

Cancer Association of South Africa (CANSA)



Fact Sheet on Cancer of the Lips

Introduction

Lips are a visible body part at the mouth of humans and many animals. Lips are soft, movable, and serve as the opening for food intake and in the articulation of sound and speech. Human lips are a tactile sensory organ, and can be erogenous when used in kissing and other acts of intimacy.

[Picture Credit: Lips]



The upper and lower lips are referred to as the 'Labium superius oris' and 'Labium inferius oris', respectively.

The juncture where the lips meet the surrounding skin of the mouth area is the vermilion border, and the typically reddish area within the borders is called the vermilion zone. The vermilion border of the upper lip is known as the cupid's bow. The fleshy protuberance located in the center of the upper lip is a tubercle known by various terms including the procheilon (also spelled *prochilon*), the 'tuberculum labii superioris', and the 'labial tubercle'. The vertical groove extending from the procheilon to the nasal septum is called the philtrum



[Picture Credit: Lips 2]

The skin of the lip, with three to five cellular layers, is very thin compared to typical face skin, which has up to 16 layers. With light skin colour, the lip skin contains fewer melanocytes (cells which produce melanin pigment, which give skin its colour). Because of this, the blood vessels appear through the skin of the lips, which leads to their notable red colouring. With darker skin colour this effect is less prominent, as in this case the skin of the lips

contains more melanin and thus is visually darker. The skin of the lip forms the border between the exterior skin of the face, and the interior mucous membrane of the inside of the mouth.

The lip skin is not hairy and does not have sweat glands. Therefore it does not have the usual protection layer of sweat and body oils which keep the skin smooth, inhibit pathogens, and regulate warmth. For these reasons, the lips dry out faster and become chapped more easily.

Cancer of the Lips

Lip cancer is cancer that develops in the tissue of the lips. It is the most common form of oral cancer, and mostly affects men. There are two types of lip cancer: squamous cell and basal cell. The most common type of lip cancer begins in the squamous cells, the thin, flat cells that line the lips and mouth.

Mummudi, N., Agarwal, J.P., Chatterjee, S., Maljick, I. & Ghosh-Laskar, S. 2019.

“Oral cavity cancer (OCC) poses a global challenge that plagues both the Orient and the Occident, accounting for an estimated 350 000 new cases and 177 000 deaths in 2018. OCC is a major public health problem in the Indian subcontinent, where it ranks among the top three cancer types in both incidence and mortality. Major risk factors are the use of tobacco, betel quid and alcohol consumption. OCC is a heterogeneous group of multiple histologies that affects multiple subsites. The oral cavity includes the lips, buccal mucosa, teeth, gingiva, anterior two-thirds of the tongue, floor of the mouth and hard palate. OCC is defined as cancer of lips, mouth and tongue as defined by the International Classification of Diseases coding scheme. The epidemiology, aetio-pathogenesis and treatment philosophy are similar within this group. Although salivary gland malignancies, sarcomas, mucosal melanomas and lymphomas can also arise within the oral cavity, this review will focus on squamous cell cancer, which is the predominant histology in OCC. We review and contrast data from developing and developed countries. We also highlight the unique regional challenges that countries in the East face; citing India as an example, we elaborate on the opportunities and scope for improvement in the management of OCC.”

Salan, A.I., Camen, A., Ciuca, A., Patru, A., Scriciu, M., Popescu, S.M., Alexandru, D.O. & Turcu, A.A. 2018.

PURPOSE: The objective of this study was to review lip tumor diagnosed subjects from Oltenia region, in the past 5 years according to gender, age, home environment, profession, geographic area, smoking habit, associated diseases, tumor location, macroscopic aspect and histological type.

MATERIAL AND METHODS: The study was done at the Oral and Maxillo-Facial Clinic of the Emergency Clinical County Hospital of Craiova, and involved the analysis of patient file records, surgical registers, histopathological bulletins, from 2012-2016.

RESULTS: Of the 175 subjects included in this study, all of them diagnosed with lip tumor pathology, 109 (62.29%) were men, and 66 (37.71%) were women, all of them with ages between 6 and 92 years, with a mean age of 61 years. Distribution of study participants according to the home residence showed that majority of the subjects lived in rural area. The most frequently localization of lip tumors in study participants was at the lower lip-140 cases (80%), than at the upper lip-35 cases (20%).According to histological characteristics, distribution of the malignant lip tumors was 87.39%-squamous cell carcinoma (SCC), 5.41%-basal cell carcinoma (BCC) and 7.20%-other type of tumors.

CONCLUSIONS: The lower lip was the most affected, by lip cancer, and squamous cell carcinoma represents the most frequently histological type of these tumors.

Incidence of Cancer of the Lips in South Africa

According to the outdated National Cancer Registry (2016), known for under reporting, the following number of cases of cancer of the lips was histologically diagnosed in South Africa during 2016:

Group - Males 2016	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All males	38	1:4 695	0,10%
Asian males	2	1:10 153	0,20%
Black males	13	1:13 514	0,10%
Coloured males	3	1:3 553	0,07%
White males	20	1:1 714	0,10%

Group - Females 2016	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	10	1:16 805	0,02%
Asian females	0	-	-
Black females	3	1:52 632	0,02%
Coloured females	1	-	0,02%
White females	6	1:4 396	0,04%

The frequency of histologically diagnosed cases of cancer of the lips in South Africa for 2016 was as follows (National Cancer Registry, 2016):

Group - Males 2016	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All males	0	0	3	5	9	9	7	5
Asian males	0	0	0	1	0	0	1	0
Black males	0	0	2	4	3	2	0	2
Coloured males	0	0	0	0	1	1	1	0
White males	0	0	1	0	5	6	5	3

Group - Females 2016	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All females	0	0	0	1	3	1	3	1
Asian females	0	0	0	0	0	0	0	0
Black females	0	0	0	0	2	1	0	0
Coloured females	0	0	0	0	0	0	0	1
White females	0	0	0	1	1	1	3	0

N.B. In the event that the totals in any of the above tables do not tally, this may be the result of uncertainties as to the age, race or sex of the individual. The totals for 'all males' and 'all females', however, always reflect the correct totals.

Causes of Cancer of the Lips

The exact cause of cancers is unknown, but certain risk factors are associated with specific types of cancer. The risk factors for lip cancer are synonymous to the risk factors of oral cancer. These include:

[Picture Credit: Cigarette Smoke]



Smoking and tobacco - has been the most often associated factor

for lip and oral cancers. Cigarettes contain various carcinogens including tar. The chemical substances found in cigarettes damages the lining of the lip, which causes abnormal cells to proliferate. Almost all patients who suffered from lip cancer are smokers.

The Vast Chemicals of Cigarettes Cause Lip Cancer.

The intake of alcohol - leads to the penetration of DNA-damaging substances in the cells of the lip and mouth. When alcohol is paired by smoking, there is higher risk for the development of lip cancer.

Exposure to the harmful ultraviolet radiation from the sun - in prolonged periods can cause skin cancers, including lip cancer.

Warts caused by HPV - can contribute to the development of lip cancer. HPV commonly affects the vagina, penis and cervix. The practice of certain sexual practices contributes to the spread of the virus in the lips and oral cavity.

Chronic irritations on the lip - caused by poor fitting dentures and other dental appliances may cause changes on the cells on the mouth and lips.

Lack of fresh vegetables and fruits in the diet - these foods have antioxidant properties and it is thought that a lack of these in the diet may predispose someone to have lip cancer.

Males - have higher percentage of smokers and alcoholic drinkers, which predisposes the male population to oral cancers.

Immunosuppression - immunosuppressed populations in particular must remain extremely vigilant about lip cancer. Kidney transplant patients have a 30-fold increased risk due to use of immunosuppressive anti-rejection drugs. People receiving higher doses of immunosuppressants tend to develop more non-melanoma skin cancers (NMSCs) than those on lower doses, and patients with

HIV also demonstrate higher skin cancer risk. Immunocompromised patients, especially those with chronic sun exposure (which further suppresses the immune system), must be monitored closely.

Adults - who have reached the age of 40 have higher risk because of more exposure to carcinogens and ultraviolet rays.

Dombrowski, N.D., Wolter, N.E., Irace, A.L., Robson, C.D., Perez-Atayde, A.R., Mack, J.W. & Rahbar, R. 2019.

OBJECTIVE: To discuss the presentation, evaluation, and management of squamous cell carcinoma of the head and neck in the pediatric population.

METHODS: Medical records of pediatric (≤ 20 years) patients treated for squamous cell carcinoma of the head and neck between 1996 and 2016 were reviewed. Data pertaining to clinical presentation, diagnostic methods, treatment plan, complications, recurrence, follow-up, or outcome were collected.

RESULTS: Eleven patients were diagnosed with squamous cell carcinoma. Seven of these patients had medical histories significant for prior malignancies, immunosuppressant therapy, and/or genetic syndromes. Lesions were identified in the oral cavity ($n = 5, 45.5\%$), lip/upper lip ($n = 3, 27.3\%$), larynx ($n = 2, 18.2\%$), and nasal cavity ($n = 1, 9.1\%$). Tumors were most commonly treated with surgical excision alone. Three patients underwent irradiation (2 adjuvant and 1 without surgery) and chemotherapy (1 adjuvant, 1 neoadjuvant, and 1 without surgery). Of these patients, one reported complications of hearing loss, loss of dentition, and laryngeal stenosis. Two patients developed local recurrence at 1 month and 5 years post-operatively, respectively. One patient developed an orocutaneous fistula and subsequently died. No other complications were reported. Median follow-up time was 4.6 years (interquartile range: 2.4-8.4 years). Complications of radiation included: laryngeal stenosis, wound breakdown, and orocutaneous fistula.

CONCLUSION: Squamous cell carcinoma is rare in the pediatric population. Most frequently, it is associated with previous malignancies, immunosuppressant therapy, and/or genetic conditions. Complete surgical excision is recommended to obviate the need for radiation whenever possible.

Lowering the Risk of Cancer of the Lips

Regular use of photoprotective lip blocks (lip products that contain sunscreen) reduce the risk of lip cancer. However, many people remain unaware how important consistent lip protection is. In a study of 299 beachgoers, 94 percent demonstrated a high awareness of the risks of UV damage to the skin in general, but only 69 percent demonstrated a high awareness of risk factors specifically for lip cancer. Seventy percent of beachgoers used no lip protection whatsoever, and even among those who otherwise properly applied sunscreen, only 37% used any lip protection.

Furthermore, while photoprotective lip blocks can be effective in reducing UV exposure, most people do not apply them properly. From a practical standpoint, the actual Sun Protection Factors (SPFs, which measure protection against the sun's UVB rays) provided by lip blocks are almost always lower than the number on the package because the blocks are not applied thickly or frequently enough. Additionally, many commercially available photoprotective lip blocks may be poorly absorbed and can be broken down quickly by UV light, losing their effectiveness — two compelling reasons for frequent reapplication.

Despite being exposed to large amounts of UV light, the lips are often overlooked as a potential site for skin cancers. It is critical to exercise careful sun protection through a combination of sun avoidance and shade-seeking; frequent application of a high-SPF lip block; and careful monitoring of skin changes. Any changes to the lip that concern you should be brought to the attention of your physician immediately.

Signs and Symptoms of Cancer of the Lips

The lips are a not uncommon, but often overlooked site for non-melanoma skin cancers (NMSC), including the two most common skin cancers, basal and squamous cell carcinoma (BCC and SCC). Most frequently occurring in fair-skinned males over the age of 50, cancer of the lip comprises approximately 0.6 percent of all cancers in the US. Studies have shown that males are 3-13 times more likely to develop lip cancers, likely due to occupation-related sun exposure combined with greater tobacco and alcohol use.



The lower lip is approximately 12 times more likely to be affected, owing to its greater exposure to sunlight. A recent 25-year retrospective study of 2,152 patients with lip cancer revealed that 81 percent occurred on the lower lip, with males predominating by 3 to 1. Large epidemiological studies have shown that up to 95 percent of NMSCs on the lower lip are SCCs.

Given their highly visible location, the majority of lip cancers are easily detectable and treatable at an early stage. The most commonly employed treatments include surgery, radiation, and cryotherapy (freezing with liquid nitrogen), with cure rates for early lesions nearing 100 percent. Although cancers of the lip have relatively low rates of spread to nearby lymph nodes and distant sites, the relapse rate after treatment can range from 5-35 percent, and the mortality associated with large or recurrent SCC of the lip is as high as 15 percent in some studies. Once these cancers spread to local lymph nodes, five-year survival rates decrease to approximately 50 percent (Skin Cancer Foundation).



[Picture Credit: Lip Cancer]

Lip cancer symptoms are very similar to those of other types of oral cancer. It can often be mistaken for a cold that won't go away, or a persistent toothache. Other symptoms and signs include:

- a sore in the mouth or on the lips that does not heal
- persistent pain around the lips
- a lump or thickening in the cheek or near the lips
- a white or red patch on or near the lips

Diagnosis of Cancer of the Lips

Tests and procedures used to diagnose mouth cancer include:

- physical exam - the doctor or dentist will examine the lips and mouth to look for abnormalities
- areas of irritation, such as sores and white patches (leukoplakia)
- biopsy - removal of tissue for testing. If a suspicious area is found, the doctor or dentist may remove a sample of cells for laboratory testing in a procedure called a biopsy. Unusual cells can be scraped away with a brush or cut away using a scalpel. In the laboratory, the cells are analysed for cancer or precancerous changes that indicate a risk of cancer

Mello, F.W., Melo, G., Modolo, F. & Rivero, E.R. 2019.

BACKGROUND: To investigate the prevalence of malignant and potentially malignant lesions of the lip in an oral pathology service and to compare these data with a literature review.

MATERIAL AND METHODS: A total of 3173 biopsy reports and histopathological records were analyzed. Cases with a histological diagnosis of actinic cheilitis (AC) with or without epithelial dysplasia, in situ carcinoma, or lip squamous cell carcinoma (LSCC) were included. A comprehensive literature review was conducted to investigate the prevalence of AC and/or LSCC.

RESULTS: 124 cases (3.91%) were included, 75 (60.5%) had some degree of epithelial dysplasia and 31 (25.0%) were LSCC. Clinically, most of the lesions were diagnosed as AC (50.8%); however, eight cases clinically reported as AC were histologically diagnosed as LSCC. Regarding clinical characteristics, most individuals were fair-skinned male, with mean age of 54.3±12.3 years, and with a history of long-term solar exposure. Furthermore, 18 articles were selected from the literature, showing that the lower lip was predominantly affected and that most individuals were males, fair-skinned, and older than 40 years.

CONCLUSIONS: Since most of the cases diagnosed clinically as AC presented some degree of epithelial dysplasia, it is important to emphasize the value of biopsy and the histological evaluation of this lesion. **Key words:** Actinic cheilitis, Precancerous conditions, In situ carcinoma, Oral diagnosis, Mouth neoplasms.

Recurrent Oral Cancer

Recurrent or relapsed disease means that the cancer has returned after treatment. Recurrent disease does not have a TNM classification or a staging system number. When oral cancer recurs in the mouth or throat, it is called a local recurrence. When it recurs in the lymph nodes, it is called a regional relapse. When other parts of the body, such as the lungs, are involved, it is called a distant recurrence. Although early-stage oral cancer may be easier to treat than more advanced disease, treatment options are available for all patients. Your doctor will explain the options that may work for you, so that your treatment can be as effective as possible.

Zhao, R., Jia, T., Qiao, B., Liang, J., Qu, S., Zhu, L., Feng, H., Xing, L., Ren, Y., Wang, F. & Zhang, H. 2019.

“Our study was designed to construct nomograms to predict the overall survival (OS) and cancer-specific survival (CSS) of lip carcinoma patients. A search of the Surveillance, Epidemiology, and End Results (SEER) database provided us with detailed clinical data of the 1780 lip carcinoma patients. On the basis of the credible random split-sample method, the 1780 patients were placed into 2 groups, with 890 patients in the modeling group and 890 patients in the counterpart's group (proportion = 1:1). By employing Kaplan-Meier univariate and Cox multivariate survival analyses based on the modeling cohort, the nomograms were developed and then used to divide the modeling cohort into low-risk cohort and high-risk cohort. The survival rates of the 2 groups were calculated. Internal and external evaluation of nomogram accuracy was performed by the concordance index (C-index) and

calibration curves. With regard to 5- and 8-year OS and CSS, the C-indexes of internal validation were 0.762 and 0.787, whereas those of external validation reached 0.772 and 0.818, respectively. All the C-indexes were higher than 0.7. The survival curves of the low-risk cohort were obviously better than those of the high-risk cohort. Credible nomograms have been established based on the SEER large-sample population research. We believe these nomograms can contribute to the design of treatment plans and evaluations of individual prognosis.”

Treatment of Cancer of the Lips

Lip cancer is classified as oral cancer, or a cancer of the oral cavity, which also encompasses cancer of the throat, tongue, tonsils and salivary glands. It is estimated that there will be 29,000 new cases of oral cancer diagnosed this year, with approximately 10 to 15 percent of the cases being cancers found specifically on the lip. Risk factors for developing lip cancer include heavy tobacco and alcohol use, exposure to the sun and HPV infections.

Surgery

Surgery to remove the tumor is a common treatment for lip cancer. Depending on the size of the cancer on the lip, part of the tongue, jaw and palate also may be removed. This can affect the way many talk, swallow or chew, so reconstructive surgery is usually takes place to help rebuild these sections of the mouth that were removed.

Ant, A., Kilic, C., Baltu, Y., Duran, A.B., Tunccan, T., Ozlugedik, S. & Bozdogan, N. 2019.

OBJECTIVES: This study was aimed to overview the treatment protocols of lip cancer and find out a cutoff point of tumor diameter and depth of invasion (DOI) for the survival parameters.

MATERIALS AND METHODS: One hundred and ninety-one patients with lip SCC were studied.

RESULTS: The average age of the patients was 62 years. Among 191 patients, 82.7% of the patients were men, 96.4% of them had lower lipcancer, and 84% were staged as early (pT₁, pT₂). Primary tumor excision with neck dissection was applied to 62.3% of the patients. Lymph node metastases rate was found to be 11%, and recurrence rate was 6.3%. There was statistically significant difference in between the tumor diameters and DOI values of patients with and without metastasis, and recurrence ($p < 0.01$, $p < 0.05$, respectively). Regarding to the lymph node metastasis, the optimal cutoff point was found to be 7.5 mm for DOI and 21.5 mm for tumor diameter. Regarding to the recurrence, the optimal cutoff point was found to be 7.5 mm for DOI and 24.5 mm for tumor diameter.

CONCLUSION: T₂ lip cancer patients also seem to be in at-risk group for metastasis and recurrence. As a conclusion, elective neck dissection and frequent follow-up are recommended for these early-stage lip cancer patients.

Radiation Therapy

An option for very small tumours on the lip or people who cannot tolerate surgery, radiation therapy can be given internally or externally. It also is used prior to surgery to reduce the size of the tumour as well as after surgery to destroy any remaining cancer cells in the area.

Chemotherapy

Typically given at the same time as radiation therapy to treat lip cancer, the use of chemotherapy can result in infection and pain in the mouth and gum area. Commonly used chemotherapeutic drugs include 5-fluorouracil, bleomycin, carboplatin, cisplatin, docetaxel, ifosfamide, methotrexate and paclitaxel.

Targeted Therapy

A targeted anticancer therapy called Erbitux also can be used to treat lip cancer. It is usually given in combination with radiation or chemotherapy. Designed to bind to a substance called epidermal growth factor receptor (EGFR) that is found on the surface of lip cancer cells, targeted therapies can cause less harsh side effects as compared to chemotherapy.

Miskinli, R. & Ozgursoy, O. 2018.

“The aim of this study is to evaluate the general demographic and clinical features, and our treatment outcomes in our patients with lipcancers, during the last 15 years. This study was conducted as a retrospective chart-review, and included a total of 59 patients with lipcancer, who were diagnosed, treated, and followed-up at the otorhinolaryngology department of Ankara University, Faculty of Medicine, Ibn-i Sina Hospital between 2000 to 2015. 91.5% of cases were male with a mean age of 61.2 years, 39% were farmers, 87% were smoking, 40.7% had dental prosthesis and 67.8% had poor oral hygiene. 93.2% of the cases had lower-lip tumors and 72.9% had stage 1 tumors. Postoperative pathological assessments revealed well-differentiated squamous-cell carcinoma in 58.3% of cases. Neck dissection was performed in 52.5% of patients. Five-year survival rate was 96.1% and 10-year survival was 72.1%. Patients with and without neck dissection had similar survival rates. Lip cancers are frequent cancers, and constitute a significant health problem regarding functional and esthetic roles of the mouth region. Early-diagnosis provides effective treatment, but advanced cases require complex resection and reconstruction techniques. Neck dissection in early-diagnosed cases did not contribute to survival in our cases.”

About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The **South African National Clinical Trials Register** provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

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Cancer Treatment Centres of America

<http://www.cancercenter.com/oral-cancer/lip-cancer.cfm>

<http://www.cancercenter.com/oral-cancer/oral-cancer-staging.cfm>

CancerTreatment.net

<http://lip.cancertreatment.net/>

Cancer8

<http://www.cancer8.com/lip-cancer/stages.html>

Cigarette Smoke

<http://cancerwall.com/lip-cancer-photos-symptoms-pictures-signs-treatment/>

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Lips

<http://www.bing.com/images/search?q=images+lips&view=detail&id=048A8457C382797BB2E23B589CB820E5ED10A005&first=179&FORM=IDFRIR>

Lips 2

<http://www.bing.com/images/search?q=images+lips+dark+skin&view=detail&id=6DAD24EFD02E3C15355AABCBCDC237B97F53BF7D&first=144&FORM=IDFRIR>

Lip Cancer

<http://www.bing.com/images/search?q=staging+lip+cancer&view=detail&id=489F278FE0485480967A92F746E8E7A5B572254B&first=75&FORM=IDFRIR>

Mayo Clinic

<http://www.mayoclinic.com/health/mouth-cancer/DS01089/DSECTION=tests-and-diagnosis>

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<http://www.cancer.gov/clinicaltrials/learningabout/what-are-clinical-trials>

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