

6. DISCUSSION.

The present study represents a retrospective review of a small patient cohort of all cases of oral and oro pharyngeal tongue cancer recorded in University Malaya Medical Centre and Department of Oral and Maxillofacial Surgery , Dental Faculty, University Malaya, Kuala Lumpur. There were total 30 cases of squamous cell carcinoma of tongue out of 48 which recorded between January 1992 to December 2005 included in this study. From the number of patients, it was indicated that not many of them with the respective disease turn up to this centre for treatment.

More than 37% (n=18) of sample had to be excluded due to several reasons; one of the main reason was the uncompleted documentation of the factors related to disease. In most of patients' folder, no proper documentation about the size, neck disease, missing histological records and clinical staging of the disease as well as type of treatment performed. Another important reason was, most of the patients loss in follow up or no longer active in reviewed. The above problems can be avoided if respective person really carried out their duty and knew how important patient's information in medicine which can be used for medical audit and also for study. A few data regarding the patient's registration number was wrongly written or incomplete leading to irretrievable records. This also can be overcome if the personnel who deals with data of patients were regularly update and double checkup.

Sociodemographic characteristic.

Total 30 cases of squamous cell carcinoma of tongue were recorded from January 1992 until December 2005. Over 14 years of period of times, if range of time was considered, it was indicated that not many patients turn up to this centre for treatment. Gender ratio female (56.7%) to male ratio was 1.3:1(**Table 7**). This finding was not in line with the earlier study by Lisetta L et al (2005) and in Regional Cancer Centre, Trivandrum, Kerala (2003) which found male preponderance. Traditionally, oral cancer was a disease of males but trend of decreasing incidence in male with an increase incidence in females has been previously reported (Stell & Maran's 2000).

In the present study, the age of patients range from 16 to 74 years old. The most common age group diagnosed with tongue cancer was 46- 69 years (56.7% ,n=17) (**Table 6**). This figure was consistent with the study by Lisetta et al (2005) which reported , older patient (60 to 69) was the common group affected. In general, oral cancer incidence mainly occurs in 5th and 6th decade of live.

In term of ethnicity, Chinese group represented 43.3% (n=13) (**Table 8**) of sample and was the predominant ethnic affected with this disease as compared to other ethnics. This finding was equivalent with study done by Ramanathan et al (1976) and Ng et al (1985) in Malaysia, which reported tongue cancer was the commonest oral cancer in Chinese ethnic and it was ranked 2nd after buccal mucosa cancer which was common among Indians.

Disease characteristic.

Squamous cell carcinoma of tongue was the second commonest oral cancer in Malaysia and it was mostly affect female in the sixth decade of life. The finding of this study was incomparable with other study which most of their findings more on male. The difference could be due to sample of study which was too small or being biased in sample selection.

Based on the site, oral tongue cancer represented 80% (n=24) in which most of it were occurred on lateral border (n=23) and one on dorsum. The remaining 20% (n=6) (**Table 9**) was contributed by base of tongue group. This finding was comparable with findings by Lisetta et al (2005) which established that oro pharyngeal tongue cancer contributed 30% of all tongue cancer cases. Manuel et al (2003) reported that the commonest site of oral tongue cancer was the lateral border (80.3%).

Of 30 patients, 36.7 %(n=11) of patients were at aged of 46 years or less at time of diagnosis (**Table 6**).The figure was higher with study by Lisetta et al (2005) which reported about 15 % of patients diagnosed with tongue cancer at age of 45 or below. This situation currently much anecdotal and some evidence suggesting that incidence of head and neck cancers, particularly oral tongue cancer are increasing in young adults, many of them who had no exposure to traditional risk factors such as tobacco and heavy alcohol used or that duration of exposure maybe too short for malignant transformation to occur. In other retrospective study, they concluded that the etiology of oral cancer in the young group of patients to be multi factorial. Suggested factors that might implicated the tongue cancer were occupational, genetic / familial risk , immune defects and infections (B.S.M.S. Siriwardwardena et al 2005).

In present study , about 55 % (n=6) of young patient (< 46) turn up to this centre with advanced disease (stage III and IV).This figure was quite true and many studies had found that young patient have tendency to present with advanced stage of tumour (Stage III and IV) and related to poor outcome (Manuel S et al 2003, Friedlander et al 1998). This suggested that, the early lesion may be neglected by patients or even dentist and physician also not aware on that. Due to the nature of tumours itself, which not bothering patient much in early stage also part of reasons why patients delay in seeking professional consultation and hence advanced in disease presentation.

It has had been suggested that patients without typical risk factors for developing tongue cancer may have a worse prognosis as compared with patient whom has typical risk factor for disease to develop and also, biological behaviors of tumour in young patients may be distinct from the one occurring in older patient. With no history of exposure, the particular patient could inherited predisposition to chromosome breakage/ abnormalities which may lead to a more rapid disease progression (Llewellyn C.D. et al 2000).

Of the 30 patients, clinical positive nodes was seen in 14 (46.7%) (**Table 11**) of the sample. In young group (< 46), of the 11 patients, 55% of them have positive neck node. This finding was in line with statement by Manuel et al (2003) and Randall et al (1986), which concluded that young patient have a greater incidence of neck nodes metastasis. Cancer which presented infiltrative in nature, may reflect to high incidence of lymph nodes metastasis (Manuel S et al 2002, Kuriakose et al 1992).

Neck involvement was highly related to site, size, histological grading and the tumour thickness (depth). The advanced of the disease characteristics, the higher chances in

neck involvement (Oral Cancer 2003). The more invasive of the tumour, the more frequent regional metastasis to occur (Dedivitis R. A 2003). For stage I/II, all of them (n=13) have negative neck node and 82.4% (14/17) of sample in advanced stage (III / IV) have positive neck node. It's means that the more advance disease patient's have, chances for neck metastasis were more higher.

Histological grading in this study recorded 56.7% (n=17) of disease in moderately differentiated , 40% (n=12) well differentiated and 3.3% poorly differentiated (**Table 13**). The above figure was comparable with the value reported by study in Australia by Lisetta Let al (2005), which quoted 50% of sample in moderate grade. The histological characteristic for oral cancer usually well or moderately differentiated, it was very rare where the disease shows poorly differentiated (Stell & Maran's 2000)

Treatment.

Treatment of tongue cancer requires a multidisciplinary approach to obtain optimal results in term of curing and better quality of life. Generally, treatment of cancer were surgery, radiotherapy and chemotherapy or in combination.

In the present study, 40% (n=12) and 26.7% (n=8) of patient had surgery and radiotherapy alone (**Table 14**).Another 30% (n=9) had combination therapy (surgery & radiotherapy). It was revealed that surgery remains the first choice of treatment in tongue cancer with curative intention especially for oral tongue cancer. The choice of treatment modality was depending on cancer characteristic (such as- staging, HPE grading and neck involvement).Umeda et al (2005) reported , for stage I and II tongue cancer, the out come of treatment either by surgery (partial glossectomy) or radiation therapy (brachytherapy) were equally same.

A total of 30 % (n=9) (**Table 14**) of patients received combination treatment (Surgery and radiotherapy).Currently, there was significant increase in the use of combined modalities; surgery , radiotherapy and chemotherapy. Several reports have demonstrated improved locoregional control rates with combined therapy suggesting that an integrated program of multimodality therapy was superior to any single therapy modality, particularly in advanced disease (Iguchi H et al 2005, Lisseta L et al 2005).

The reason for giving adjuvant radiotherapy at this centre may be divided into planned preoperatively / postoperatively and unplanned postoperatively. The former was given due to advanced stage of disease (stage III & IV) while the latter was given to whom who have had unexpectedly aggressive primary disease , margin not clear (< 1cm) or microscopic aggressive neck nodal disease and also for recurrence prevention .

Base of tongue cancer, which contributed 20% (n=6) of this study (**Table 9**). 83.3% (n=5) of patients with the disease received primary radiotherapy alone as treatment and the rest had combination of surgery and radiotherapy. The proper management of the disease still controversial. The major treatment options were external beam radiation therapy (EBRT) with or without interstitial beam radiotherapy (IRT) or surgery combined with post operative radiotherapy. Surgical resection of base of tongue cancer frequently results in poor swallowing and inadequate speech function. In other word, surgery will increased patient morbidity and reduced quality of life.

Of 6 patients with base of tongue, 5 (83%) of them received radical radiotherapy to primary site together to neck region. The treatment performed to base of tongue cancer patients in this centre was in line with Van de Pol .M et al (2004) reported that , radical radiotherapy to primary site and neck dissection (ND) as compare to surgery

with or without radiotherapy were all non significant different, but with the radiotherapy and neck dissection give patients better quality of live. Functional outcome in term of understanding speech, eating in public and normalcy of diet which definitely affected in patient who underwent surgery.

Only one patient (3.3%) (**Table 14**) with oral tongue cancer received other method of treatment (chemotherapy or chemo-radio). Concurrent chemo-radiotherapy holds promise as an effective treatment modality in mucosal squamous cell carcinoma in head and neck region. In this case, chemotherapy may be used as palliative treatment because of advancement of disease.

Neck dissection was part of treatment modalities in head and neck cancer. About 44 % (n=13)(**Table15**) of sample in this study received neck dissection even various in types. Of 16 patients with N0 neck, 3 patients had undergone neck dissection. Neck treatment had to perform in case of positive node or in case of occult metastasis suspected. Current management for N0 neck is anecdotal. About 20%-30% of early tongue carcinoma (T1 and T2) and about 70%-80% of advanced tumour (T3 and T4) will have nodal metastasis at diagnosis, and of these, 15%- 20% have bilateral involvement (PW Booth 1999). Clearly the goal of neck treatment was for regional control of disease but the most frequent causes of treatment failure following surgical removal of oral tongue cancer was regional recurrence.(Sparano A et al 2004)(Yuen APW et al 1997).

Survival.

The present study examined 5 year disease specific survival according to various tumour characteristic and treatment modalities. The survival rates of this study were comparable to other international studies using actuarial or Kaplan Meier analysis. Despite improvements in locoregional disease control with combined modalities therapy, disease specific survival rate for tongue cancer (SCC) has not improved over 20 years of period.

Overall 5 year-survival from this study was 26.7%. 5 year survival of patient with oral tongue and base of tongue cancers were 33% and 0% respectively (**Table 18**). These values relatively were low if compared to study by Gorsky et al (2004) .In their study, they established that, overall 5 year survival for tongue cancer was 40% with 5 year survival of oral tongue and base of tongue cancers were 43% and 27% respectively. The 5 year disease specific survival for oral tongue cancer was about 33% and much better as compared to oropharyngeal tongue which recorded nil in percentage.

Patients in the youngest age group had drastically better 5 year survival (42%) compared to the middle group (18 %) and the oldest age group (0%) (**Table 19**). These findings were consistent with study reported by Lisetta L et al (2005) which shows much higher in percentage of survival in younger group of patient. (Statistical analysis shows that $p = 0.2045$ (>0.05)).It means that survival was not influenced by age.

In the present study, about 64% (n=7) in young group died cause of disease. Currently, many literatures have reported that cancer in younger age was associated with poor

prognosis and this statement strongly supported by B.S.M.S. Siriwardena et al (2005) which quoted that squamous cell carcinoma of tongue in the younger group had a poor prognosis than the older group. On the other hand, about 36% (n=4) of patients in young group (< 46) still alive with good quality of life.

Disease specific survival for oropharyngeal tongue cancer was significantly worse than the oral tongue cancers (0% versus 33%).The poor survival figures from this study were much worse compare to other study done in other country (25.9% -RAH Cancer Registry (1987-1998) and 40.3% - National Cancer Database USA) (Lisetta L et al 2005).The poor outcome of this disease considered to be multi factorial , reflecting both the aggressive nature of the disease and the impact of additional co morbidities in the patient population.

Base of tongue was a difficult part to visualize and these cancers frequently asymptomatic, leading to delay in diagnosis and advanced presentation of the malignancy. In addition, the incidence of second primary tumour within the upper aerodigestive tract in patient with this disease was rather high (17% to 30%) and had significantly negative impact on survival (Lisetta L 2005).

Table 20 revealed that, 5 year-survival rates was 75% and 33.3% in clinical stages I and II , compared to 33.3% and 7.7% for stages III and IV. There was a progressive decline in survival with little plateau for advanced stage tumour (**Figure 14**).These pattern suggests that the vast of majority of death during the first 40 months were attribute to failure in control the regional disease. These finding seems comparable with study reported by Lisetta L (2006); 5 year survival rates of 50% or more for

clinical stages I and II, compared to 40% or less for those with advanced disease. (p=0.0027 (< 0.05)).

A 5 year survival by treatment shown that about 42% with surgery, 100% for combination treatment with radiotherapy followed by surgery (1 patient) and 20% for surgery followed by radiotherapy (**Table 22**).The above values were in line with study by Van de Pol M et al (2004) which reported that comparing surgery combined radiotherapy vs radiotherapy combined neck dissection 49% to 52% which was not significant. Before rendering any treatment to patient, many factors have to take into consideration and hopefully the decision taken will give a good outcome to patient. Statistical analysis gives p=0.3330 (> 0.05) ,which means that type of treatment modalities does not influence the survival.) .

In present study, it was shown that in NO neck patient 5 year survival rate was about 43.8% and about 7% in positive neck nodes(**Table 21**). In view of neck nodes involvement, 5 year survival rates in N0 neck was the highest (~ 44%) and decreased in case of neck node positive. A study done in Taiwan population, reported that the size, nodal involvement, distant metastasis, staging, differentiation and habit has a direct relationship with survival (Lo WL et al 2003).(Statistical analysis of neck node was p=0.0008 (< 0.05))

Histological grading also closely related to survival. 5 year- survival by HPE grading shows that 37.5% in well differentiated, 23.5% in moderate and none in poorly differentiated (**Table 24**).These findings were comparable with study in UK by O-charoenrat et al 2002 , which found that advanced pathological stage related to poorer prognosis.(Statistical analysis for this study gives p=0.5117 (p>0.05)).

A total of 11 patients (36.7%) experience more than 2 years disease free period (DFP) while 8 patients (26.7%) had less than 6 months. In the present study, most of the cases with the disease free period less than 6 months occurred in patient with advanced disease and underwent radiotherapy and these complications arise due to residual disease. A better 2 year-disease free period in well differentiated (67%) as compared to moderate (35 %) and poor (0%)(**Table 26**). By staging, 2 year-disease free period recorded 100% in stage I, 33.3% in stage II, 75% in stage III and 7.7% in stage IV (**Table 25**). The above figures were comparable with earlier study by Gorsky et al (2004) which reported that the advanced disease patients have, the poorer prognosis and the high chances for recurrence.

Recurrences occurred in 13 patients (43.3%) (**Table 16**) in this study and about 61% of that occurred in the neck (**Table 30**). This figure indicated that, even neck dissection performed in indicated cases, but because of the nature of the disease itself with extra capsular and perineural spread or in multiple nodes involvement which can stimulate the recurrences. Out of 13 patients, 4 patients (30.8%) was in stage II and 9 (69.2%) of them in stage III / IV. Manuel S et al (2003) and Siegelmann - Danieli et al (1998) reported, stage of disease to be a significant predictor; earlier stage were associated with favourable outcome. Of 13 patients who had recurrent, 6 of them occurred in primary site.(Log Rank Test : $p= 0.0045 (< 0.05)$). 8 patients have had less than 6 months DFP. This situation occurred due advanced of the disease or incomplete removal of primary disease (closed margin).

Of the 11 patients in young group, 45.5% (n= 5) of them have recurrence. Manuel S et al (2003) and Vargas et al (2000) reported that the time interval in young patients was significantly shorter than in older patients. Manuel S et al (2003) pointed out that disease free period of patients who underwent salvage surgery for recurrent disease

was significantly higher than patients who underwent salvage surgery for radio residual disease. This was in line with the findings of other author, which reported that young patients have a greater incidence of neck node metastasis, but will respond well to salvage surgery if identified early.