

## Cancer Association of South Africa (CANSA)



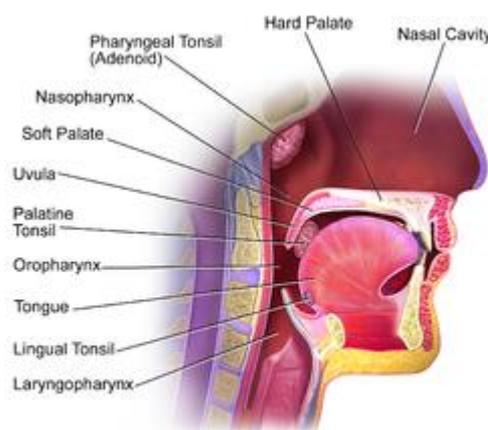
### Fact Sheet on Cancer of the Tonsils

#### Introduction

Tonsils are collections of lymphoid tissue facing into the aerodigestive tract. The set of lymphatic tissue known as Waldeyer's tonsillar ring includes the adenoid tonsil, two tubal tonsils, two palatine tonsils, and the lingual tonsil.

[Picture Credit: Tonsils and Throat]

When used unqualified, the term most commonly refers specifically to the palatine tonsils, which are masses of lymphatic material situated at either side at the back of the human throat. The palatine tonsils and the nasopharyngeal tonsil are lymphoepithelial tissues located near the oropharynx and nasopharynx (parts of the throat).



Tonsils and Throat

Tonsils are part of the lymphatic system and protect the body from harmful germs and contaminants. They lie strategically, just behind the mouth and nose, and form the first station of defense against all ingested and inhaled pollutants. The loose pieces of hanging tissue located on either side of the throat are called palatine tonsils. Those that lie within the throat, near the posterior opening of the nasal cavity are the adenoids, or pharyngeal tonsils. The paired structures that lie at the base of the tongue are called lingual tonsils.

Provide Immunity - tonsils function to trap bacteria and antigens and allow the body to produce antibodies against them. The primary function of the tonsils is to provide local immunity. They trap viruses, bacteria and other infectious contaminants and hold on to them before the immune system goes in for the kill.

Process Lymphatic Fluid - tonsils process lymphatic or lymph fluid in unison with other lymphoid tissue. Lymph fluid is circulated in the tissues of the lymphatic system. The lymphatic system functions to remove interstitial fluid from tissues and adjacent organs, to absorb fatty acids and transport them into the circulatory system, and to transport immune cells to and from lymph nodes. Lymph fluid contains fats, proteins and lymphocytes, which are a type of white blood cells. It plays a primary role in filtering and destroying germs and toxins.

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October 2021

Produce Antibodies - tonsils produce antibodies that neutralise respiratory infections (e.g. pneumonia, bronchitis, ear infections, laryngitis, sinusitis and rhinitis) that enter through the throat, mouth or nose. Antibodies (or immunoglobulins) are proteins that are found in the blood and other bodily fluids. They are produced by various components of the body's immune system and provide protection against chemicals, viruses, parasites, fungi and bacteria. They produce specific antibodies against staphylococcus aureus, haemophilus influenzae, streptococcus pneumoniae, poliovirus and diphtheria toxoid.

### **Cancer of the Tonsils**

Cancer of the Tonsils occurs when there is uncontrolled division of the tonsillar cells. Cancer of the tonsils usually involves the palatine tonsils on the sides of the throat. [Picture Credit: Cancer of the Tonsils]

Most tonsil cancers are squamous cell carcinomas but some are lymphomas.



### **Tumour Grade and Tumour Stage**

Tumour grade and stage are terms used to describe the severity of a tumour, while tumour grade describes the appearance of cancerous cells in the tissue by examining them under a microscope.

Tumour stage encompasses:

- The location of the tumour.
- The size and/or extent of the original tumour.
- Whether cancer cells have spread to lymph nodes or anywhere else in the body.
- The number of tumours present.

Doctors use tumour grade, cancer stage, and a patient's age and general health to decide the course of treatment for the patient and determine prognosis. Prognosis describes all factors including the disease course, cure rate, chances of survival, and risk of recurrence of cancer.

### What are the cancer stages?

Different systems of cancer staging are used to describe the types of cancer. Below is a common method in which stages are ranged from 0 to IV.

- Stage 0: The tumour is confined to its place of origin (in situ) and has not spread to nearby tissue.
- Stage I: The tumour is located only in the original organ, is small, and has not spread.

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- Stage II: The size of the tumour is large but has not spread.
- Stage III: The tumour has become larger and may have spread to surrounding tissues and/or lymph nodes.
- Stage IV: The tumour has spread to other distant organs of the body, which is known as the metastasis stage.

### TNM staging

Another common staging method used for cancer is the TNM system, which stands for tumour, node (which means spread of the tumour to lymph nodes), and metastasis. When a patient's cancer is staged using the TNM system, a number will be present along with the letter. This number signifies the extent of the disease in each category - tumour, node, and metastases.

Another system of cancer staging divides cancer into five stages, which include:

- In situ: Abnormal cells are present but have not spread to nearby tissue.
- Localized: Cancer is located only in the original organ and shows no sign of its spread.
- Regional: Cancer has spread to nearby lymph nodes, tissues, or organs.
- Distant: Cancer has spread to distant parts of the body.
- Unknown: The stage cannot be figured out due to a lack of enough information.

### What are the cancer grades?

Cancer grades are based on examination of the suspected tissue sample under a microscope. This involves surgically removing a piece of the suspected cancerous tissue and sending it to the lab for analysis. The entire procedure is known as a biopsy.

A doctor who specializes in diagnostic tests (pathologist) examines the cells of the tissue and determines whether they are harmless (benign or noncancerous) or harmful (malignant or cancerous). They describe the microscopic appearance of the cells and assign a numerical "grade" to most cancers. Generally, a lower grade indicates slow-growing cancer and a higher grade indicates fast-growing cancer.

The most commonly used grading system is as follows:

- Grade I: Cancer cells that look like normal cells but are not growing rapidly.
- Grade II: Cancer cells that don't look like normal cells with their growth being faster than normal cells.
- Grade III: Cancer cells that look abnormal and have the potential to grow rapidly or spread more aggressively.

Sometimes, the following system can be used:

- GX: Grade cannot be assessed (undetermined grade)
- G1: Well-differentiated (low grade)
- G2: Moderately differentiated (intermediate grade)
- G3: Poorly differentiated (high grade)
- G4: Undifferentiated (high grade)

## **Incidence of Cancer of the Tonsils in South Africa**

The outdated National Cancer Registry (2017), known for under reporting, does not provide any information regarding the incidence of cancer of the tonsils.

## **Signs and Symptoms of Cancer of the Tonsils**

Patients with cancer of the tonsils may have one or more of the following symptoms:

- A sore in the back of the mouth that will not heal
- One tonsil is larger on one side
- Blood in the saliva
- Mouth pain
- Difficulty chewing, swallowing or speaking
- Persistent sore throat
- Intolerance to eating or drinking citrus foods
- Severe ear pain
- A lump in the neck
- A pain in the neck
- Pain when swallowing (dysphagia)
- Bad breath

## **Causes and Risk Factors for Cancer of the Tonsils**

Men are diagnosed with tonsil cancer three to four times more often than women. Cancer of the tonsils are diagnosed at age 50 or older, although it can develop at any age. The most significant risk factors for tonsil cancers are:

- Tobacco use
- Smokeless tobacco (snuff and betel nut) use
- Alcohol consumption

## **Broglie Däppen, M.A. 2020.**

“In the past decades, an increasing incidence of oropharyngeal squamous cell cancer could be observed. More than twenty years ago, a correlation between a pharyngeal Human papillomavirus high-risk type infection and the development of oropharyngeal cancer has been suspected. Especially younger patients without the former risk factors smoking and alcohol have a higher prevalence for this cancer type. HPV-associated cancer is developing in the lymphatic tissue of the tonsils and the base of the tongue. HPV-driven tumors can be defined as a clinical and morphologic distinct tumor entity with a significantly better prognosis compared to tumors based on smoking and alcohol consumption. They are demonstrating a clearly better treatment response irrespective of the treatment modality. The tumor development is assumed to be comparable to cervical cancer, probably through a step-wise process from dysplasia to invasive cancer. In the pharynx, no HPV-associated precursor lesions have been detected so far. Therefore, Screening program proven to be very successful in the cervix have not could not have been implemented so far. The reduction of HPV-associated tumor burden in the cervix is likely to be compensated by the rising number of HPV-driven oropharyngeal cancer. P16 as a surrogate marker for HPV has been implemented in the 8th edition of

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the TNM classification for oropharyngeal cancer. A worldwide accepted definition of an HPV-driven tumor is lacking so far. P16 immunohistochemistry or HPV-DNA detection by PCR as single markers have an insufficient sensitivity and specificity. A combination of both markers demonstrates a higher accuracy compared to the gold standard RNA. Antibodies to HPV oncoproteins are reliable diagnostic and prognostic markers that could in the future possibly serve for early tumor detection.”

Other potential causes include people with certain infections or decreased immunity such as:

- Exposure to human papilloma virus (HPV), especially strains 16 and 18
- Organ transplant recipients
- People with Human Immunodeficiency Virus (HIV) disease

**Wittekindt, C., Wagner, S., Bushnak, A., Prigge, E.S., von Knebel Doeberitz, M., Würdemann, N., Bernhardt, K., Pons-Kühnemann, J., Maulbecker-Armstrong, C. & Klussmann, J.P. 2019.**

“Increasing incidences of head and neck cancers and rising proportions of these associated with human papillomavirus (HPV), especially in the oropharynx, have been reported in international studies. So far, the trends and contribution of HPV to the number of newly diagnosed cases of oropharyngeal squamous cell carcinomas (OPSCC) in Germany are uncertain. We investigated HPV association and incidence rates in a cohort of consecutively included patients with OPSCC in Giessen 2000-2017, and compared our results with regional (Giessen and the federal state of Hesse), national (Germany), and international (United States) databases. Regional data show a significant increase in the overall incidence rates of oropharyngeal cancers and in the incidence of HPV-associated cancers of the subsites tonsils and oropharynx, whereas other oropharyngeal subsites show no significant change. Analysis of national databases shows a significant incidence increase in Germany and in the United States. The rise in incidence is predominantly attributable to male patients in the US population, whereas in Germany rising OPSCC incidence is more associated with females. There is a significant elevation of OPSCC incidence rates in Germany, which corresponds to the recognized incidence increase of HPV-related oropharyngeal cancers based on experimental data from consecutively included patients of our cohort. Our investigation shows different patterns of this increase in Germany and in the United States, which demonstrates spatial heterogeneity and the need for population-based investigations regarding the role of HPV in oropharyngeal cancer.”

### **Treatment of Cancer of the Tonsils**

Patients may have either surgery or radiotherapy to treat early tonsil cancer. Early means a small tumour that is still contained within the tonsil. If one has a cancer that is larger, has grown throughout the tonsil, or has started to grow outside it, one may have surgery followed by radiotherapy. More advanced cancers that have grown outside the tonsil may need shrinking before they can be removed. One may have chemotherapy or radiotherapy or both to try to shrink the cancer. This is called down staging. If the cancer does shrink, one may then be able to have an operation to remove it.

Advanced cancers cause symptoms such as pain, bleeding and difficulty swallowing. Patients are given radiotherapy or chemotherapy or both to help control symptoms.

There are other experimental treatments being investigated, for example, photodynamic therapy (PDT). For this treatment, patients have to take a drug that concentrates in the cancer cells. The drug is harmless until a bright light is shone onto the cancer cells. This then kills the cells.

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Treatment depends on how far the cancer has grown.

The first step is to find out:

- How far the cancer has grown into local tissues
- Whether it has spread to nearby lymph glands
- Whether it has spread to any other part of the body

This is called staging the cancer. The doctor will be able to tell which treatment is best once the cancer has been staged.

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A common treatment for tonsil cancer involves using radiation therapy in combination with chemotherapy.

Surgery – the patient may be able to have an operation to remove the part of the throat that contains the cancer. There are different types of operation. The part of the throat removed depends on the exact site of the tumour. If the cancer is very small, the patient may only need a very simple operation. This can be done using local anaesthetic or with laser surgery, and overnight stay in the hospital.

For larger more extensive cancers one may need a more complicated operation and need to stay in hospital for a while. For the most complicated surgery, one may have to have part of the soft palate or the back of the tongue removed. The surgeon will rebuild this with tissue taken from another part of the body.

All types of treatments have side effects. Sometimes surgery to the throat causes a lot of swelling in the area and makes it difficult to breathe normally. If this is the case then the surgeon may need to

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make a hole in the patient's windpipe, at the base of the neck. This hole is called a tracheostomy and will allow the patient to breathe while the swelling is there. It is usually only temporary and will be removed once the wound has healed.

Some operations on the throat can affect speech. We take it for granted that it is easy to speak, but it is actually a very complicated process. To produce sound humans use their throat, soft palate, lips, nose, mouth and tongue. If one has surgery to any of these, speech may change. This may not be very noticeable and may only be temporary. But sometimes the change is permanent. If a patient has any speech difficulties at all, a speech and language therapist can help you manage.

**Spellman, J., Coulter, M., Kawatkar, A. & Calzada, G. 2020.**

**Purpose:** To compare treatment costs and cost-effectiveness for transoral robotic surgery (TORS) and definitive intensity-modulated radiotherapy (IMRT) in managing early stage tonsil cancer.

**Materials and methods:** Direct treatment costs for surgery and IMRT were calculated from SEER-Medicare data for a cohort with clinically early stage (cT1/2N0) p16+ tonsillar squamous cell carcinoma from Kaiser Permanente Southern California Health Plan between 2012 and 2017. A Markov decision tree model with a 5-year time horizon was then applied to the cohort which incorporated costs associated with treatment, surveillance, and recurrence.

**Results:** IMRT cost up to \$19,000 more (35%) than TORS in direct treatment costs. When input into the Markov model, TORS dominated IMRT with lower cost and better effectiveness over a range of values.

**Conclusion:** TORS is a more cost-effective treatment method than IMRT in early stage (cT1/2N0) tonsil cancer.

**Williamson, A.J., MULLangi, S. & Gajra, A. 2020.**

"Tonsil cancer is the most common form of oropharyngeal malignancy, and its incidence is sharply rising due to the increasing prevalence of human papillomavirus (HPV)-induced cancers. The presence of HPV can dramatically alter the prognosis of tonsillar cancer, and there have recently been significant changes made to the WHO classification and TNM staging to reflect this. Tonsil cancer can be managed by both surgical and oncological approaches, although the optimal treatment regimen remains an area of ongoing research."

**Patel, E.J., Zhu, A.W., Oliver, J.R., Cornwell, M., Jacobson, A.S., Hu, K.S., Tam, M., Vaezi, A., Morris, L.G.T. & Givi, B. 2020.**

**Objective:** To investigate the patterns of care and outcomes of treatment of early stage tonsil cancers, controlling for human papillomavirus (HPV) status.

**Study design:** Historical cohort study.

**Setting:** National Cancer Database (NCDB).

**Methods:** Review of the NCDB between 2010 and 2017 for all T1-2N0M0 tonsillar squamous cell carcinoma (SCC). Demographics, clinical characteristics, HPV status, treatment regimens, and survival were analyzed.

**Results:** A total of 4720 patients were identified with early stage SCC of the tonsil. Most were tested for HPV (2759 [58.5%]). Among tested patients, 1758 (63.7%) were positive for HPV and 1001 (36.3%) were negative for HPV. HPV-positive patients had higher 3-year survival compared to HPV-negative patients (93.2% vs 77.8%,  $P < .001$ ). Among HPV-positive patients, there was no significant difference in survival between treatment cohorts. However, in the HPV-negative cohort, 3-year survival was higher in both bimodality surgical-based settings (tonsillectomy + neck dissection + radiotherapy, 86.0% vs chemoradiotherapy, 69.6%,  $P = .01$ ) and for all surgical-based treatments when compared to nonsurgical management (84.6% vs 69.3%,  $P < .001$ ). This difference was maintained in multivariable

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regression controlling for age, sex, comorbidities, clinical T stage, and treatments. In a subpopulation of HPV-negative patients propensity score matched by all factors significant in multivariable analysis, 3-year survival remained higher in the surgically treated group compared to the nonsurgically treated cohort (84.9% vs 67.1%,  $P < .001$ ).

**Conclusions:** Surgical- or radiation-based treatment resulted in similar survival in early stage HPV-positive tonsil cancer. Surgical-based treatments were associated with longer survival in HPV-negative cancers. These findings should be further investigated in a randomized prospective trial.

**Meccariello, G., Montevicchi, F., D'Agostino, G., Iannella, G., Calpona, S., Parisi, E., Costantini, M., Cammaroto, G., Gobbi, R., Firinu, E., Sgarzani, R., Nestola, D., Bellini, C., De Vito, A., Amadori, E. & Vicini, C. 2019.**

**PLAIN-LANGUAGE-SUMMARY:** “Trans-oral robotic surgery (TORS) has changed surgical management of patients with oropharyngeal squamous cell carcinomas (OPSCC). In this study we present surgical and oncologic outcomes of patients with oropharyngeal squamous cell carcinomas, treated using TORS, with and without an adjuvant therapy. Sixty patients with oropharyngeal squamous cell carcinomas treated with TORS between January 2008 and December 2017 have been retrospectively evaluated considering clinicopathologic features, disease characteristics, adjuvant treatments and oncological outcomes. TORS was performed for OPSCC to the base of tongue in 41.7%, tonsils in 46.7%, soft palate and posterior pharyngeal wall in 3.3% and 5%, respectively. Neck dissection was performed in 43.3% of patients. Management strategies included surgery alone in 30%, TORS and adjuvant radiotherapy in 33.3%, and TORS plus adjuvant chemotherapy in 36.7%. The 5-year overall survival of the total group was 77.6%, the 5-year disease-free survival rate was 85.2%, and the 5-year local recurrence-free survival rate was 90.6%. Finally, in selected patients TORS appears to yield similar oncologic outcomes and functional outcomes to traditional techniques and non-operative treatment with a possible benefit on long-term quality of life. The future offers exciting opportunities to combine TORS and radiotherapy in unique ways. However, further research is urgently needed to clarify the indications for adjuvant therapy following TORS resections.”

Radiotherapy – patients may have radiotherapy:

- On its own to treat a small tonsil cancer
- Either before or after surgery to treat a larger cancer
- To help relieve the symptoms of advanced tonsil cancer

Doctors may use both external radiotherapy and internal radiotherapy (brachytherapy) to treat tonsil cancer. External radiotherapy treatment is usually given once a day for a few weeks. Brachytherapy is most likely to be used for small cancers. Patients may have brachytherapy if the cancer has come back after earlier treatment with external beam radiotherapy.

There are several types of radiation used in radiation therapy such as:

- High-energy X-rays
- Electron beams
- Radioactive isotopes

Chemotherapy - chemotherapy uses anti-cancer (cytotoxic) drugs to destroy cancer. Chemotherapy has not always been a treatment of choice for tonsil cancer. But recent research has suggested that

combining chemotherapy with radiotherapy may help as much as surgery for large cancers of the head and neck, including tonsil cancer. Further research is needed in this area.

If one has tonsil cancer, one may have chemotherapy before the main treatment to help shrink the cancer. This is called neo adjuvant treatment. When a cancer is shrunk before further treatment, this is called down staging.

### **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](http://www.sanctr.gov.za/) 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.

For additional information, please visit: [www.sanctr.gov.za/](http://www.sanctr.gov.za/)

### **Medical Disclaimer**

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### Tonsils and Throat

<https://en.wikipedia.org/wiki/Tonsil>

### Tonsil Cure

<http://tonsilcure.com/cancer.html>

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**Tumour Grade and Tumour Stage**

[https://www.medicinenet.com/cancer\\_101\\_pictures\\_slideshow/article.htm](https://www.medicinenet.com/cancer_101_pictures_slideshow/article.htm)

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