2. LITERATURE REVIEW.

2.1. General.

The oral cavity is defined as the area that extend from the skin vermillion border of lip to the junction of hard and soft palate above and to the line of circumvallate papillae below (Head and Neck ,AJCC 1992).Tongue is a structure located partly in oral cavity and another part in pharynx. It can be divided into anterior 2/3 of tongue so called the oral or mobile tongue and is bounded by the ‘ V shaped ’ line of circumvallate papillae. Posterior to this line is base of tongue which is part of oropharynx (PW Booth 1999).

The International Classification of Disease (ICD) was developed by World Health Organization (WHO) for the purpose of statistical analysis of various disease. The ICD now become the basis for global standardization in definition of oral cancer. The ICD is a coding system based on anatomical origin of the primary cancer. According to the ICD system , specific areas related to the mouth were marked with specific codes, which include the lip, tongue, floor of mouth, soft palate, buccal mucosa and gingival/alveolus(including the retromolar region) (WHO 1978).

2.2. Oral Cancer In Malaysia.

Oral cancer in Malaysia was reported by Hirayama in 1966.He estimated that 3.1 new cases per 100 000 population were diagnosed for the year 1963.Based on the information from his study, the highest rate was in Selangor (8.2 per 100 000), while in other states like Kelantan, Terengganu and Kedah had the lowest rates (1.9 per 100 000 or less) (Hirayama 1966).

In 1976, a total of 898 cases were recorded for over six years (1967-1972), showing the incidence rate of about 150 cases per year (Rama and Lakshimi 1976) and between 1978 and 1984 (six years) ,749 cases were recorded and resulting in incidence rate of about 125 per year (Ng et al 1985). In Malaysia, the overall prevalence for oral cancer was reported as 0.04% (Zain et al , 1997).

Between 1967 – 1972 ,Oral Pathology Division , Institute Medical Research, Kuala Lumpur reported tongue cancer (15.1%) was the 2nd commonest oral squamous cell carcinoma after buccal mucosa (43.2 %) from all 1031 biopsy cases. For tongue cancer, Chinese male and female has the highest number while in Malay , it was common in male.(Ng et al 1985) In study of oral cancer incidence (1994-1998) in five states in Malaysia , tongue cancer also reported as 2nd commonest oral cancer (16.2%) (Dissertation of Hamdan. M. 2004).

2.3. Oral cancer in Global.

Cancer was a major cause of disease and death throughout the world.(Dambi C et al, 2001) and it becomes one of the five causes of death in all societies .Globally , oral cancer was one of the six most frequently occurring cancer related death , although many people were unaware of its existence. In ranking, lung, breast, colon , stomach and oral (Jatin P. Shah et al, 2003) .The frequency of cancer was more in developed country compared to developing country. (Melrose RJ, 2001) .

However, in countries of southern Asia, oral cancer was the most common cancer affecting males and the third one affecting females, after breast and cervix uteri tumors. Other geographic areas with high incidences were eastern, western and southern Europe, Australia and New Zealand and Melanesia.(Parkin DM et al 1997). Latin America and the Caribbean have intermediate incidence rates for oral cancer.

However, the rate among countries of the region varies widely.(Wu¨nsch-Filho V, Camargo EA, 2001). Oral cancer may occur at any age, but was primarily a disease of the elderly; more than 95% of oral cancers occur in persons older than age of 40 . (Langlass R, Miller C.1998). The common age for patient to has oral cancer (tongue) was 60 to 69 (Lisetta L et al 2005).

The most common type of oral cancer was Squamous cell carcinoma (SCC).(Neville B.1995). Approximately 94% of all oral malignancies were Squamous cell carcinoma. In United States, oral carcinoma has been reported as 25 most common oral mucosal lesion and about 21000 new cases were diagnosed annually.(Oral & Maxillofacial Pathology, 2002 by Saunders). Squamous cell carcinoma is a malignant neoplasm of mucosal origin.(Langlass R, Miller C,1998).

Fifty years ago, it was predominantly a disease of man and there was no good explanation for this change in the gender ratio. Recently, the disease affected equally man and woman.(Stell & Maran's.2000). In study done in Royal Adelaide Hospital, Australia, it was clearly male predominance resulted male to female ratio 2.1: 1 (Lisetta L et al 2005). Regional Cancer Centre (RCC) , Trivandrum, Kerala , India also found that male preponderance in their study (Manuel S et al 2003).

The most common site of intra oral squamous cell carcinoma was the lateral border and ventral surface of the tongue, followed by the oropharynx, floor of the mouth, gingiva, buccal mucosa, lip, and palate. (Langlass R, Miller C.1998) (Neville B ,1995). In case of tongue cancer which can be divided into two anatomical origin; oral and oropharyngeal tongue. The latter gives incidence about 30% of cases as compared to oral tongue (Lisetta L et al 2005).Which means that oral tongue cancer was more common. 80.3% of oral tongue cancer occurs at lateral border (Manuel S et al 2003)

2.4. Etiology

The exact causes of oral Squamous Cell Carcinoma was obscure but now generally accepted that causes of oral SCC were multi factorial.(Dambi C et al ,2001). It was accepted in the light of current literature that both extrinsic and intrinsic factors may be responsible for the malignancies. Extrinsic factors include the agent such as tobacco smoke, alcohol, syphilis, poor oral hygiene and sunlight (vermilion cancers only). Intrinsic factors including systemic or generalized disorders such as genetic / familial risk, immune defence, infection, malnutrition, general resistance and iron-deficiency anemia. (Neville B ,1995).

Despite, cigarette smoking and alcohol consumption were the two strongest etiological factors for the development of head and neck squamas cell carcinoma both independently and synergistically.(Stell and Maran's , Fourth Edition 2000). In China, there was significantly increased risk of tongue cancer associated with tobacco smoking and with increasing life time kilograms of alcohol consumed.(Zheng T et al .1997). Personnel oral hygiene also plays a role in oral cancer development. There was a case where patient free from any medical problem (Intrinsic factors) except has had very poor oral hygiene with dental trauma, developed tongue cancer.(Orbak R.et al , 2005).

Squamous Cell Carcinoma (SCC) of tongue **(ICD 141)** was the most common oral cancer, about 40% of disease arise over anterior 2/3 of tongue and about 85% of that from lateral border.(Stell & Maran's, Fourth Edition .2000). Base on study in United States, more than 50% of intra oral cancers were cancers of the tongue.(Oral & Maxillofacial Pathology, 2002 by Saunders).

2.5. Tumour characteristic

Cancer of tongue is a malignant tumour that begins as a small lump, a firm white patch, or a sore (ulcer) on the tongue. If untreated, the tumor may spread throughout the tongue to the floor of the mouth and to the gum (jaws). As a tumour grows, it becomes more life threatening by spreading (metastasizing) to lymph nodes in the neck and later to the rest of the body. The true causes of tongue cancer are obscure but it is one of the more common and serious types of mouth cancer. It commonly occurs in people who smoke cigarettes, pipes or cigars or use smokeless tobacco. People who took large amounts of alcohol and tobacco are especially at risk. Tongue cancer was rare in people under age 40 and people whom do not use tobacco or alcohol. It was most common after age 60.(Head & Neck Cancer Information, University of Michigan, Comprehensive Cancer Center ,Update May 2006).

Patients younger than 45 less likely been a smokers or alcohol drinkers, to have a greater percentage of well-differentiated tumours and to have a more favorable survival rate in comparison to older tongue cancer patients(Mathew Provanzano et al 2004) .

According to study in Sri Lanka, 40% of cancers in younger group were not associated with any habit or identifiable risk factor and 70% of the carcinoma of the tongue had no habits associated. The commonest site of occurrence for younger group appears to be the tongue whilst buccal mucosa and alveolar mucosa were the common sites for older group. It appears that SCC of the tongue in the younger group had a poor prognosis than that of the older group (Siriwardena BSMS et al 2006). SCC among young adults was rare and thought to have aggressive biological behavior and poor prognosis (Manuel S et al 2003).

Even patient present to clinic with the above symptoms, the confirmation of the diagnosis has to do by biopsy, usually incisional if the size was big. The diagnosis of SCC always made with light microscopy and with that the grading can be made. Tumour size and the extent of metastatic spread of oral squamous cell carcinoma was the best indicator of patient's prognosis. Quantifying these clinical parameters was call staging and base on TNM System set up by UICC and AJCC 1997.(Oral & Maxillofacial Pathology,2002 by Saunders).

Classification of tumour based on clinical presentation was used as one of method to predict the clinical outcome of disease. Ideally, the system should be easily understood and accurate. As mentioned above, the TNM system is the most reliable and ideal. TNM system gathers all the factors of disease such as primary site, regional and distant metastasis. This system was developed by American Joint Committee on Cancer (AJCC) and International Union Against Cancer (UICC).TNM system was modified a few times , and now the TNM system was modified in 1997(UICC 1997).

Table 1: TNM Classification (UICC and AJCC 1988) of tumour size (T).

Tis	Tumour in situ
T0	No primary tumour visible
T1	Less than 2 cm in diameter
T2	Between 2.1 cm to 4 cm in diameter.
T3	More than 4 cm
T4	Invades adjacent structures.

Source : Churchill Livingstone, PW Booth 1999.

Table 2: TNM Classification for regional metastasis (N).

Nx	Node cannot be assessed
N0	No nodes involved
N1	Ipsilateral single node < 3 cm
N2a	Ipsilateral single node > 3 cm to 6 cm
N2b	Multiple nodes ipsilateral < 6cm
N2c	Contra lateral / Bilateral nodes < 6cm.
N3	More than 6 cm

Source :Churchill Livingstones, PW Booth.1999.

Table 3: TNM Classification for metastasis (M).

Mx	Distant metastasis cannot be assessed
M0	No distant metastasis.
M1	Distant metastasis.

Source : Churchill Livingstone, PW Booth.1999

Table 4 : Staging grouping for oral cancer (UICC 1997)

Stage 0	Tis	N0	M0
Stage 1	T1	N0	M0
Stage 2	T2	N0	M0
Stage 3	T3 T1 T2 T3	N0 N1 N1 N1	M0 M0 M0 M0
Stage 4A	T4 T4 Any T	N0 N1 N2	M0 M0 M0
Stage 4B	Any T	N3	M0
Stage 4C	Any T	Any N	M1

Source: Butterworth Heinemann, Stell & Maran's 4th Edition (2000)

Histological grading was useful in providing clue to prognosis and should be considered in designing a treatment policy (Athur and Farr 1972). There was system developed in 1972 by Brodes, but his classification does not show a significance correlation between histological differentiation and prognosis. One of the main reason being squamous cell carcinoma usually exhibit a heterogenous cell population with differences in degree of differentiation (Anneroth et al 1995) .

A tumour was said to be well differentiated / low grade / grade 1 when its histological pattern closely resemble its tissue of origin. This type of tumour usually slow growing and late metastasis during its course. A tumour where there was much cellular and nuclear pleomorphism and with little or no keratin production may be so immature that it becomes difficult to identifies the tissue origin. Those tumour was classified as high grade / grade III or poorly differentiated / anaplastic. Tumour of this classification often enlarge rapidly and metastasis early along it course. Tumour that shows histological behavior in between this two grades will be classified as moderately differentiated / grade II (Neville et al 2002).

Table 5: Histological Grading**.**

Grade	Differentiation
1	Well differentiated
2	Moderately differentiated
3	Poorly differentiated
4	Undifferentiated

Source : Churchill Livingstone , PW. Booth 1999

Squamous cell carcinoma (SCC) of tongue has high incidence of neck metastasis. Involvement of regional lymphatics by primary SCC of oral cavity was depend on various factors related to the primary tumour including the size, site and in addition, histomorphologic features of primary tumour also influence the risk of nodal metastasis.(Oral cancer ,2003).

Basically, oral squamous cell carcinoma spreads by local extension / invasion or by way of lymphatic vessels (Orbak R et al 2005). The more invasive the tumour, the more frequent regional metastasis are; the more invasive tumors were indicative of a poorer prognosis; the mode of invasion of the deep invasive margins of SCC of the oral tongue has prognostic value.(Dedivitis R. A. 2003).

Evaluation of the tumour thickness in early oral tongue cancer may allow the identification of a subset of patient who more susceptible to metastatic spread via lymphatic pathway and permit suitable therapy to be offered accordingly.(O-charoenrat P et al 2003). Lymphatic drainage from tongue and floor of mouth were to the jugulo-digastric and mid-jugular regions of the neck.(Lindberg R 1972).

Neck nodes involvement could be unilateral or bilateral. Tumour size (T), multi-involvement of the ipsilateral node and histopatological grading were the significant predictors for occurrence of contra lateral neck metastasis. So, it was unlikely for contra lateral neck metastasis to occur if ipsilateral neck nodes negative.(Kurita H et al,2004). Occult metastasis is a worry in oral cancer. This event was depending on tumour site and stage. Infiltration of muscular layers had higher occult metastasis rates and lesser disease free survival time.

Therefore, the incidence of this event was much higher in tongue and floor of mouth cancer (Amaral TMP et al , 2004). Squamous Cell Carcinoma of oral tongue has high

incidence of nodal metastasis even in the early stages. Treatment options of early oral tongue carcinoma include surgery, radiation therapy or a combination of both. Until now, management of the clinically negative neck remains controversial. The AJCC/UICC staging systems have been used as international standards for cancer reporting, prognosis evaluation, planning and comparison of therapeutic strategy. Exceptional for T4 size, the maximum tumour diameter was the only parameter used in the classification of size T1–T3 oral tongue cancer. Since cancer can spread in different planes to invade the surrounding structures, the greatest diameter alone therefore cannot reflect the overall aggressiveness of tumour.(P .O- charoenrat et al .2003)

2.6.Treatment modalities.

Basically, treatment of tongue cancer requires a multidisciplinary approach to obtain optimal results in terms of cure and quality of life. There is a significant increase in the use of combined surgery and radiotherapy and decrease in the use of surgery as a single modality. Several reports have demonstrated improved locoregional control rates with combined therapy suggesting that an integrated program of multimodality therapy was superior to any single modality treatment plan alone, particularly for advanced disease or oropharyngeal tongue cancers (Lisetta L et al, 2005). Main treatment for tongue cancer were surgery, radiotherapy and chemotherapy but the choosing of treatment was depend on tumour staging, grading and neck nodes involvement. Optimal treatment for early carcinoma of tongue remains a controversial issue. Primary tumour control can be achieved equally with partial glossectomy or radiation therapy.(P. O-charoenrat et al,2003).

Base on retrospective study done in Japan , a comparison of treatment brachytherapy and surgery in stage I-II shows that surgery was the optimal treatment method for patient with the above stage of tongue cancer.(M.Umeda et al ,2005). Stage I disease can be treated by radiotherapy alone because in term of outcome almost same with surgery, but the latter method can lead to functional and cosmetic defect.(Ichimiya Y et al ,2005).

Surgery and radiotherapy are the mainstays of treatment of oral cavity cancer, and equivalent result have been reported using either modality for early stage tumours (Oral Cancer 2003).In spite of this two treatments, the advantage of surgical therapy is that it immediately eradicate the disease and provides information on both histology and clearance in the early stage cancer.

This modality might useful for younger patient where as for older, radiotherapy can give obvious advantages.(Stell & Maran's 2000).When surgeon decided to ablate the tumour , consideration to margin of clearance is important in order to prevent regional recurrence. Based on study done in Amsterdam, the purposed of study to asses the relation of local recurrence with distance of marginal resection. The result shows that tumour cell in the margin less than 5mm, but not into deep surgical margin. To be safer, better the margin of resection was more (at least 1cm) (Weijers M et al 2003)

The status of the surgical margins is probably the single most factor determining the local control. It is interesting that in one report margins were classified as positive if they meet one of the following four criteria: closed margin (tumour with in 0.5 cm), premalignant change, in situ carcinoma and invasive microscopic cancer in margin (Oral Cancer 2003). In patient with close or positive surgical margins, adjuvant radiotherapy in doses of 60Gy or more yields local control rates comparable to those in patient with negative margins. When patients who received radiotherapy of 60 Gy

or more were analyzed , the control rate exceed 90%. However, the efficacy of postoperative radiotherapy was dependent on site of primary tumour; floor of mouth had better 5 years local control rate compared to oral tongue tumour (89% vs 62%) respectively (Oral Cancer 2003).

On top of that, for stage I disease, surgery excision was effective and expenditious with good preservation of function and for stage II lesion that were infiltrative, hemiglossectomy achieves excellent tumour control rates and can be combined with modified neck dissection for neck nodes to provide accurate staging information and determination of the need of adjuvant radiotherapy.(G.Aksu et al 2006).

For advanced stage of cancer, the treatment preference might be changed. Base of Tongue (BOT) cancer treatment is still controversial. In study for comparing of radiotherapy and surgery modalities in stage III and IV base of tongue cancer, result shows that surgery was better in control disease advancement as compared to radiotherapy but, reconstructive surgery also play an important role in benefit patient. However both treatment modalities were reasonable in locoregional tumour control.(Van de Pol et al M ,2004). On the other hand, surgical resection of BOT frequently result in poor swallowing and inadequate speech function but better tumour control can be achieved.(van de Pol M et al 2004).

Until now, surgical excision still the mainstay treatment for tongue cancer, even now combination of surgery and adjuvant radiotherapy routinely used in control primary site as well as neck nodes in advanced stage (III & IV) of disease, and is being used increasingly in lower stage (II) that exhibit pathologic indicators of nodes metastasis and perineural invasion.(G.Aksu et al 2006). Furthermore, histopathological sign which has been correlated with local control was the presence of perineural invasion. Patient with the histological evidence of perineural invasion have a lower control rate

(77%) compared to others (91%). When perineural invasion was seen in surgical specimen, consideration should be given to the use of adjuvant radiation therapy to enhance local control (Oral Cancer 2003).

For advanced tumour but operable, the combination of chemotherapy and radiotherapy preoperatively and followed by surgery. This combination treatment widely used for head and neck cancer including advanced stage of lingual squamous cell carcinoma.

Chemotherapy drugs, intra-arterial pirarubicin and intravenous 5-flourouracil 1 hour before radiotherapy (2Gy /day). Pirarubicin introduced into lingual artery via superficial temporal artery .This procedures was continues for 20 days. After chemoradiotherapy completed, surgical ablation performed including glossectomy, neck dissection (en-bloc resection with pull through approach) and reconstruction. The best advantage of the concurrent chemoradiotherapy with intraarterial approach for tongue cancer , it was appears very useful for tongue cancer (Iguchi H et al 2006).

Radiotherapy can be used preoperatively, the outcome of subject patient to radiotherapy prior to surgery for stage II tongue cancer shows a remarkably high rate of pathological local control and acceptable adverse effect.(mucositis & leukopenia).(Iguchi H et al 2006). In some centre, a combination of external beam radiotherapy (EBRT) and interstitial radiotherapy (IRT), supplemented by 2 courses of concomitant chemotherapy was the best treatment modality which can surpassed the tolerance of salivary glands.(van de Pol et al 2004).

Furthermore, treatment method for tumors located in the base of tongue is more difficult especially surgical resection. Mandible-sparing procedures is used more often, and significantly more patients received primary and adjuvant radiotherapy in the early study period. At the same time, there were fewer composite neck, tongue,

and jaw resections and fewer laryngectomies, although more patients had elective treatment of the neck.(Charles D et al ,1984).

When patients with oral tongue primary lesions were compared with those with tumors in the base of the tongue, the prognosis seemed to be better in those with oral primary lesions when the patient had stage I or II disease. In fact, patients with tongue cancer have at least a 1 in 5 chance of development of a second aerodigestive tract malignancy and require lifelong scrutiny. Although current therapy results in lower morbidity, the proportions of patients with stage III and IV tumors remain high, and the cure rates remain disappointingly stable. (Charles D et al,1984).

2.7. Neck treatment.

Squamous cell carcinoma of tongue has high incidence of nodal metastasis even in early stage. Tumour thickness is something difficult to determine accurately. Imaging study (Ultra sound, CT scan & MRI) can be used to measure it. If tumour thickness more than 5mm, the surgeon might consider for elective neck dissection avoid lymphatic spread later.(P.O-charoenrat et al,2003). About 20%-30% of early tongue carcinoma (TI and T2) and about 70%-80% of advanced tumour (T3 and T4) will have nodal metastasis at diagnosis, and 15%- 20% of that have bilateral involvement (PW Booth 1999).

Clearly, the goal of node treatment was for regional control of disease but, the most frequent cause of treatment failure following surgical removal of oral tongue cancer was regional recurrence.(Sparano A et al 2004)(Yuen APW et al 1997).Generally, treatment modality of neck node were surgery or radiotherapy. For surgery, it can be divided into comprehensive radical neck and selective radical neck dissection. (Oral cancer 2003)

Minimal gross metastasis may be controlled by radiotherapy alone. However, surgery remains the mainstay treatment of cervical nodes metastasis since it provides comprehensive clearance of grossly enlarged nodes and offers accurate histological information on lymph nodes at risk of having micrometastasis in clinically negative neck.(Oral cancer,2003).

Currently, when regional metastases are clinically palpable, comprehensive clearance of all regional lymph nodes at risk is mandatory. Classical radical neck dissection remain the gold standard of surgical management of clinically apparent metastasis lymph nodes. The current indications for radical neck dissection are N3 disease, multiple nodes involving multiple level, recurrent metastatic disease in radiated neck, extra nodal spread and involvement of accessory nerve.(Oral cancer 2003).

Selective neck dissection may be sufficient for many N+ patients with SCC of the oral tongue, but some patients with extensive nodal disease may benefit from more aggressive treatment of the neck. Radiotherapy may be beneficial for all of the node-positive patients (Schiff BA et al 2005). In advanced stage of base of tongue cancer (Stage III & IV), it seems that treatment with radiotherapy for primary site and neck give almost the same outcome in term of locoregional control as well as less morbidity to patient.(van de Pol et al 2004).

In certain disease condition, elective neck dissection is undertaken in excise nodes at risk of harboring micrometastasis (occult metastasis). Elective neck dissection of patient with early oral tongue cancer with a clinically negative neck node (TI /T2 NO) still generated controversy for more than 3 decades. Although this treatment may benefit patient with occult metastasis, it is also produces unnecessary morbidity in others with out metastasis.(Sparano A et al ,2004). Occult metastasis was a factor that always causes regional recurrence. Preoperative used of CT scan and ultra sound

imaging offer negligible added sensitivity in identifying occult metastasis.(Sparavo A et al 2004)(Byers et al 1998) (Yuen et al 1997).Thus, an elective operation for primary tumours with N0 neck requires dissection of nodes at level I, II and III if the primary tumours cross the midline. The pattern of cervical lymph nodes metastasis was predictable and sequential, with involvement of first echelon lymph nodes before dissemination occurs to other levels (Oral cancer 2003).

Even until now, management of tongue cancer with negative neck node remains controversial. Nevertheless, it is recommended that for SCC of oral cavity in general, any clinically negative neck should be treated when the incidence of occult metastasis is greater than 20%. Other factors that involved in consideration were primary site (especially tongue- vascularised and muscular), tumour size and characteristic of tumour (histopathologic features)(William I. Wei et al 2006).

When a significant risk of micrometastasis to regional lymph nodes is present based on the characteristics of the primary tumour, an elective dissection of regional lymph nodes at risk should be considered (Oral cancer 2003). Assessments of the clinical and histopathologic factors enable more informed decision addressing elective neck treatment than does presurgical evaluation of early N0 oral tongue cancer. (Sparano A et al 2004).

In certain condition, even surgery is performed over neck region, but sometimes surgeon might thought of further modality like radiotherapy for adjuvant. A few indications might be considered such as in case of extra capsular spread , case of perivascular or perineural invasion, multiple neck nodes, gross residual disease following neck dissection and other ominous findings such as tumour spread to base of skull and cranial nerve invasion (Oral cancer 2003).

Furthermore, treatment of advanced neck lesion (N2 and N3) required combination of multimodal technique involving surgery, radiotherapy and chemotherapy although brief understanding regarding distant metastasis should be emphasize before initiating any treatment (Pitman and Bradley 2003).

Positive neck node will reduce the survival of patient drastically. In reviewed of 123 patient diagnosed with squamous cell carcinoma of oral / oropharynx and treated by primary radical surgery and simultaneous neck dissection. All of the subjects were followed up for at least 5 years. In patient presented without histologically positive node, the 5 years survival probability was constantly around 80%. In patient with presence of histologically positive node, the 5 years survival reduced to 44%. Present positive node need aggressive or extensive management. Radical neck dissection required. Modified neck dissection performed in selective cases (Woolgar et al 1995).

Invasion of tumour also significant in prognostic value. Preliminary investigations suggest that the initial diagnostic biopsy can classify the tumour according to it mode of invasion. So the prognosis could be determined earlier. The more invasive tumour, the more frequent regional metastatic are, the more invasive tumour indicative of poorer prognosis. (Dedivitis RA 2003).

Eventually, patient with advanced tumours, multi involvement of the ipsilateral neck nodes, or a higher degree of histopathological grading were at a higher risk of contralateral lymph nodes metastasis (Kurita H 2004). Patients with nodal metastases, particularly in advanced stages, seem to be at highest risk for the development of distant metastases. This has implications for the longevity of follow-up. Unfortunately, the surgical salvage in patients who have failed a primary treatment for advanced stage disease or oropharyngeal tongue cancer was very difficult and the results are extremely poor (Lisetta L et al 2005).

2.8. Prognosis and Survival

Survival analysis refers to the techniques used to study the time to occurrence of event in a population, and is usually called time to event analysis. The outcome of interest is the elapsed time between a well defined starting point and a well defined end point (Dickman et al, 2000). In this study, the starting point was defined as a time of diagnosis of squamous cell carcinoma of tongue confirmed. The event of interest was the duration between the first diagnosis and death occurred. The survival period was defined as the duration between diagnosis and death and is the principle measure of effectiveness of cancer care (Dickman et al ,2000).

In cancer patient, survival is defined as duration or elapsed time from the time of first diagnosis is made until patient death. Survival is better in patient with early stage cancer and no node involvement .In patient with negative histological node , 5 years survival probably constantly around 80%, but in the presence of positives nodes, 5 years survival will reduced to 44% (Woolgar et al 1995).

In spite of advances in cancer therapy, the worldwide trend in five-year survival rates of tongue SCC since the early 1970s has remained relatively constant. The Tumour, Node and Metastasis (TNM) stage is the single most important predictor for survival. Survival rate is much higher in patients with early stage tongue cancer than in those in whom the cancer had spread to regional lymph nodes or to more distant site at time of diagnosis. Oropharyngeal tongue cancer also has a poorer survival than oral tongue cancer. According to population-based cancer registries data, five-year survival for oropharyngeal tongue cancer around 33–40%, compared with 53% for oral tongue cancer (Lisetta L et al 2005).

A study done in Taiwan population, reported that the size, nodal involvement, distant metastasis, staging, differentiation and habits have a direct relationship with survival (Lo WL et al 2003).But some believe that thickness is the most important determinant of survival in early oral cancer and that, any tendency for tumors in advanced T stage to show an increased mortality, albeit insignificant. (Sheahan P et al 2003) but advanced pathological stage also related to poorer survival outcome (O-chroenrat . P et al 2002) .

In the study done in one of the hospital in Spain, the data indicate that patients with tumours less than or equal 3 mm thickness have a significantly higher survival rate (85.7% at 5 years) than those with tumours of greater thickness. The result also shows that no differences in survival between patients with tumours of 4–7 mm thickness (58.3% at 5 years) and those with tumours of >7 mm thickness (57% at 5 years).

This analysis showed that the thickness of the tumour had the greatest influence on the survival of the present patients, more significant than that of the superficial measurement of the tumour or the pathologic size (T). Other studies have reported the influence of tumour thickness on survival (Gonzales – Moles et al 2002).

In case of T3/T4 tumour, the survival rate definitely will reduce. In analysis done , comparing treatment result in North America academic institution using surgery combined radiotherapy vs radiotherapy combined neck dissection, local control was about 79% vs 76% .Overall survival at 5 years (49% vs 52%) were all non significantly different (van de pol M et al 2004) (Parsons et al 1994). Sometimes, relaps in local and regional are inevitable and in certain cases, salvage treatment will give a good out come. The actuarial survival rates at 2 years post relaps were 35% for local and 17% for locoregional (Wada M , Peters LJ 2001).

In Sri Lanka, study was done in comparing of oral cancer in younger and older group. Result shows that prognosis of oral squamous cell carcinoma was determined by a number of factors. Patient and professional delay, clinical stage, tumour size and histopathological properties of the tumour were some of the important factors in this context. The clinical stage is a well-known prognostic factor and it reflects both the local disease and the spread to lymph nodes. It has been concluded that the delay in diagnosis of oral squamous cell carcinoma is mainly caused by the patient due to asymptomatic nature of oral cancer in early stage and incapability of patient to distinguish between ominous and innocuous symptom in oral cavity.

This study also showed that the recurrences in younger and older patient were 39% and 30% respectively. The three years survival rate looks more or less equal in younger and older patient (91% and 85.7%) respectively (Siriwardena BSMS et al 2006).

In review of the literature indicates that the present series show that more or less similar three years survival rate in both groups (Siriwardena BSMS et al 2006) (Iype EM 2001). The results of study in Kerala India also indicate that the outcome in younger age patients was comparable to that in older patients (Manual S et al 2003).

There was no significant difference between different sites of oral mucosa with three-year survival rate in both younger and older groups in the present study. The three-year survival rate of women in the younger group is better (90%) than that of the older group (75%).But three-year survival rate of men was almost equal in both younger (88%) and older (86%) groups (Siriwardena et al 2006). In Switzerland, the 5-year relative survival rate of women is little higher than men (Levi F et al 1992). Higher three-year survival rate was observed in patients with no habits (94%) compared to the patients who practiced habits (85%). There was no difference in survival among each

habit such as betel chewing, smoking and / or alcohol consumption. In the young group, three-year survival rate of habits practiced and not practiced were 81% and 94% respectively. In contrast older group shown higher survival with no habits (Siriwadena et al 2006).

Extra-capsular spread (ECS) has been previously reported as a prognostic indicator of recurrence and survival with the relative risk of death increasing with increasing T stage. Some authors, though, have found no significant prognostic value for ECS. Other factors which can affect survival include surgical excision with or without neck dissection and histological grade (Chandu A et al 2005).

Some author reported an overall survival (OS) of 64% at 5 years and 5-year survival rates of 85%, 90%, 82% and 42% for stages I, II, III, and IV, respectively in 200 patients with oral squamous cell carcinoma (Chandu A et al 2005)(Woolgar et al 1999).The result of study in Australia, overall survival at 5 years was 83.8% and 5 year-disease specific survival probability were 88.7%, 83.8%, 83.3% and 76.5% for stage I, II, III and IV respectively. The result of study in Kerala, shows that the overall survival is about 78% and disease free survival is 57.4% in young patient (< 45) with tongue cancer (Manuel S et al 2003).

The disease free survival (DFS) of patients who underwent salvage surgery for recurrent disease (74.5%) was significantly higher than patients who underwent salvage surgery for radio residual disease (20.2%) (Manual S et al 2003). This is 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 (Randall CJ and Shaw HJ 1986).

In other study, the author concluded that the time interval for recurrence in young patients is significantly shorter than in older patients (Manuel S et al 2003) (Vargas et al 2000) . It is the tumour status, pathological node status, type of primary surgery, surgical clearance, and the selection of appropriate treatment that influences survival, irrespective of age. It is time to think of appropriate treatment modality for this type of disease.