

RESEARCH ARTICLE

Profile and Survival of Tongue Cancer Patients in "Dharmais" Cancer Hospital, Jakarta

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Abstract

Background: Tongue cancer is still a major health problem in most developing countries around the world. Statistics shown the number of tongue cancers, especially in early age, to be increasing, with poor survival. **Objective:** To analyze the characteristic profile of tongue cancer patients in Indonesia as well as the survival rate. **Materials and Methods:** A cross sectional study was conducted in Dharmais National Cancer Hospital by collecting general, clinical, and survival data of tongue cancer patients from medical records for January 2009 to April 2012. **Results:** Tongue cancer incidence increased year by year. The average age of tongue cancer patients was 47.5 years, and males predominated, accounting for 64.5% of cases. Most patients presented at an advanced stage (69.6%). The histopathology type was squamous cell carcinoma in the vast majority (96.8%). The therapies applied were surgery (45.6%), radiation (63.6%) and chemotherapy (57.6%). The survival rate after one year is 60.6% and after two years was 12.1%. In addition, median survival of tongue cancer patients was 20 months (95% confidence interval 9.07-30.9). The significant factor affecting survival was size of tumor with a hazard ratio of 3.18 (95% CI, 1.02-9.93; p 0.046) for largest versus smallest categories. **Conclusions:** In each year, the number of tongue cancer incidents in Indonesia is increasing. The age of tongue cancer patients in Indonesia is younger compared to other countries. Moreover, the survival rates are not high.

Keywords: Tongue cancer - patient characteristics - survival - Indonesia

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Introduction

Oral cancer located in the mouth, tongue or oropharynx is a serious health problem in the world (Rana et al., 2011). Oral cancer is at the 9th position in the world and 8th in developing countries with the case numbers respectively 170,900 and 107,700 (Jemal et al., 2011). Tongue cancer is one of the most common oral cancers with various incidents in some countries, India, for instance, the incidence rate is 6.5 per 100,000 per year, whereas France's incidence rate is 8 per 100,000 per year (Moore, et al., 2000). In US, it has been estimated that 13,590 patients (9,900 males and 3,690 females) will be diagnosed and 2,070 will die because of tongue cancer in 2013 (Howlader et al., 2012). Meanwhile in Asia, especially in South Asia and South East Asia, the incident rate of oral cancer is quite high (Wamakulasuriya, 2009). According to the data from Dharmais National Cancer Hospital (DNCH), national cancer referral center, there are 163 cases of tongue cancer from 2003 to 2007 in Indonesia. The number has increased 52.8% from the period 1993-1997 (Sinuraya, 2012a; 2012b).

Several risk factors of oral cancer are coming from smoking habit and alcohol consumption (Dahlstrom et al., 2008; Rao et al., 2013). Data stated that for the

past 30 years, the incidents of mouth cancer in western countries have been decreasing, due to higher awareness towards the danger of smoking habit (Reddy et al., 2010). Nevertheless, it is a different case compare to tongue cancer. In England, the number of tongue cancer incidents is increasing 6.5-6.7% per year since 1985 (Reddy et al., 2010). Generally, tongue cancer strikes old males, however, recent research found that it has started to attack younger age especially females. Patel et al. also analyzed that there are increment of tongue cancer incidents on young white females aged 18 to 44 years old (Patel et al., 2011). Furthermore, American Cancer Society (ACS) reported that oral cancer related with infection of human papilloma virus (HPV), such as oropharynx cancer, tonsil and tongue base, is increasing in young adult patients in US and some other countries (Jemal et al., 2011), like Iran (Magi et al., 2012) and India (Krishnamurthy and Ramshankar, 2013).

Modalities therapy of tongue cancer is the same with other cancers, which consists of surgery, chemotherapy, and radiotherapy. In early stage, surgery therapy is the main treatment option, and continues by chemotherapy or radiotherapy. Meanwhile, for advanced stage patients, chemotherapy is the main treatment, and continue by radiotherapy (Shim et al., 2010). Even though various

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modalities have been developed rapidly, the prognosis of tongue cancer is still very bad. A study in Colorado showed that squamous cell carcinoma of tongue had the worst prognosis compared to the same carcinoma in other parts of oral cavity (Rusthoven et al., 2007).

There is no research of epidemiology and survival of tongue cancer in Indonesia prior to this. Therefore, this research's objective is to identify the characteristics and survival rate of tongue cancer patients that came to DNCH as well as the affecting factors

Materials and Methods

Cross sectional study used in this research, with patients who came for treatment to DNCH in the year 2009 to February 2012 as the target population. Data are taken from tongue cancer patients who received therapy in DNCH through patients' medical records, which consist of general data (age, sex, weight, height, body mass index/BMI and symptoms), clinical data (diagnosis, stage, histopathology, and therapy) and survival data. The survival data that were not available in the medical records are collected through phone interview. Data of survival patients are evaluated until April 2013.

The data is analyzed using SPSS for windows version 19. Descriptive analysis is conducted to get patients' characteristics consisting of age, sex, body mass index (BMI), symptoms, tumor size (T), the involvement of lymph node (N), metastasis (M), stage, histopathology type, therapy, and survival. For survival analysis, the variable of the study are the influence of age (<40 years old and >40 years old), stage (early and advanced), and tumor size (small and big). The tongue cancer survival is analyzed using Kaplan Meier and the significance by Cox Regression test. The test will be significant if p<0.05.

Dead-subject incidents are categorized into event category, and alive or loss-follow-up-subject incidents into censored category. The duration of survival is counted from the diagnose date to the last follow up based on medical records or per call.

Results

Research found that 62 patients positively diagnose with tongue cancer came to DNCH since 2009 to April 2012. However, only 36 out of 62 patients could fulfill the inclusion criteria, and only 33 patients with sufficient data that could be participate in the study.

There were 5 patients in 2009, 8 patient in 2010, 16 patients in 2011, and 4 patients in 2012 (until April). The general characteristics of tongue cancer patients are shown in Table 1 below. The average age of the patients is 47.5 years old with standard deviations of 13.93; the youngest is 25 years old and the oldest is 70 years old. There are 66.6% of tongue cancer patients in productive age (21 to 50 years old). Most of the tongue cancer patients are males (63.4%). The average of body mass index (BMI) is 21.25 kg/m² with standard deviations of 5.11, and the lowest BMI is 14.1 kg/m². More than half of the tongue cancer patients complained the pain in the tongue, followed by hard intake and other complaints like fatigue, oral

bleeding, mass on the tongue, and stomatitis.

Table 2 below shows the clinical characteristics of tongue cancer patients. More than half of the patients (54.3%) came with tumor size T3 or bigger. The most often involvement of lymph node is N1 (39.4%), and only one out of 33 patients who had distant metastasis (3.1%) which is metastasis to the lungs. Almost 70% of the patients came in advanced-stage conditions, which are in stage 3 and 4. From the data collection of DNCH, the histology type of squamous cell carcinoma is found in 25 patients (75.7%). Some patients did not have the information about the histopathology type as their main purpose to come to DNCH only for radiotherapy, not diagnosed at DNCH.

Surgery therapy was given to 15 patients (45.6%) and mostly to stage-II cancer. Radiotherapy was given to 21 patients (63.6%). Other therapy alternative is chemotherapy. There are few types of chemotherapy that can be used as the tongue cancer therapy preference. At

Table 1. General Characteristics of Tongue Cancer Patients

General Characteristics		Frequency (%)
Age	21-30	3 (9%)
	31-40	12 (36.4%)
	41-50	7 (21.2%)
	51-60	6 (18.2%)
	>61	5 (15.1%)
Sex	Male	21 (63.4%)
	Female	12 (36.6%)
Body Mass Index	Underweight (<18.5)	5 (15.2%)
	Normal (18.5-22.9)	11 (33.3%)
	Overweight (23-24.9)	0 (0%)
	Obese I (25-29.9)	4 (12.1%)
	Obese II (>30)	2 (6.1%)
	No Data	11 (33.3%)
Patients' complaints	Pain on tongue	19 (57.6%)
	Hard intake	12 (36.4%)
	Others	10 (30.3%)
	No Data	3 (9.1%)

Table 2. Clinical Characteristics of Tongue Cancer Patients

Clinical Characteristics		Frequency (%)
Tumor size (T)	T1	4 (12.1%)
	T2	10 (30.3%)
	T3	5 (15.2%)
	T4	14 (42.4%)
KGB involvement (N)	N0	10 (30.3%)
	N1	14 (42.4%)
	N2	7 (21.2%)
Metastasis (M)	N3	2 (6.1%)
	M0	32 (96.9%)
	M1	1 (3.1%)
Stage	1	4 (12.1%)
	2	6 (18.2%)
	3	8 (24.2%)
	4	15 (45.4%)
Histopathology types	Squamous cell carcinoma	25 (75.7%)
	No data	9 (24.3%)
Therapy types	Surgery only	5 (15.2%)
	Surgery+Radiation	5 (15.2%)
	Surgery+chemotherapy+radiation	5 (15.2%)
	Chemotherapy+Radiation	7 (21.2%)
	Radiation only	4 (12.1%)
	Chemotherapy only	7 (21.2%)

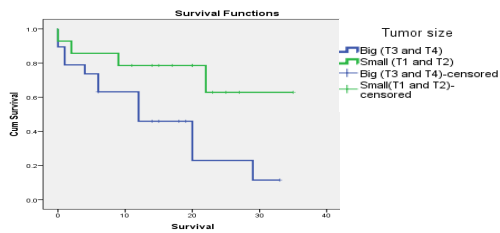


Figure 1. The Graphic of Kaplan-Meier with Hazard Ratio and Survival Comparison of p between Subjects and Classifications of Small and Big Size of Tumor

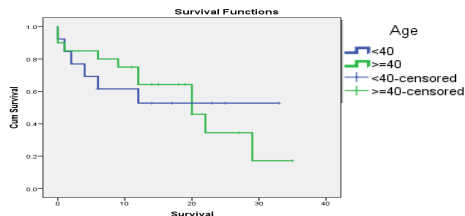


Figure 2. The Graphic of Kaplan-Meier Subject with Age Classifications

DNCH, chemotherapy was given to 19 patients (57.6%) and some patients received combined therapy. Nearly all regimen of given chemotherapy is based on platinum, and only 1 patient received palliative chemotherapy. The most often combination is platinum with 5-fluorouracil (5-FU)-to 11 patients (57.9%).

Based on followed up survival, one-year survival is found 66.7% and two-year is 12.1%. There are 12 patients reported died in the period of a year and 28 patients died in two years after the patient's first visit to DNCH. The median survival of tongue cancer patient at DNCH is 20 months (95%CI 9.07-30.93). Bivariate analysis that shows significance is tumor size: it is found that subjects with big size of tumor (T3 and T4) 3.18 times higher risk of death than subjects with small size of tumor (T1 and T2), with the average of survival big size tumor is 14.73 months and small size tumor is 26.24 months. Even though the stage did not show statistically significant result ($p=0.08$), it is found that the average of advanced stage survival is shorter (16.02 months) than early stage (26.3 months).

Albeit age does not show significant influence towards survival ($p=0.91$), it is shown in Figure 2 below that there is a difference of survival in age group below 40 years and 40 years and above in the 20th month. In the interval 0 to 20 months, subjects with the age 40 and above have better chance to survive than subjects below 40 years old. Yet when it passes 20 months, the survival of subjects with the age 40 and above gets worse compared to subjects below 40 years old.

Discussion

Tongue cancer is one of major health problems in the world, including in Indonesia. This research has discovered that there is incremental number of patients every year, with 5 patients in 2009, 8 patients in 2010, 16 patients in 2011, and 4 patients in the first four month of 2012. The data collected by DNCH cancer registration also describe the similar: the case had been increased more than 50% from the period of 1993 to 1997 and 2003 to

2007 (Sinuraya, 2012a; 2012b). This result is comparable with other researches in other countries such as in England (Reddy et al., 2010), United States (Howlader et al., 2012), and Scandinavia (Annertz et al., 2007).

DNCH cancer reported the registration from 2003-2007, which is 63.8% of tongue cancer was found in the age below 50, which could falls into young category (Sinuraya, 2012a). On the contrary, global data showed that tongue cancer is often found in the age above 50 years old (Wamakulasuriya, 2009). Data from American Cancer Society (ACS) in United States from 2006 to 2010 claimed that the median age of tongue cancer is 61 years old and only 27.7% in the age below 55 (Howlader et al., 2012). Nevertheless, it is reported that tongue cancer incidents on young age have a tendency to increase. Shiboski (2005) studied the squamous cell carcinoma of the tongue and found the increase in the period age of 20-44 years old. Similarly, Patel (2011) discovered that there is an increase of incidents in the age 18 to 44 years old of white skin females.

Most tongue cancer patients are males (63.4%), comparable with other studies (Lam et al., 2006; Wamakulasuriya, 2009; Saba et al., 2011; Howlader et al., 2012). It is possible as continuous exposure of risk factors on males are higher than on females. However, this does not mean that an increase of tongue cancer on females cannot happen for they start to expose with risk factors alike with males, which are cigarettes and alcohol.

Nearly 70% of the all cancer patients who came to DNCH are in advanced stage conditions (stage 3 or 4) (Sinuraya, 2012a). Similar with tongue cancer, where most of the patients already have tumor size T3 or bigger and reached advanced stage when they came to DNCH. Generally, patients will seek medical help when tumor size is already big or disturbing. This is described in most complaints of the patients, which are pain in the tongue (57.6%), followed by difficulty of food intake (36.4%) that makes the patients seek for help from a doctor. This discovery shows that people awareness about tongue cancer is still limited because most of them consider early lesion of cancer like stomatitis is not dangerous. Besides that, many people still prefer alternative medicine that just worsens the condition and prognosis of the patient.

Therapies for tongue and other cancer are alike, which consist with surgery, radiotherapy, and chemotherapy. Surgery therapy is done mostly to early stage tongue cancer cases since the more aggressive therapy in the early stadium, the higher survival of the patient is. A study in Hannover found that there is an increase of five-year survival which is 54.5% on patients who received surgery, compared to 13.7% without the surgery. This is possibly caused by 83.5% patients had tumor size T1 and T2 (Kokemueller et al., 2011). At DNCH, surgery therapy was done to 45.6% patients because more than half of the patients were already in stage 3 and 4 that were non-operable. Other study found that tongue cancer is easier treated by radiotherapy (Yamazaki et al., 2010), whilst Weijers (2011) added that the combination of surgery and radiation therapy could reduce local recurrence to nearly 0% (Weijers et al., 2011). At DNCH, radiotherapy was done to 19 patients (63.6%). Radiation

with chemosensitization was only given to 2 patients due to huge side effects. Tongue cancer patients usually have stomatitis, thus giving radiation with chemosensitization would only worsen the stomatitis.

Platinum-based chemotherapy is mostly chosen at DNCH. Study in Japan found that response rate 83.3% on stage 3 and 4 patients by using docetaxel, cisplatin, dan 5-fluorouracil chemotherapy (Shibuya et al., 2004). Meanwhile, the use of Cetuximab as a target therapy is still limited due to its high price. Weekly chemotherapy was given to patients with weak general conditions and only in the palliative condition.

A study in Brazil found that a year survival for an early-stage tongue cancer patient who received a surgery is 62% (Biazevic et al., 2010). That is in line with the finding of this research which is 66.7% for a year survival. However, two-year survival of this research's subjects is very low, which is 12.1%. Furthermore, the median survival of tongue cancer patient in all stages is 20 months. This result is less than that what reported in a Singaporean study: median survival of tongue cancer patient in all stages is 36.9 months (CI 95% 5.6 – 68.2) (Yip et al., 2010). This probability due to two thirds of the subjects had advanced stage when they came to DNCH. Another reason is there are 4 patients came firstly in the year of 2012, as the result follow up survival cannot be done for two years.

Stage is one of the prognostic factors to tongue cancer patients' survival. This research found that advanced stage has 10 months shorter survival than early stage, even though it is not significant in the statistics. On the other hand, tumor size is one of the components to decide the stage; showing significant linkages to survival of tongue cancer patients. This is in line with the study reported by Davidson (2001).

The effect of age towards survival is still controversial. This research has not found any significant difference between young age group (below 40 years old) and older group (40 and above), but if it is analyzed further, the young group has better survival. Patel et al. reported that there is no difference in survival between young age patients (18-44 years old) of squamous tongue cancer and older (above 44 years old) patients (Patel et al., 2011). This also strengthens by Siegelmann-Danieli (1998) who found that the prognosis of a patient is not decided by the age when he/she diagnosed. Yip (2010) also found that younger patients do not show any worse pathological characteristics and worse clinical outcomes than older patients. However, there is a study found that the survival of tongue cancer is worse in the young age. Sarkaria (1994) reported that five out of six patients in Wisconsin University Hospital who had squamous carcinoma (SCC) tongue in the age below 40 years received therapy from 1971 to 1991, and those who received the therapy had locoregional recurrence although it was in the early stage. In contrast, Davidson (2001) found that an increase in age would predict bad prognosis; an age increase of 10 years would increase the death risk of 18%.

The weakness of this research is the data collection that was done retrospectively from the medical records and there are some unrecorded data there. Besides, there are some patients who had not come to DNCH anymore

so they should be called to get the survival data. We took the newest data of tongue cancer, which is the latest two years so that we could minimize the probability patients could not be contacted. Also, there are four patients who came in 2012 so that the follow up cannot reach two years, and might affect the number of 2-year survival.

In conclusion, tongue cancer is a growing major health problem in Indonesia. This cancer deserved to be taken into further attention because of the increasing incidence in young patients, low sensitivity towards cancer therapies (chemotherapy and radiotherapy) and the low rate of survival. Tongue cancer incidents in this research show relatively young age compared to the age in other countries. Besides, the death rates of tongue cancer are also relatively high, in which the survival rate of tongue cancer in a year is 60.6% and the survival rates of tongue cancer in two years is only 12.1%, also the survival median is 20 months. Tumor size and the age of patients are found to have influences towards the survival of tongue cancer patients. Therefore, further steps need to be taken; such as prevention and early detection especially for people who have high-risk factors towards tongue cancer like people with the habits of smoking, drinking alcohol and HPV infections.

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