow-up after treatment in other institutions were included in this study.

The Kaplan-Meier (K-M) product limit estimate of survival was used to estimate the survival rate. The significant difference between survival curves when grouped according to all specified explanatory variable was tested using the log-rank test of significance. Level of significance was set to 5%, with observed p values <0.05 considered significant. Pearson product moment of correlation was used to determine the association of survival with gender, tumor site and grade, tumor and node stages, and treatment received. Additionally, multi-regression analysis was performed to produce a model appropriate for estimating survival as influenced by the defined factors of this study. Statistical analysis was performed using SPSS v20.0.

Results

A total of 150 previously untreated patients with histologically-confirmed squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx, or larynx were included in this retrospective study. Upon termination of the study (October 31, 2012), only 80 (53.3%) were still living, as confirmed by the Civil Registration Department of the National Statistics Office of the Philippines. Age of cases at initial diagnosis ranged from 37 to 94 years, with median of 61.5.

Male predominance was evident with a 7:3 male to female ratio. Among males, 47, 8, 4, and 46 had tumor in the oral cavity, oropharynx, hypopharynx, and larynx, respectively. Only 29, 5, 2, and 9 of the females had cancer in the same sites, correspondingly. Using log rank statistics, survival of SCCHN cases grouped according to sex was measured. At 5% level of significance, survival rate of males was not statistically different from that of the females (Table 1). Thus, sex was not associated with survival (log rank=1.94; p value/α=0.16).

Tumor in the oral cavity was seen in 76 (50.7%) of the cases, hence, making it the most common tumor site. Oropharyngeal, hypopharyngeal, and laryngeal tumors were seen in 13 (8.67%), 6 (4%), and 55 (36.7%) cases, respectively. The difference in the survival rate between having tumor in the oral cavity and larynx (Table 2), irrespective of other factors, was not significant (log rank=0.02; p value/α=0.90).

As to tumor grade, only 1 case had poorly-differentiated tumor (G3). Well-differentiated (G1) and moderately-differentiated (G2) tumors were seen in 112 case (74.7%) and 37 (24.7%) cases, respectively. Tumor grade was not proven to be statistically associated with the survival of our cases (log rank=1.74; p value/α=0.42).

Of the 150 patients, 105 (70.0%) were already in their

Table 1. Estimated Cumulative Survival Rate of Male and Female SCCHN Cases*

Survival (in months)	Male	Female
12	86.1%	96.8%
24	69.6%	89.6%
60	34.9%	51.9%
106	2.4%	7.4%

*Using log rank statistics measure, survival rate between sexes was compared. At 5% level of significance, the difference was not proven to be statistically significant (log rank=1.937, p value/α=0.164)

Table 2. Mean Survival Time in Months Based on Tumor Site, Tumor and Node Stages, and Treatment Received

Factor for Survival	Mean*			
	Estimate	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
Tumor Site				
Oral cavity	51.4	4.86	41.9	61.0
Larynx	51.4	5.89	39.9	63.0
Overall	51.4	3.72	44.2	58.7
Tumor Stage				
Tis, T1, T2	35.0	5.91	23.4	46.6
T3, T4a, T4b	54.2	4.10	46.2	62.3
Overall	48.8	3.51	41.9	55.6
Node Stage				
NO and N1	58.0	29.0	29.0	50.0
N2a, N2b, and N2c	89.0	38.0	51.0	57.3
Overall	147.0	67.0	80.0	54.4
Treatment				
No treatment received	54.2	5.29	43.9	64.6
With treatment received	44.5	4.68	35.3	53.7
Overall	48.8	3.51	41.9	55.6

*Estimation is limited to the largest survival time if it is censored

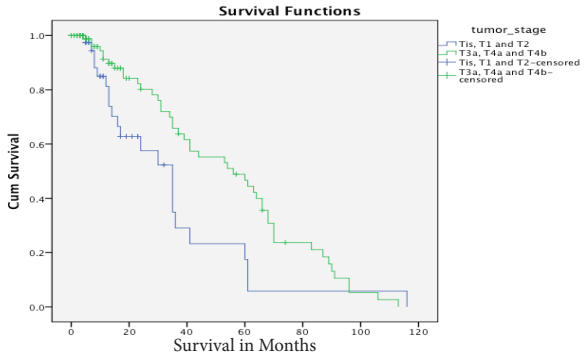

Figure 1. Comparison of Survival Rate of Tis, T1, and T2 with T3, T4a, and T4b (log rank=5.337; p value/α=0.021)

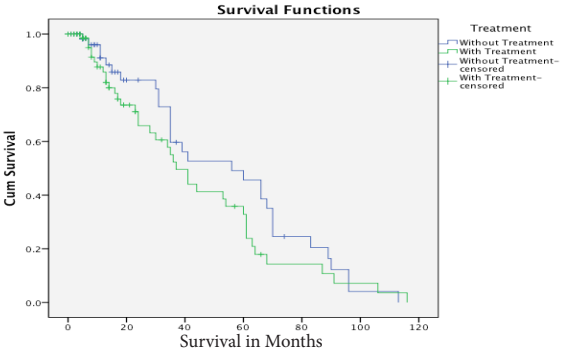

Figure 2. Comparison of the Survival Rate of Cases who have Received Treatment (Surgery Alone, Surgery with Radiation Therapy, or Radiation Therapy Alone) with Cases without having Received any Treatment (log rank=1.65, p value/α=0.20)

Table 3. Estimated Cumulative Survival Rate of SCCHN Patients

Time (months)	Estimated Cumulative Survival Rate
12	88.3%
24	73.6%
36	56.1%
60	39.3%
90	10.9%
106	3.6%
113	1.8%

advanced stages (T3, T4a, or T4b) at initial presentation: 30 with T3; 69 with T4a; and 6 with T4b stage. Tis, T1, and T2 were seen in 1, 13, and 31 cases, respectively. When comparing the survival rate of early stage with late stage cases (Table 2, Figure 1), the difference was found to be statistically significant (log rank=5.33; p value/α=0.02). Ironically, the late stage cases had better survival than the early stage ones.

No regional lymph node involvement (N0) was seen in 45 (30.0%) of the cases. Nodal stages N1, N2a, N2b, and N2c were found in 15 (10.0%), 22 (14.7%), 39 (26.0%), and 28 (18.7%) patients, respectively. Only 1 (0.67%) had N3 during initial diagnosis. When survival rate of N0 and N1 cases was compared with N2a, N2b, and N2c (Table 2), difference was not proven statistically significant (log rank=0.07; p value/α=0.80). Only 12 (8.00%) had distant metastasis, mostly in the lungs. K-M survival analysis was not performed since the number of cases having distant metastasis was not sufficient for comparison with those without.

Among our SCCHN patients, 72 (48.0%) were not able to receive treatment of any kind. Among the 45 patients initially diagnosed as Tis, T1, or T2 stage, 33 underwent surgery with radiotherapy; 4 with radiotherapy alone; 3 with surgery alone; and 5 did not undergo any treatment. Among those with advanced stage (T3, T4, or T4b) at presentation, 67 did not receive any treatment; 3 with surgery alone; 1 with radiotherapy alone; and 34 with surgery followed by radiotherapy. At 5% level of significance, difference in the survival rate (Table 2) between cases that have and have not received treatment (surgery, radiotherapy, or combination of both) was not proven to be statistically significant (log rank=1.65; p value/α=0.20) (Figure 2).

The overall mean survival was 49.25 months. As time progressed, survival rate diminished from 88.3% during the first year to 1.80% by end of the study (Table 3).

Discussion

To date, the only available published data on cancer incidence and survival among Filipino patients were based from two population-based cancer registries: the Philippine Cancer Society-Manila Cancer Registry (PCS-MCR) and Department of Health-Rizal Cancer Registry (DOH-RCR). Said registries included only cases from the National Capital Region (NCR) or more commonly known as Metro Manila and the nearby Rizal province, accounting for merely 7% of the Philippine population (Laudico et al., 2010; Medina et al., 2010; Redaniel et al., 2010; 2011). Based on the above reports, the incidence of oral cavity cancer decreased strongly during the period 1980-2002 among Metro Manila and Rizal residents (Laudico et al., 2010).

Meanwhile, the hospital-based cancer registry of the MMMH-MC (unpublished) has identified head and neck cancer as the second (23.7%) most common malignancy among its 1147 cases from January 2007 to February 2013; followed by colon/rectum/stomach (14.2%), ovary/uterus (8.89%), and lungs (3.40%), respectively. Breast cancer (30.8%) ranked highest in incidence among its cases. MMMH-MC is a 200-bed capacity government-run hospital that caters to the health needs of patients, majority of whom are residents of Ilocos Norte (population as of May 2010 was 568,017) (National Statistics Office, 2010). Of the 150 cases included in the study, 119 (79.0%) were residents of Ilocos Norte and 31 (20.7%) were from nearby towns where medical facilities and specialists may not be available.

The age of our cases was similar to what has been observed in other populations; i.e. incidence increased with age (Dobrossy, 2005; Warnakulasuriya, 2009). Studies have associated survival with patient's age, being better if diagnosed at age 40 or younger (Pruegsanusak et al., 2012; Udeabor et al., 2012; Listl et al., 2013). A K-M survival analysis of our samples based on age, however, could not be assessed since SPSS motioned all cases as censored.

Similar to what has been observed in other countries, our SCCHN cases were mostly men, probably due to their longer term and heavier indulgence in tobacco and alcohol (Warnakulasuriya, 2009). Said behaviours have been greatly identified as major risk factors in the development of cancer in these anatomical regions (Warnakulasuriya, 2009). Our findings agreed with the United States-based matched-pair analysis wherein sex was not associated with improved survival (Roberts et al., 2010). In Europe, however, women were found to have higher relative survival rates than men (Dobrossy, 2005; Listl et al., 2013).

Majority of our cases had tumors in their oral cavity. It has been estimated that about 275,000 oral cavity cancers occur annually worldwide, with two-thirds coming from developing countries (Warnakulasuriya, 2009). Chen et al. (2009) proved a negative correlation between gross domestic product (GDP) per capita and rate of oral cavity cancer, thus associating the latter with low economic, social, and educational status. Laryngeal tumor ranked second among our cases in terms of frequency. We did not find any association between survival and having tumor in the oral cavity or larynx. The incidence of oropharyngeal squamous cell carcinoma among our cases was relatively low compared to the steady increase especially in younger populations seen in more developed nations (Marklund and Hammarstedt, 2011; Johnson-Obaseki et al., 2012).

Tumor grade and tumor stage are known to be associated with survival, i.e. decreased as grade or stage advanced (Warnakulasuriya, 2009; Laudico et al., 2010; Redaniel et al., 2010; Listl et al., 2013). Our analysis shows that cases with Tis, T1, or T2 stage at initial presentation had lower survival rates than the T3, T4a and T4b. This may seem inconsistent with the fact that the clinical stage is the strongest prognostic factor for survival (Noguti et al., 2012; Pruegsanusak et al., 2012). However, a number of our cases diagnosed with early stage SCCHN had delayed treatment, mainly due to financial reasons. MMMH-MC as a government hospital offered subsidized services but was limited due to insufficient public funds allocated to health care (Laudico et al., 2010; Redaniel et al., 2010). Lack of education about the advances in the management and treatment of cancer also resulted in our patients' fatalistic attitude towards their condition, treating it like a "death sentence". Delay in treatment especially of the T1, T2, and T3 cases was also due to consultation with other clinicians for second to third opinion followed by a long period of denial and bargaining. Based on our experience, several patients would only come back for their planned treatment when their condition was worst and tumor stage has probably advanced. Moreover, some patients resorted to complementary and alternative medicine in the forms of herbal medicine and religious or faith healing, a practice suggestive of their socio-cultural heritage (Maskarinec et al., 2000).

A great majority (70.7%) of our cases were already in their advanced stage (T3, T4a, and T4b) at presentation, an observation similar to that of Thailand (Pruegsanusak et al., 2012). Since most of the signs and symptoms associated with SCCHN were non-specific and could be mistaken for common ailments (Kademani, 2007), patients opted for self-medication. This delay in diagnosis was also a reflection of how diagnostic and treatment facilities in the Philippines, while accessible, could be costly for an average Filipino cancer patient (Redaniel et al., 2009).

Surgery with radiotherapy is the most common practice and has been proven to improve locoregional control and overall survival of T1 or T2 stage SCCHN patients. In our study, 32 (74.4%) of the 43 T1 or T2 cases were able to undergo this recommended treatment. While chemotherapy is recommended for T3, T4a, and T4b stages (Lybak et al., 2011), none of our cases was able to avail said treatment, again due to financial constraints.

Our analysis shows that the survival rate of our patients who underwent treatment (surgery, radiotherapy, or combination of both) was not significantly different with that of patients who did not undergo treatment of any kind. Although a high percentage (74.4%) of our T1 and T2 cases was able to undergo surgery with radiotherapy, treatment was usually not only delayed but intermittent or pre-terminated, depending on the availability of funds. Health insurance of our low-income cases was not sufficient for treatment in private institutes where more modern and better radiation treatment facilities were available (Tatsuzaki and Levin, 2001). Like in other low and middle income countries where radiotherapy services were restricted to a few centers (Barton et al., 2006), MMMH-MC currently has no radiotherapy services. Thus, the cost of transportation and accommodation in areas where machines were available added to our patients' financial burden. Some also resorted to religious or faith healing and herbal medicine, the consequence of which was uncertain.

Among our cases, 70.0% had already regional lymph node involvement at presentation, proving further their late diagnosis. Only about 25-40% of patients with lymph node metastasis are said to achieve 5-year survival (Mizumachi et al., 2012). Incidence of distant metastasis in SCCHN is usually relatively low (Dragovic et al., 2013). Among our cases, only 12.0% had distant metastasis, mostly in the lungs.

It is important to note that our study made generalizations on hospital- and not population-based data. Thus, it does not make any representation of the totality of SCCHN patients from the Philippines. Also, a weakness of our study was that we failed to present data on the epidemiologic risks associated with SCCHN development. Thus, a prospective cohort study was recently initiated to investigate on SCCHN patient's tobacco exposure, alcohol intake, betel nut chewing, and even sexual practices. Filipinos are identified reverse smokers (cigars with lit end inside the mouth) and betel nut chewers, habits which are particularly popular among rural folks of lower socio-economic class and proven to increase risk of developing SCCHN (Ngelangel and Wang, 2002; Laudico et al., 2010; Wen et al., 2010). Molecular analyses will also be done on our tumor samples to verify if the human papillomavirus (HPV) plays a role in their development. Epidemiologic and molecular data have demonstrated HPV to promote head and neck tumorigenesis (Holzinger et al., 2012) and have associated it with changes in sexual practices (D'Souza et al., 2007) .

Survival estimates of SCCHN patients in the Ilocos

region are low because of poor access to diagnostic and treatment facilities (Redaniel et al., 2009; 2011). The Philippine Health Insurance Corporation, moreover, does not cover the cost of head and neck cancer treatment based on the premise that it is lifestyle-associated (Philippine Health Insurance Corporation, 2012). Hence, the immediate need to educate high-risk individuals about the primary prevention and early detection of this disease. The Philippines has been identified as among the world's nations with high tobacco smoking prevalence but weak control programmes (Alechnowicz and Chapman, 2004). And the Ilocos region where our SCCHN cases originate is the top tobacco producer in the country (Philippine Bureau of Agricultural Statistics, 2006-2013). Moreover, since patient decision as regards his treatment is influenced by his religious and socio-cultural beliefs, it is also significant to educate SCCHN patients not to have fatalistic attitude towards their condition as not to lose belief that they would be cured if diagnosed early and given quality treatment.

Acknowledgements

Our thanks go out to the: University of Santo Tomas Research Center for the Natural and Applied Sciences, University of Santo Tomas College of Nursing, Mariano Marcos Memorial Hospital and Medical Center (Department of Pathology and Department of ENT Head and Neck Surgery), Civil Registration Department of the National Statistics Office, Anna Karenina Rosana for the help in the statistical analysis and Dr. Michael Pawlita of the German Cancer Research Center (DKFZ), Heidelberg, Germany for his comments and suggestions. Pia Marie Albano is being supported by the Department of Science and Technology-Science Education Institute and the Commission on Higher Education thru its PhD Sandwich Program.

References

Alechnowicz K, Chapman S (2004). The Philippine tobacco industry: the strongest tobacco lobby in Asia. *Tob Control*, **13**, 71-8.

Barton MB, Frommer M, Shafiq J (2006). Role of radiotherapy in cancer control in low-income and middle-income countries. *Lancet Oncol*, **10**, 797.

Brown LM, Check DP, Devesa SS (2012). Oral cavity and pharynx cancer incidence trends by subsite in the United States: changing gender patterns. *J Oncol*, **2012**, 649498.

Chaturvedi AK, Engels EA, Pfeiffer RM, et al (2011). Human papillomavirus and rising oropharyngeal cancer incidence in the United States. *J Clin Oncol*, **32**, 4294-301.

Chaudhary AK, Singh M, Sundaram S, Mehrotra R (2009). Role of human papillomavirus and its detection in potentially malignant and malignant head and neck lesions: updated review. *Head Neck Oncol*, **1**, 22.

Chen DT, Chou YF, Wu HP, et al (2009). Income and the incidence of oral cavity cancer: cross-national study. *J Otolaryngol Head Neck Surg*, **2**, 208-11.

de Souza DL, de Camargo Cancela M, Perez MM, Curado MP (2012). Trends in the incidence of oral cavity and oropharyngeal cancers in Spain. *Head Neck*, **5,** 649-54.

Dobrossy L (2005). Epidemiology of head and neck cancer: magnitude of the problem. *Cancer Metastasis Rev*, **1**, 9-17.

Dragovic AF, Caudell JJ, Spencer SA (2013). Locoregional failure and the risk of distant metastasis after modern radiotherapy for head and neck cancer. *Head Neck*, **35**, 381-7.

D'Souza G, Kreimer AR, Viscidi R, et al (2007). Case-control study of human papillomavirus and oropharyngeal cancer. *N Engl J Med*, **356**, 1944-56.

Hertrampf K, Wiltfang J, Katalinic A, et al (2012). Recent trends in incidence and mortality of oral and pharyngeal cancer in Schleswig-Holstein in Northern Germany. *Community Dent Health*, **4**, 268-73.

Hocking JS, Stein A, Conway EL, et al (2011). Head and neck cancer in Australia between 1982 and 2005 show increasing incidence of potentially HPV-associated oropharyngeal cancers. *Br J Cancer*, **5**, 886-91.

Holzinger D, Schmitt M, Dyckhoff G, et al (2012). Viral RNA patterns and high viral load reliably define oropharynx carcinomas with active HPV16 involvement. *Cancer Res*, **19**, 4993-003.

Johnson-Obaseki S, McDonald JT, Corsten M, Rourke R (2012). Head and neck cancer in Canada: trends 1992 to 2007. *Otolaryngol Head Neck Surg*, **1**, 74-8.

Kademani D (2007). Oral cancer. *Mayo Clin Proc*, **7**, 878-87.

Kim L, King T, Agulnik M (2010). Head and neck cancer: changing epidemiology and public health implications. *Oncol*, **10**, 924.

Laudico AV, Mirasol-Lumague MR, Mapua CA, et al (2010). Cancer incidence and survival in metro manila and rizal province, Philippines. *Jpn J Clin Oncol*, **7**, 603-12.

Listl S, Jansen L, Stenzinger A, et al (2013). Survival of patients with oral cavity cancer in Germany. *PLoS One*, **1**, 53415.

Lybak S, Liavaag PG, Monge OR, Olofsson J (2011). Surgery and postoperative radiotherapy a valid treatment for advanced oropharyngeal carcinoma. *Eur Arch Otorhinolaryngol*, **3**, 449-56.

Marklund L, Hammarstedt L (2011). Impact of HPV in oropharyngeal cancer. *J Oncol*, **2011**, 509036.

Maskarinec G, Shumay DM, Kakai H, Gotay CC (2000). Ethnic differences in complementary and alternative medicine use among cancer patients. *J Altern Complement Med*, **6**, 531-8.

Medina VM, Laudico A, Mirasol-Lumague MR, Brenner H, Redaniel MT (2012). Cumulative incidence trends of selected cancer sites in a Philippine population from 1983 to 2002: a joinpoint analysis. *Bri J Cancer*, **9**, 1411-4

Mizumachi T, Kano S, Sakashita T, et al (2012). Improved survival of Japanese patients with human papillomavirus-positive oropharyngeal squamous cell carcinoma. *Int J Clin Oncol,* [Epub ahead of print].

National Statistics Office website. Retrieved 12 Mar 2013 http://www.census.gov.ph/sites/default/files/attachments/hsd/pressrelease/Ilocos.pdf.

Ngelangel CA, Wang EH (2002). Cancer and the Philippine Cancer Control Program. *Jpn J Clin Oncol*, **32**, 52-61.

Noguti J, De Moura CF, De Jesus GP, et al (2012). Metastasis from oral cancer: an overview. *Cancer Genomics Proteomics*, **5**, 329-35.

Philippine Bureau of Agricultural Statistics website. Retrieved 8 Mar 2013. http://countrystat.bas.gov.ph/?cont=16 and r=1.

Philippine Health Insurance Corporation website. Retrieved 8 Mar 2013. http://www.philhealth.gov.ph/circulars/2012/circ30_2012.pdf.

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*, **3**, 885-90.

Redaniel MT, Laudico A, Mirasol-Lumague MR, et al (2009). Cancer survival discrepancies in developed and developing countries: comparisons between the Philippines and the

United States. *Bri J Cancer*, **5**, 858-62.
Redaniel MT, Laudico A, Mirasol-Lumague MR, Gondos A, Brenner H (2011). Cancer survival differences between European countries and an urban population from the Philippines. *Eur J Public Health*, **2**, 221-8.
Reddy VM, Cundall-Curry D, Bridger MW (2010). Trends in the incidence rates of tonsil and base of tongue cancer in England, 1985-2006. *Ann R Coll Surg Engl*, **8**, 655-9.
Roberts JC, Li G, Reitzel LR, Wei Q, Sturgis EM (2010). No evidence of sex-related survival disparities among head and neck cancer patients receiving similar multidisciplinary care: a matched-pair analysis. *Clin Cancer Res*, **20**, 5019-27.
Rosenquist K (2005). Risk factors in oral and oropharyngeal squamous cell carcinoma: a population-based case-control study in southern Sweden. *Swed Dent J*, **179**, 1-66.
Sturgis EM, Cinciripini PM (2007). Trends in head and neck cancer incidence in relation to smoking prevalence: an emerging epidemic of HPV associated cancers? *Cancer*, **110**, 1429-35.
Tatsuzaki H, Levin CV (2001). Quantitative status of resources for radiation therapy in Asia and Pacific region. *Radiother Oncol*, **1**, 81-9.
Udeabor SE, Rana M, Wegener G, Gellrich NC, Eckardt AM (2012). Squamous cell carcinoma of the oral cavity and the oropharynx in patients less than 40 years of age: a 20-year analysis. *Head Neck Oncol*, **4**, 28.
Warnakulasuriya S (2009). Global epidemiology of oral and oropharyngeal cancer. *Oral Oncol*, **4**, 309-16.
Wen CP, Tsai MK, Chung WS, et al (2010). Cancer risks from betel quid chewing beyond oral cancer: a multiple-site carcinogen when acting with smoking. *Cancer Causes Control*, **9**, 1427.
Zhang M, Marugame T (2010). Comparison of time trends in larynx cancer mortality (1990-2006) between countries based on the WHO mortality database. *Jpn J Clin Oncol*, **8**, 820-1.