IS REHABILITATION OF OLFACTION NECESSARY IN PATIENTS UNDERGOING TOTAL LARYNGECTOMY

A DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF M.S BRANCH IV OTORHINOLARYNGOLOGY EXAMINATION OF THE TAMIL NADU DR. M.G.R.MEDICAL UNIVERSITY TO BE HELD IN APRIL 2016.

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DEPARTMENT OF OTORHINOLARYNGOLOGY
CHRISTIAN MEDICAL COLLEGE
VELLORE

CERTIFICATE

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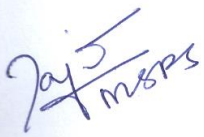

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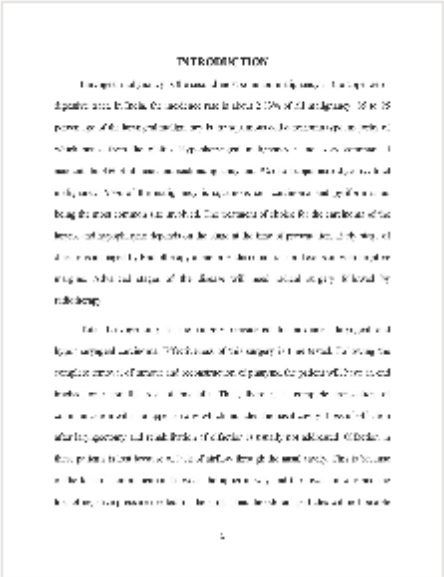

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INTRODUCTION

Laryngeal malignancy is the second most common malignancy in the upper aero-digestive tract. In India, the incidence rate is about 2.63% of all malignancy. 85 to 95 percentage of the laryngeal malignancy is the squamous cell carcinoma type, majority of which arises from the glottis. Hypopharyngeal malignancy is not very common. It accounts for 4% of all head and neck malignancy and 7% of all upper aero-digestive tract malignancy. 95% of the malignancy is squamous cell carcinoma and pyriform sinus being the most common site involved. The treatment of choice for the carcinoma of the larynx and hypopharynx depends on the stage at the time of presentation. Early stage of disease is managed by Radiotherapy alone or Endoscopic transoral excision with negative margins. Advanced stages of the disease will need radical surgery followed by radiotherapy.

Total Laryngectomy is the surgery considered for advanced laryngeal and hypopharyngeal carcinoma. Effectiveness of this surgery is time tested. Following the complete removal of tumour and reconstruction of pharynx, the patient will have an end tracheostome for the rest of his life. Thus, there is a complete transection of communication with the upper airway which includes the nasal cavity. Loss of olfaction after laryngectomy and rehabilitation of olfaction is usually not addressed. Olfaction in these patients is lost because of lack of airflow through the nasal cavity. This is because of the loss of communication between the upper airway and the lower air way and the loss of negative pressure needed for the sniff. Thus the odorant particles will not be able

to reach the olfactory epithelium situated in the roof of the nasal cavity and perception of smell will not occur.

Olfaction, being one of the special senses, enhances the quality of life. There is not only loss of smell for laryngectomised patients, but also significant loss of taste. Loss of smell also leads to loss in appreciating the flavour of the food and hence there is significant loss in the quality of life of these patients.

Olfaction also helps in analysing danger which is essential for daily living. As a result of loss of smell, the danger of leaking gas, smell of burnt substances, smell of toxins etc. will not be appreciated.

This prospective study was conducted to assess olfaction after total laryngectomy. Olfaction was assessed prior to and after surgery to document the loss of smell in these patients.

Olfaction rehabilitation using Nasal Airflow Inducing Manoeuvre (NAIM) called as Polite Yawn technique was used to study the effectiveness of this simple manoeuvre in improving olfaction following laryngectomy.

Loss of smell and loss of appetite also affects the quality of life. Quality of life (QOL) assessment was done using a questionnaire called Appetite, Hunger and Sensory Perception (AHSP) in this study.

AIM AND OBJECTIVES

AIM OF STUDY

- To assess whether olfactory rehabilitation is necessary in patients following laryngectomy
- To assess the effectiveness of Nasal Airflow Inducing Manoeuvre (NAIM) also known as Polite Yawn Technique in improving olfaction in laryngectomised patients

OBJECTIVES

- To compare the olfactory acuity of patients prior to and after total laryngectomy
- To assess effectiveness of nasal airflow inducing maneuver (NAIM) – Polite yawn technique in laryngectomised patients, in improving olfaction by comparing olfaction following laryngectomy and after teaching the patient NAIM.
- To assess the quality of life of laryngectomised patients with relation to olfaction, taste and appetite

REVIEW OF LITERATURE

Malignancy of Larynx is the second most common malignancy of the upper aerodigestive tract (1). This accounts for approximately 1.7% of all new cancer diagnosis and 30% of all head and neck malignancies (2,3). 90% of laryngeal malignancy is squamous cell carcinoma (2).

Laryngeal carcinoma in India constitutes about 2.63% of all malignancies with incidence of 3.29 new cases in males and 0.42 new cases in females for one lakh population(4). Laryngeal carcinoma is ten times more common in males than females (4.79% vs 0.47%) (4). Peak incidence of laryngeal malignancy occurs in seventh decade in men and before the sixth decade in women (5).

Laryngeal malignancy is classified as supra glottis, glottis and subglottis malignancy. The glottic malignancy being the most common site involved and squamous cell carcinoma is most common type (6). It is staged based on the TNM staging developed by the International Union against Cancer(7).TNM classification describes tumour staging from T1 to T4, regional metastasis from N0 to N3 and distant metastasis as M0 and M1, and further staged based on this.

Malignancy of hypopharynx is relatively rare. It accounts for 4 % of all head and neck malignancies and 7 % of malignancies of the upper aerodigestive tract (8,9). It has the highest mortality rate among the malignancy of the head and neck, with overall 5 year survival rate of 30 to 35 % (8,9). Tumours of the hypopharynx present at an advanced stage when there is neural invasion causing pain or when there are symptoms of airway or digestive tract obstruction (10).

At the time of presentation about 60 to 80 % of the patients have cervical metastasis (11–15). Sub-mucosal spread occurs in hypopharyngeal malignancy making it difficult for clinical staging. More than 75% present with stage III or IV disease (8).

Hypopharynx is divided into three subsites – the pyriform sinus, posterior pharyngeal wall and post cricoid region. Of the three subsites, malignancy of the pyriform sinus is the most common, accounting for more than 60 % of hypopharyngeal malignancy. The least common is the post cricoid malignancy, representing less than 5 % of the cases (9).

EMBRYOLOGY, ANATOMY AND HISTOLOGY OF LARYNX AND HYPOPHARYNX

EMBRYOLOGY

The larynx is divided into three regions or sites: supra glottis, glottis and sub glottis. It is divided based on the embryologic structure of the larynx and the anatomical barriers to spread of laryngeal cancer. The pattern of spread of tumors within the larynx is guided by the ligaments, connective tissue membranes and cartilages of the larynx that contain the spread of tumour. The soft tissue spaces within the larynx also act as pathways within and outside of the larynx.

The characteristic tumour pattern can be explained by the embryologic development of the larynx. The supra glottis is derived from the buccopharyngeal primordium, which develops from the third and fourth branchial arches. The glottis and sub glottis are developed from the tracheobronchial primordium. Based on the development, the larynx has a dual blood supply and lymphatic drainage.

The supra glottis is supplied by the superior laryngeal arteries and its lymphatic drainage follow these vessels into the carotid sheath into the deep cervical nodes in level 2 and level 3. The glottis and sub glottis are supplied by the inferior laryngeal arteries, and lymphatic drainage from these regions follow these arteries to drain into pre laryngeal and pre tracheal nodes, and finally drains into deep cervical nodes in level 4 (16).

The glottic region is formed by the paired structures that fuse in the midline. So the lymphatics drain unilaterally. The vocal folds have sparse lymphatics. This explains the lower incidence of lymphatic metastasis in glottis squamous cell carcinoma. But the supra glottis is formed without a midline union, its lymphatics drain bilaterally and this causes the increased likelihood of bilateral lymphatic metastasis from supra glottic carcinoma (17).

ANATOMY

The larynx is divided into three sites - supraglottis, glottis and subglottis (Fig 1). This division reflects the embryologic structure and the anatomic barriers to spread of laryngeal cancer.

The supraglottis is composed of the suprahyoid and infrahyoid epiglottis (both the lingual and the laryngeal surfaces), aryepiglottic folds (laryngeal surface only), arytenoids and the ventricular bands (false cords). The inferior limit of supra glottis is a horizontal plane through the lateral margin of the ventricle at its junction with the superior surface of the true vocal cords.

The glottis consists of bilateral true vocal cords including the anterior and posterior commissures. The inferior surface of the glottis is 5 mm below the level of vocal folds anteriorly and 10 mm posteriorly (18). The subglottis extends from the inferior limit of the glottis to the inferior edge of the cricoid cartilage (Fig 1).

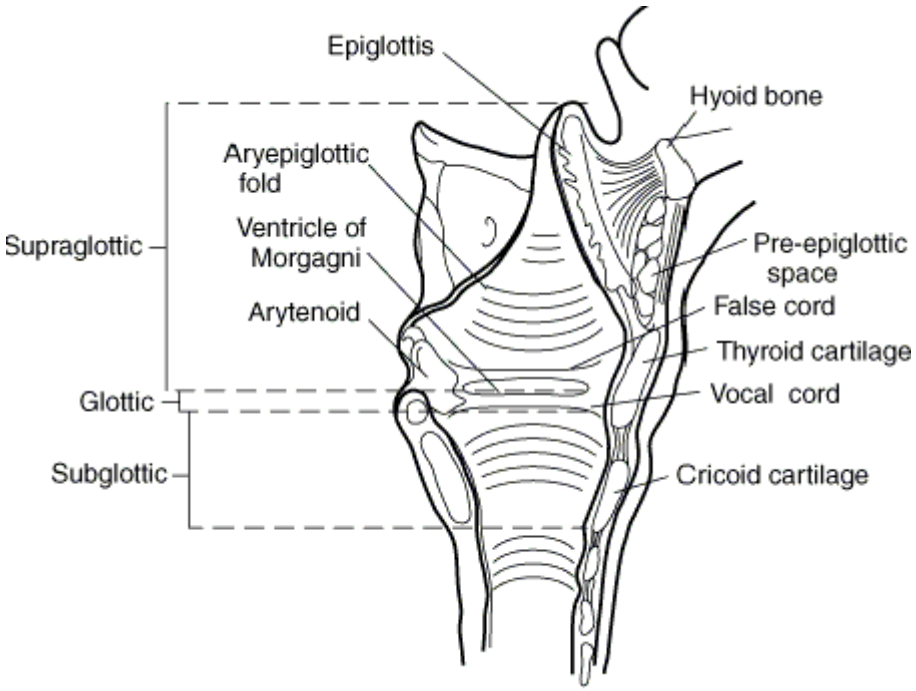

Figure 1 – Cross section anatomy of larynx (Adopted from Current Diagnosis & Treatment in Otolaryngology - Head & Neck surgery. 2nd Edition)

The hypopharynx is divided into three parts – Postcricoid area, Pyriform sinus and the Posterior pharyngeal wall (Fig 2) (19).

Postcricoid area forms the anterior wall of the hypopharynx. It extends from the level of the arytenoid cartilage to the lower border of cricoid cartilage.

The pyriform sinus is bounded laterally by the thyrohyoid membrane and the thyroid cartilage and medially by the aryepiglottic fold and the cricoid cartilage. It extends from the pharyngoepiglottic fold to the upper end of oesophagus (19).

Posterior pharyngeal wall forms the posterior wall of the hypopharynx. It extends superiorly from the level of hyoid or the floor of vallecula and inferiorly upto the level of the inferior border of the cricoid cartilage (19).

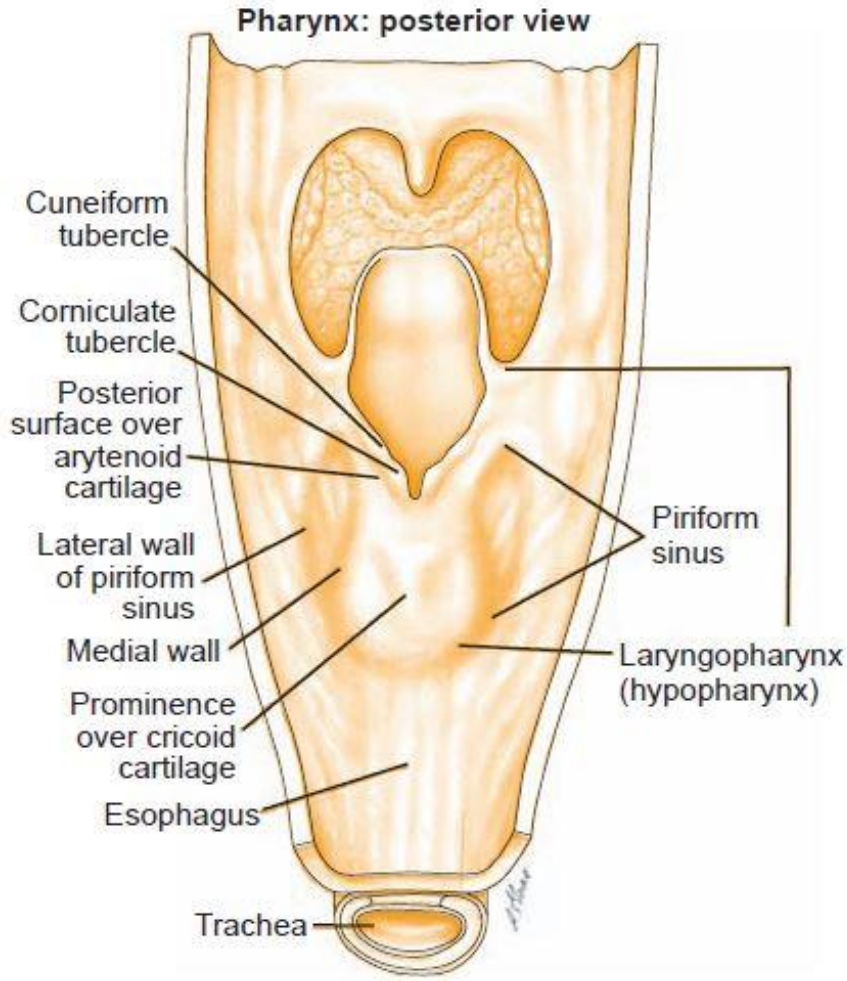

Figure 2 – Anatomy of Hypopharynx ((Adopted from Cummings Otolaryngology Head and Neck Surgery, 6th edition)

HISTOLOGY

The mucosal lining of the larynx differs in the three regions. The epithelium of the supra glottis is predominantly of the pseudo stratified columnar type. The edges of the aryepiglottic folds and the lateral borders of the epiglottis are lined by stratified squamous epithelium.

The true vocal cords have a unique structure: non keratinized stratified squamous epithelium, which covers a three layered lamina propria. The lamina propria is composed of superficial, intermediate and deep layers. The intermediate and deep layers of lamina propria form the vocal ligament.

The subglottis is lined by pseudo stratified columnar epithelium (20).

The hypopharynx is lined by non-keratinizing stratified squamous epithelium.

AETIOLOGY OF LARYNGEAL AND HYPOPHARYNGEAL MALIGNANCY

Various aetiological factors have been explained for laryngeal and hypopharyngeal malignancy. Tobacco and alcohol consumption is strongly associated with squamous cell carcinoma of larynx. An association of tobacco and alcohol with carcinoma of larynx and hypopharynx is present each acting – individually and synergistically (21,22). 98% of persons diagnosed with laryngeal malignancy are smokers, explaining the strong association of laryngeal malignancy with smoking habit (23). Alcohol consumption has contributed to hypopharyngeal malignancies more than laryngeal malignancies (24)

Workers with exposure to nickel and chromate in industries have an increased incidence of laryngeal malignancy (25). Workers exposed to asbestos, carbon and formaldehyde have increased risk of developing hypopharyngeal malignancy (26). Gastric acid reflux and Barett's oesophagus are carcinogenic cofactor for laryngeal malignancy. Galle and colleagues studied the role of acid and alkali reflux in laryngeal squamous cell carcinoma (27). They have identified association of laryngeal and pharyngeal malignancy with achlorhydria. They have also identified the increased incidence of laryngeal malignancy with acid reflux. Their study showed 81% of people with laryngeal malignancy had abnormal acid reflux on 24 hours pH monitoring (27).

Human Papilloma Virus subtypes 16 and 18 infection is also a known aetiological factor for laryngeal malignancy (28). Consumption of fruits and vegetables with higher Vitamin A and Vitamin C content is found to have a protective effect, as there is an

increased incidence among communities with ain poor nutritional status.(29). These aetiological factors act at various levels in the molecular structure of the laryngeal epithelium causing series of events transforming normal mucosa to premalignant lesions and later to invasive disease (30).

Patient with Plummer-Vinson syndrome has a 10 % chance of developing malignancy of hypopharynx (31). Plummer Vinson syndrome was first described by Plummer and Vinson in 1922 which comprises of iron deficiency anaemia, glossitis, oesophageal webs, koilonychiasis and dysphagia (32). It occurs due to mucosal changes as a result of iron deficiency anaemia and chronic mucosal irritation by the retained food (33).

Treatment of laryngeal and hypopharyngeal malignancy depends on the type, size and staging of the disease. Various treatment options like surgery, radiation, chemotherapy are effective in the treatment of laryngeal and hypopharyngeal cancer. Single modality or combined modality of these is used based on the staging of the disease. Total laryngectomy is one of the surgical treatment options available for advanced stages of the disease. Total laryngectomy results in a permanent disconnection of the upper and lower airways with breathing through a permanent opening in the trachea, a so called stoma. Consequently, the natural airflow will be totally missing or disrupted.

SPREAD OF LARYNGEAL AND HYPOPHARYNGEAL TUMOURS

Tumours of the larynx remain localized to the site of origin of the tumour during the early stage of the disease because of the embryological development of the larynx. Ligaments and perichondria form separate compartments, which limits the spread of the disease till these barriers are breached. During the late stage of the disease, tumour spreads along the pathway of least resistance (34).

SUPRAGLOTTIC TUMOURS

Supraglottic tumour spread can be divided based its location. It can be divided into four types, epiglottic tumours, false cord tumours, ventricle tumours and tumours of arytenoids and aryepiglottic fold.

Epiglottic tumours

Tumour involving the suprahyoid epiglottis is usually limited to the epiglottis. These tumours are usually over staged. This is because these lesions are usually proliferative and exophytic and are like a ball-valve causing significant airway obstruction (35).

Infrahyoidepiglottic tumours spread both inferiorly and posteriorly. Posteriorly it spreads circumferentially, spreading to the false cords, aryepiglottic fold, pharyngoepiglottic fold and the medial wall of pyriform sinus. Inferiorly it spreads to the petiole of the epiglottis. This involves the anterior commissure and thyroid cartilage.

Early invasion of thyroid cartilage and involvement of pre-epiglottic space is very common in these tumours (36).

Tumours of False cords

Isolated tumours of the false cords are rare. The inferior spread of the tumour is limited by the ventricle. At a later stage, the tumour crosses the ventricle to become a glotto-supraglottic disease. The tumour spreads posteriorly to involve the arytenoids (37).

Tumours of Ventricle

Ventricle tumours spread laterally to involve the paraglottic space. Thus a major portion of the tumour remains hidden. Spread to the thyroid cartilage, involvement of preepiglottic space is very common (38). Significant submucosal extension occurs in these tumours (Fig 3).

Tumours of arytenoids and aryepiglottic fold

These types mostly behave like a hypopharyngeal malignancy. Involvement of the postcricoid region and the pyriform sinus is very early. It is considered as a marginal zone cancer.

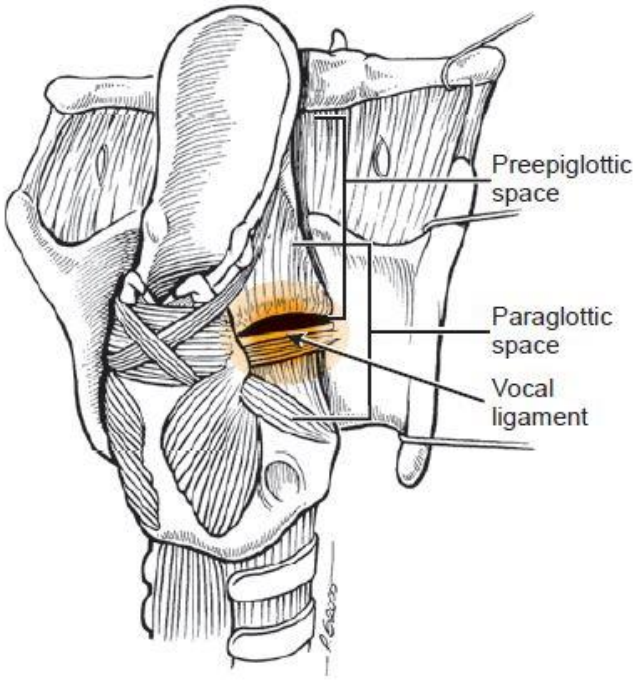

Figure 3 – Preepiglottic and paraglottic space (Adopted Cummings Otolaryngology Head and Neck Surgery, 6th edition)

GLOTTIC TUMOURS

The spread of the glottis tumours is divided into two, vocal cord lesions and anterior commissure growth

Vocal cord growth

Majority of the glottis tumours arise from the free edge of the anterior two third of the vocal cords. The first barrier is the Reinkes space, which prevents the spread to the underlying muscles (39). It also helps in easy resection without damaging the underlying muscle. Spread occurs in 3 directions, anterior, lateral and vertical (Fig 4).

Anterior growth occurs along the length of the vocal cord to the anterior commissure. The Broyles ligament functions as a barrier to this spread (36). Vertical spread can be superior or inferior. Superior spread is rare and is limited by the ventricle. Inferior spread to the subglottis is restricted by the conus elasticus.

Lateral spread occurs to the paraglottic space and early involvement of the thyroid cartilage. The thyroarytenoid muscle involvement occur causing vocal cord fixation.

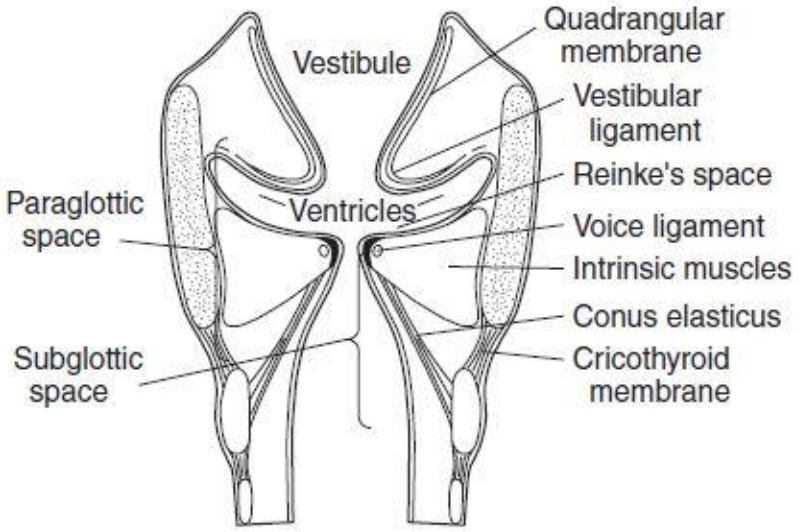

Figure 4 – Cross section anatomy of larynx (Adopted from Current Diagnosis & Treatment in Otolaryngology - Head & Neck surgery. 2nd Edition)

Anterior commissure lesion

Anterior commissure tumours invade the thyroid lamina very early and spread to the anterior epiglottic space. Also these tumours spread in a mushroom like pattern

through the anterior subglottic wedge. This erodes the cricothyroid ligament and tumour becomes extralaryngeal (36).

SUBGLOTTIC TUMOURS

Subglottic tumours are very rare. These occur in less than 1 % of all the laryngeal tumours. These tumours grow circumferentially and early involvement of the cricoid cartilage occurs.

HYPOPHARYNGEAL TUMOURS

Sub mucosal spread of tumour and skip lesions are very common in hypopharyngeal malignancy. This results in underestimation of the disease extent and under staging of the disease (11). Histopathology after excision of tumours reveals submucosal extension in 60 % of the specimen. Post radiotherapy the incidence of submucosal spread is further increased (26).

Pyriform sinus tumour

The pyriform sinus malignancy can spread superiorly to involve the base of tongue, inferomedially to reach the postcricoid region and posteriorly to involve the posterior pharyngeal wall. Tumour in the apex of the pyriform sinus spread rapidly to the paraglottic and preepiglottic space, thus causing early vocal cord fixation (40). Tumour involving the lateral wall can cause early involvement of the thyroid cartilage, causing erosion and having extralaryngeal spread involving the thyroid gland. Tumour involving the anterior and medial wall of pyriform sinus spreads superiorly to involve the

arytenoids and aryepiglottic folds. It also invades the paraglottic space at a much earlier stage, causing vocal cord fixation (41).

Posterior pharyngeal wall tumour

Growth involving the posterior pharyngeal wall attains a larger size before causing vocal cord fixity. It can extend superiorly upto the nasopharynx, inferiorly to the cervical oesophagus and posteriorly involving the prevertebral fascia (41).

Postcricoid tumour

Post cricoid growth is circumferential and causes symptoms of difficulty in swallowing. It involves the posterior cricoarytenoid muscle, the cricoid and arytenoid cartilage. The tumour can spread anteriorly to involve the paraglottic space cause vocal cord fixity either unilateral or bilateral. It spreads inferiorly to involve the cervical oesophagus. Posteriorly it spreads to involve the prevertebral fascia (41)

Lymphatic spread

Hypopharynx has a rich lymphatic network. Spread through lymphaticcs occurs first to the jugular group of lymph nodes followed by the lateral pharyngeal, retropharyngeal and trachea oesophageal nodes. At the time of presentation 60 to 70 % of the patients have a clinically palpable lymph node (11–15,42). Nodal metastasis occurs mostly in Level II (72%–75%), level III (55%–72%) and level IV (21%–45%) zones (43,44).

TREATMENT OPTIONS FOR ADVANCED LARYNGEAL AND HYPOPHARYNGEAL MALIGNANCY

Total laryngectomy has been the mainstay gold standard of treatment for several years in advanced laryngeal and hypopharyngeal malignancy. Due to the increased morbidity (like permanent tracheostomy, swallowing disturbance and loss of voice) more conservative treatment options were explored. The conservative procedures where concerned with preservation of the functions of the organs, and called the organ preservation strategies (45).

Organ preservation strategies

The concept of organ preservation started in the year 1991 after the study by the Department of Veterans Affairs Laryngeal Cancer Study Group. For advanced malignancy of the larynx and hypopharynx, combination of chemotherapy with radiotherapy as a treatment option was compared with the treatment option of laryngectomy followed by radiotherapy. The cure rate attained was equal in both groups (45). Induction chemotherapy followed by radiotherapy hence helped in preserving the larynx in approximately two thirds of the patients with advanced laryngeal malignancy.

Concurrent chemoradiotherapy, also an organ preservation strategy, increased the percentage of cure rate when compared to induction chemotherapy followed by radiotherapy or radiotherapy alone (46).

Increased effectiveness of this treatment thus reduced the need for total laryngectomy. The advantage of this treatment option was that at the end of the treatment, the patient would have a functioning larynx.

Mortality of about 4% is reported in patients undergoing concurrent chemo radiotherapy indicating the aggressive nature of the disease (47). Also at the end of the treatment, the patients could have a non-functional larynx, requiring tracheostomy.

Surgical options

Transoral laryngeal surgery

It is the surgical resection of the laryngeal tumour via an endoscopic approach. Endoscopic resection of laryngeal tumour was first performed by Chevalier Jackson for resecting an epiglottic tumour (48). It was not routinely performed due to the lack of instrumentation and difficulty in the procedure.

Srong and Jako in the year 1972 used CO2 laser coupled with the microscope by micromanipulators and performed the transoral laser microsurgery (49). Steiner developed the used of endoscopes for transoral surgery which helped in increasing the visualisation and also developed better instruments for handling tissues (50). This brought about an increased usage of laser even in later stages and different locations of the larynx.

Canis et al had performed transoral laser laryngeal surgery for T2 and T3 stages of glottis malignancy. A total of 391 patients were recruited in his study. All patients underwent transoral laser surgery. He achieved larynx preservation in 93% of patients with pathological staging of T2a and 83% in pT2b and pT3. This led to the conclusion that results of transoral laser surgery was comparable to results of total or partial laryngectomy and better than primary chemoradiotherapy(51).

Canis further expanded his usage for transoral laser surgery even for T4a glottis or supraglottic malignancy. Transoral laser surgery with or without neck dissection and postoperative chemoradiotherapy was done for 79 patients with T4a disease of glottis and supraglottis. 5 year organ preservation rate was 80 % and the local control rate was 67.2 %. Five year overall survival rate was 55.8% and was comparable with the result of total laryngectomy. Canis also mentioned the advantages of transoral laser surgery being organ preservation, low morbidity and rapid postoperative recovery (52).

HISTORY OF LARYNGECTOMY

Outcome of laryngectomies done on dogs by Czerny in the 19th century had discouraged the surgeons from performing it on humans (53). Albers documented a successful laryngectomy on a dog which survived for 9 days following the surgery. Von Langenbeck in 1854, Kòberleand Hueter in 1856 suggested the possibility of total laryngectomy in humans as a treatment for malignancy of larynx (53).

Patrick Watson of Edinburg performed the first post-mortem total laryngectomy on a patient whose larynx was destroyed by syphilis (54). Billroth of Vienna is credited with performing the first total laryngectomy for a case of laryngeal malignancy on December 31st 1873(55).

On April 11th 1874, Gussenbauer, Billroth's assistant presented this case in the 3rd Congress of German Surgical Society. It was performed on a 36 year old teacher who had a malignant lesion below the vocal cords. He had multiple cauterizations and biopsies earlier. On November 21st 1873, Billroth had performed a laryngofissure and removed the tumour. Within a month the patient had recurrence and so Total laryngectomy was done on him on December 31st1873 (55) . The surgery was done in 1 hour and 45 minutes (53). The patient died 7 months after surgery due to metastasis (56). This was the first ever documented case of Total Laryngectomy for cancer larynx.

The operative or the early postoperative mortality of the procedure was as high as 54 % in 1880(57). In a retrospective study Mackenzie reported operative and early

postoperative death in 9 cases out of 19 cases, early recurrence in 7 patients and cure in 3 patients (58). The reason for the high mortality rate was due to complications like fistula, haemorrhage, shock, mediastinitis and bronchopneumonia due to postoperative aspiration (59). Foulis in 1881 and Sendziak in 1888 reported a larger case series where the mortality rate was greater than 50 % (57).

Gluck developed a two staged procedure to reduce the mortality rate due to postoperative aspiration (60). Tracheal separation was done as a first stage procedure. Trachea was separated from the larynx and sutured on to the skin, creating a permanent trachea-cutaneous fistula. Two weeks later the second stage was performed which included laryngectomy and pharyngeal closure. This procedure was also followed by Francesco Durante of Italy and Silva Solis-Cohen in the United States (61).

Gluck and Sorenson improved upon the surgical technique of total laryngectomy. Gluck and Sorenson later abandoned this procedure, and refined the surgery to a single stage procedure. They felt that dissection of the trachea at the end of the procedure reduced the risk of local infection and so performed it as a single stage surgery. During this period from 1889 and 1900, they brought down the mortality from 44 % to 8.5 % and long term survival rose from 4% to 44 % (62). They had performed 160 total laryngectomies by 1922, with the last 63 cases without fatality (63).

George Washington Crile performed the first total laryngectomy in America in 1892. He also introduced the concept of neck dissection to remove the lymphatics which contained the tumour metastasis (64).

Radiation therapy began by early 1920s when Coutard and Regaud reported 6 successfully treated cases of laryngeal malignancy using X rays (65). From 1925 to 1940, radiation was the treatment of choice for extrinsic lesions and surgery was reserved for smaller intrinsic lesions. Later after the development of antibiotics and further surgical refinement, radiation was considered for smaller lesions and surgery was reserved for advanced disease (66). By 1950, Martin and Ogura standardised the procedure for total laryngectomy with neck dissection (67).

First performed in 1873, coded in 1950 and constantly being refined, total laryngectomy has passed the test of time. It serves as an effective treatment option for advanced laryngeal malignancy (Fig 5). It is indicated in the treatment in patients with laryngeal and hypopharyngeal cancers where:

- Organ preservation is not suitable
- As salvage surgery for disease recurrence after radiotherapy
- As salvage surgery for recurrence after partial laryngectomy

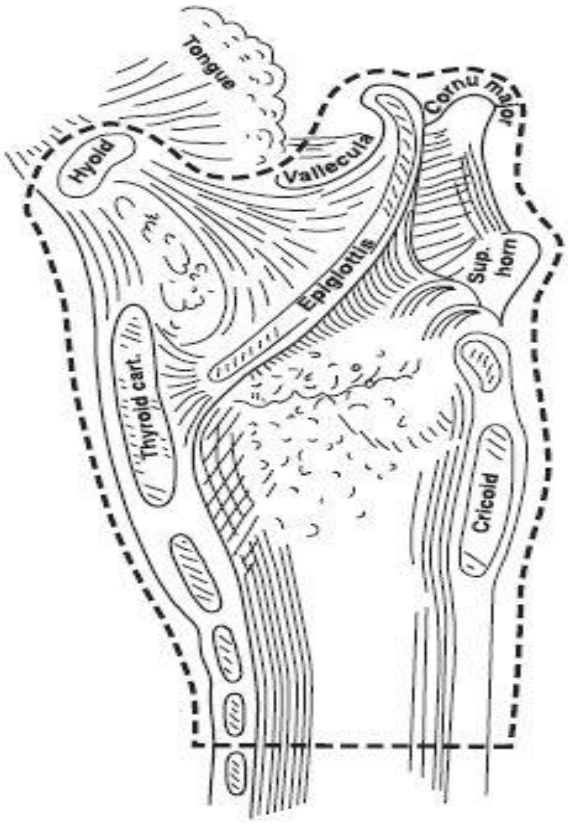

Figure 5 – The resection limits of Total Laryngectomy (Adopted from Current Diagnosis & Treatment in Otolaryngology - Head & Neck surgery. 2nd Edition)

FUNCTIONAL DISABILITY AFTER TOTAL LARYNGECTOMY

Larynx acts as an organ for sound production. Once the larynx is removed, it not only causes loss of voice but also other functional disabilities. Olfaction and gustation is lost, as the patient is not able to get the negative suction for air to reach the olfactory epithelium. Dysphagia following laryngectomy is prevented by pharyngeal myotomy. Some of the functional disabilities are discussed as follows.

VOICE AFTER TOTAL LARYNGECTOMY

Voice without a functioning larynx has been described as early as 1859 by Czermak et al. He had described voice restoration in a girt with laryngeal stenosis by bypassing airflow from tracheostomy to tongue base (68). Gussenbauer had first devised a double-lumen tracheotomy tube with a port extending into the pharynx for Billroth's first total laryngectomy patient for voice rehabilitation (69).

Voice production occurs in three main steps. Firstly, it needs air generation, which is produced by the lungs during expiration which passes through the larynx. Secondly, a vibrating voice box, the vocal cords is needed. Thirdly, the sound produced by the vibrating cords needs to be articulated to produce understandable voice. This articulation is done in the oral cavity, oropharynx and nasopharynx (70).

Voice is lost after total laryngectomy as a result of removal of larynx. The air generator and the articulation process are still functioning (71).

Three voice rehabilitation methods are commonly used - oesophageal voice, trachea-oesophageal prosthesis and artificial larynx. Based on the patient choice, the voice rehabilitation is planned.

Oesophageal speech

This manoeuvre begins with insufflation of air in the oesophagus by swallowing air. The swallowed air is made to pass through the upper oesophagus in a controlled manner, which is to be mastered by the patient, causing the pharygo oesophageal segment to vibrate (Fig 6). The sound produced is modified by the resonators and then, is articulated by the articulators in the oral cavity and oropharynx to produce voice.

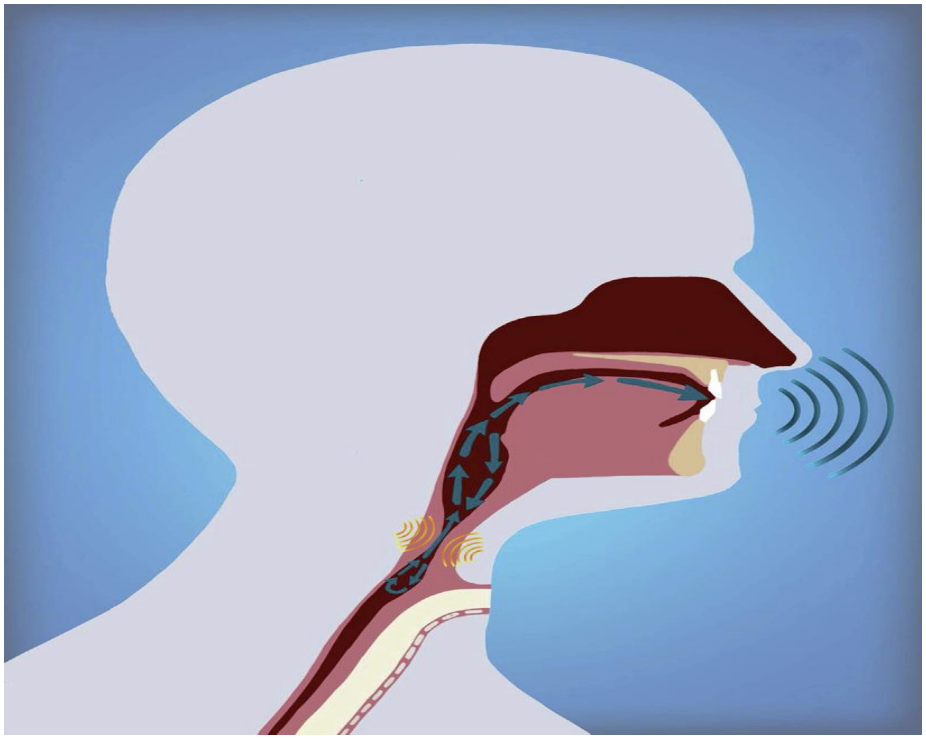

Figure 6 – Oesophageal speech (Adopted from Voice Restoration After Total Laryngectomy, Christopher G. Tang)

The advantage of this method is that it is cost effective and does not need any other device or surgery for the rehabilitation. However, it is difficult to master.

Artificial larynx

The Electrolarynx is an electronic vibrating device. The device is placed on the cheek or against the neck. This device causes the vibrations of the mucosa of the oral cavity and the pharyngeal mucosa which helps in producing sound (Fig 7). This sound is then articulated to produce voice. Its usage can be easily mastered , however the voice is produced sounds very mechanical (72,73).

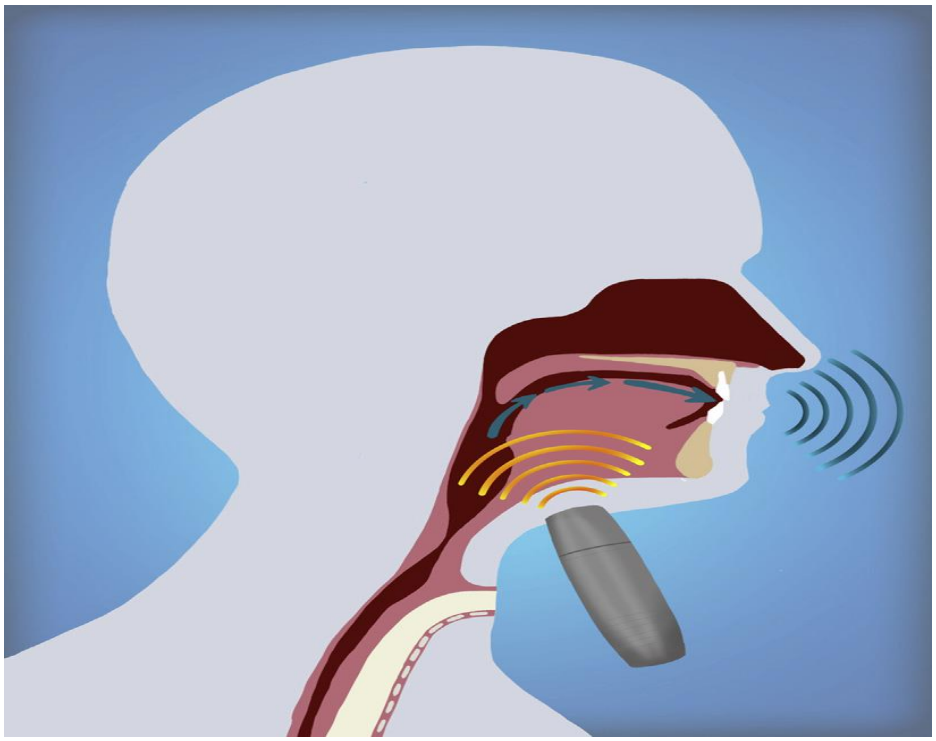

Figure 7 – Electrolarynx (Adopted from Voice Restoration After Total Laryngectomy, Christopher G. Tang)

Tracheo-oesophageal voice prosthesis

This is the gold standard for the voice rehabilitation in patients after total laryngectomy. The voice achieved using this is far superior when compared to oesophageal speech or electrolarynx (73–75). A puncture is made on the posterior wall of trachea onto the oesophagus. This is fitted with the prosthesis, which allows air to pass form the trachea into the oesophagus. This air is used to vibrate the mucosa of the oesophagus and the pharynx creating sound (Fig 8). The prosthesis can be placed primarily during the surgery, or can be planned later at a later stage.

The disadvantage of this method of rehabilitation is the cost of the prosthesis and need for care of the puncture site (76).

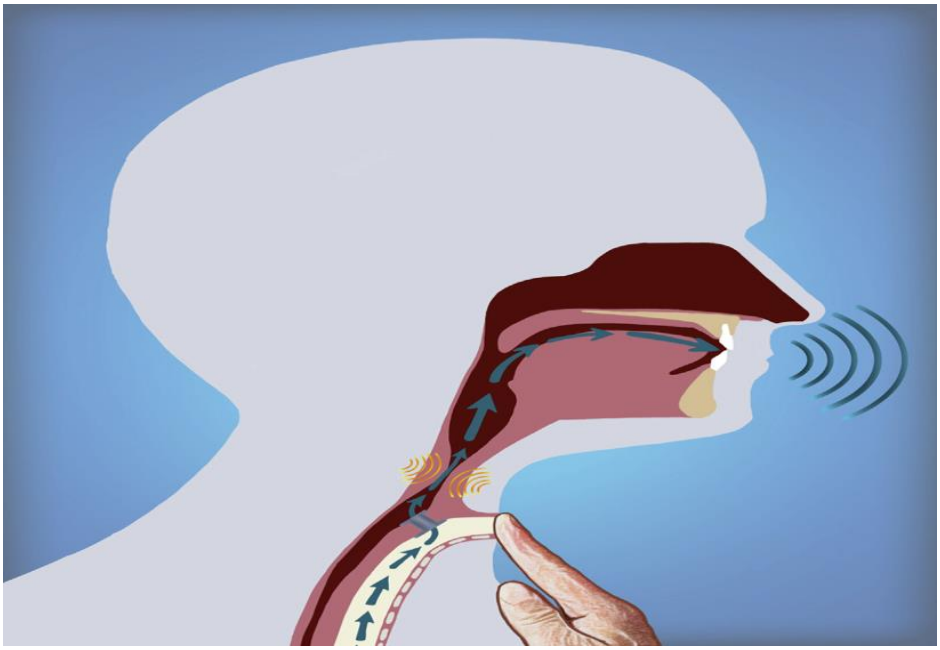

Figure 8 – Tracheo-Oesophageal puncture (Adopted from Voice Restoration After Total Laryngectomy, Christopher G. Tang)

OLFACTION AFTER TOTAL LARYNGECTOMY

After total laryngectomy there is a permanent discontinuity of upper airway with that of the lower airway. The patient will have an end tracheostomy and the normal nasal airflow will be totally lost. This results in impaired olfaction after Total Laryngectomy(77–80) . Miani et al in their study observed that the olfactory epithelium showed various degrees of degeneration after total laryngectomy and hence concluded that combination of loss ofnasal airflow and degenerative phenomena of the epithelium contributes to the olfactory deficits in patients following total laryngectomy(81) .

Moore-Gillon, in his study of the nose after laryngectomy, found a relatively denser ciliated epithelium and a faster mucociliary clearance in patients after laryngectomy. He attributed this to the loss of airflow through the nostril and reduced destruction of the cilia due to crusting. He also tested the olfactory acuity and found it to be normal and expressed the need for olfactory rehabilitation for patients after total laryngectomy (79).

Reduced airflow through the nostril after total laryngectomy is hence considered the reason behind reduction in smell. When nasal airflow is created by squeeze bottles or devices like laryngeal bypass, improvement in olfactory acuity occurs. (77,79,80).

GUSTATION FOLLOWING TOTAL LARYNGECTOMY

After total laryngectomy the taste sensation also is impaired due to impairment of the sense of smell. The loss of gustation is not to the same extent as the loss of smell. Ackerstaff et all in their study which included 63 laryngectomised patients, 15% had dysgeusia and 52% had hyposmia (82). A significant correlation was found between hyposmia and dysgeusia ($r=0.43$, $p<0.001$), implying smell and taste were closely related, where all patients with a taste problem also reported reduced sense of smell. Finizia et al also noted that 21% of laryngectomised patients had dysgeusia and 50% had hyposmia according to European Organization for Research and Treatment of Cancer Quality of Questionnaire for Head and Neck (EORTC QLQ-H&N35) (83).

OLFACTION

Olfaction is a special sense which helps us perceive pleasant and unpleasant smell. Olfaction is also considered as a chemical sense that can trigger certain specific memories and emotions. Buck and Axel's research on olfaction showed that there were about 1000 different genes for odour receptors in the mammalian genome (84). Odour is perceived when the odorants are inhaled and they bind to the olfactory receptors. Detection of hazards like fire, leaking gas and spoiled food are perceived due to the presence of olfactory system (85). Olfaction is thus responsible for better quality of life and in the assessment of danger.

The olfactory pathway starts with the olfactory epithelium. Olfactory epithelium is located on the roof of the nasal cavity and occupies a surface area of about 1 cm^2 on either side.

THE OLFACTORY EPITHELIUM

There are an estimated six million specialized olfactory receptor cells per nostril in a human nose (86). The receptor cells are present along with the matrix of supporting cells in the olfactory epithelium. It is lined by pseudo-stratified ciliated columnar epithelium. The olfactory epithelium lines the nasal aspect of cribriform plate, superior portion of the septum, the superior turbinate and a lesser extent on the anterior aspect of the middle turbinate (87).

The olfactory receptor cells are bipolar neurons, and are the first-order neurons. The limbs of the receptor cell project into the nasal cavity without having any synapse. This is the only place where a free nerve ending is present outside the body with a direct communication with the brain. Thus it acts as a pathway for viral and bacterial invasion into the brain. The olfactory receptor cells are tightly lodged between the non-neural cells in the olfactory epithelium. Knob like protrusion from the apical end project into the mucus covering the olfactory epithelium. These cells are embryologically derived from the olfactory placode (88).

The somata of the older cells are closer to the mucosal surface. The more recently differentiated cells are located away from the mucosal surface. These olfactory neurons then ascend as the olfactory bulb, olfactory tract and to the olfactory cortex (86).

There are about 25 cilia per olfactory cell. The olfactory receptors for the odorants are located on the cilia. The olfactory cilia contain the 9 plus 2 arrangements of microtubules. It contains two central microtubules surrounded by nine outer doublet microtubules. They do not have the muscle-like dynein arms required for motility and they do not beat synchronously. Dynein arm is present in the cilia of the respiratory epithelium and hence they beat synchronously. The cilia in the olfactory epithelium simply waft in the mucus.

Majority of the cells in the olfactory epithelium is the supporting cells, also termed sustentacular cells. These cells are larger cells and the main function is to insulate and protect the smaller receptor cells. Other functions of the sustentacular cells are regulating the microcomposition of the mucous and deactivation the odorants. These cells have many microvillae which are projected into the mucus.

Other types of cells in the olfactory epithelium are the lining cells of the duct of Bowman's glands, microvillar cells and basal cells. Bowman's glands are the special glands located in the olfactory epithelium. These glands secrete the mucus that bathes the olfactory epithelium.

The microvillar cells are similar to the brush cells of the airway tract present in other species. The functions of these cells are less known. They are located at the epithelial surface and extend the microvillae into the olfactory mucus (86).Ratio of the microvillar cells to the receptor cell is about1:10. There are about 600,000 microvillar cells in a normal olfactory epithelium.

There are two types of basal cells, the horizontal (dark) and globose (light) basal cells located near the basement membrane. These are the stem cells of the olfactory epithelium. All other types of cells arise from these cells (89).

OLFACTORY RECEPTORS

The olfactory receptor contains the olfactory receptor protein. These are members of the large G protein coupled receptor family. Majority (73%) of the olfactory receptor gene is distributed on six chromosomes (1, 6, 9, 11, 14, 19) and the remaining on the rest (90).

In 1991, Linda Buck and Richard Axel identified the first 18 members of the olfactory receptor genes, using the polymerase chain reaction (84). Each receptor cell can expresses only one type of olfactory receptor protein. The receptor cells help in facilitating the modulation of activity of olfaction by hormones and neurotransmitters (91).

The receptor cells expressing the same olfactory receptor protein are mapped in the same area in the glomeruli within the olfactory bulb. That is where the first synapse occurs. A functional topography thus exists in the olfactory epithelium and the olfactory bulb(92,93).

OLFACTORY BULB

Olfactory bulb is a paired thin laminate like structure. It is located in the ventral surface of frontal lobes, immediately above the cribriform plate. It is ovoid in shape with a size of about 50 mm^3. Filtration and modification of the stimulus occurs in the olfactory bulb. It is not a mere relay station.

The most superficial layer of the bulb is the olfactory nerve layer. It is made up of unmyelinated olfactory receptor cell axons. The next layer is the glomerular layer. It contains the olfactory glomeruli. Several thousands of these structures arranged in single or double layers in the younger population, these layers decrease in number with age. It is almost absent in people over the age of 80 years (94). The glomerular layer is prone to age-related damage due to environmental xenobiotics (95). Olfactory receptor cells can also get damaged due to the pinching of their axons, which occurs due to oppositional bone growth within the cribriform plate as suggested by Kalmey (96).

Initial synapse occurs between the axons of the olfactory receptors and the dendrites of the interneurons, mitral and tufted cells (97).

Deep to the glomerular layer is the external plexiform layer. This layer is mainly formed by the dendrites of the granule cells and secondary dendrites of the mitral and tufted cells. It contains very few cell bodies.

Deep to the external plexiform layer is the mitral cell layer. This is the layer with most numerous cells in the olfactory bulb. The cells are small cells without axons. There are between 50 and 100 granule cells for each mitral cell. Each granule cell has at least 50 short thorns like extensions called the gemmules. They are connected to mitral or tufted cell dendrites.

The next layer is the internal plexiform layer which is made up of myelinated axons from the mitral cells, tufted cells and a few peripheral dentrites of the granule cells. These axons exit from the olfactory bulb as the olfactory tract. Before leaving the bulb they send off collaterals. These collaterals end within the bulb's deeper regions (Fig 9).

The next layer comprises the granule cell layer containing the cell bodies of the granule cells. This arrangement thus causes excessive interaction. Cell populations within the olfactory bulb also undergo replacement over time (98). It is facilated by odorant stimulation (99).The stem cells necessary for the replacement is present in the anterior subventricular zone of the brain.

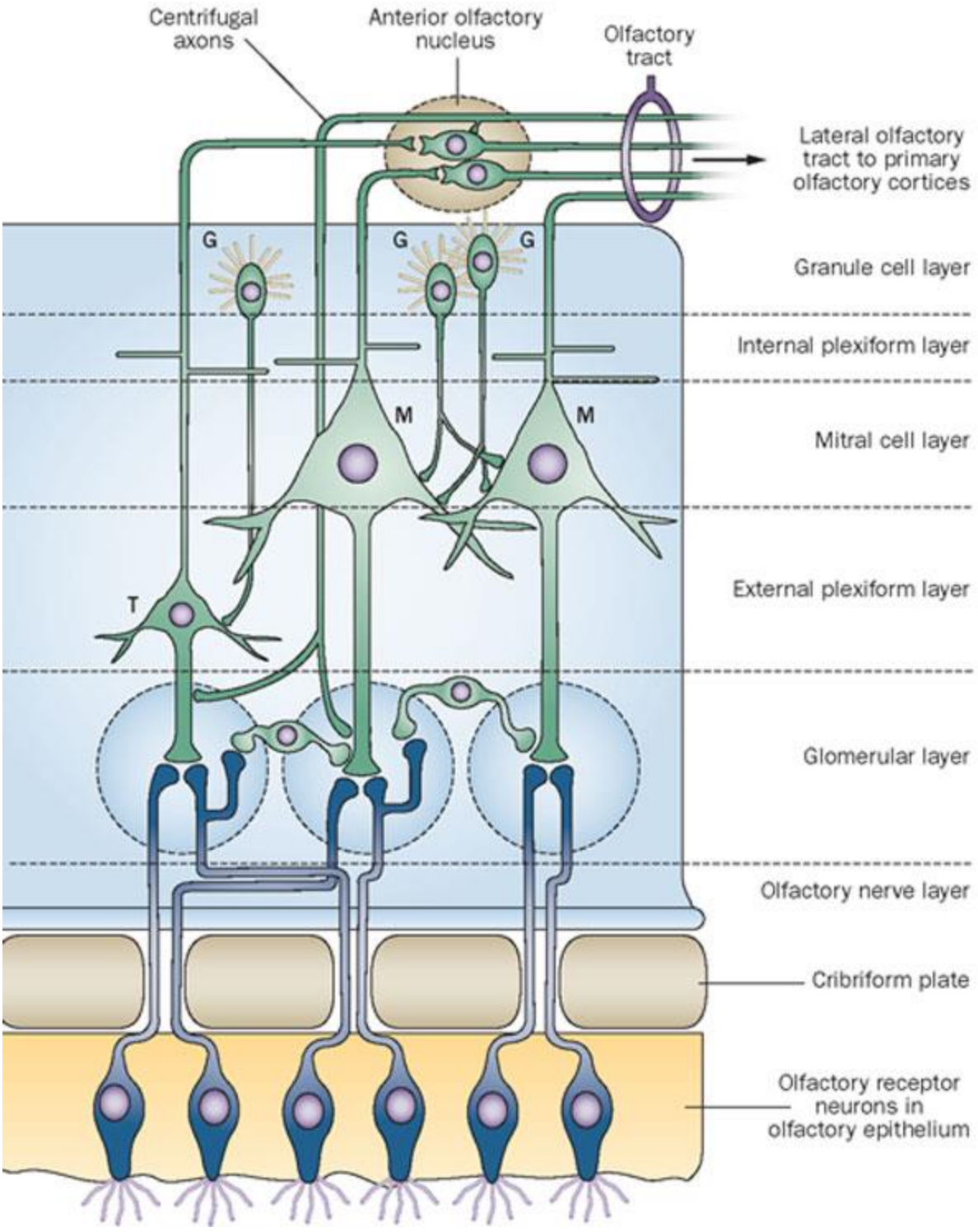

Figure 9 – Structure of olfactory bulb (Adopted from Duda, J. E. *J. Neurol. Sci.* 289, 49–54 (2010), Elsevier Ltd)

OLFACTORY BULB PROJECTION

The mitral and tufted cell axons exit the olfactory bulb and enter the olfactory tract. This tract follows the under surface of the frontal lobe to the olfactory trigone. The tract splits into three striae – the medial, intermediate, and lateral olfactory striae.

All fibers from the olfactory bulb pass through the lateral olfactory striae. The other two striae in humans are merely vestiges. Unlike other major sensory pathways, the main cortical projection of the bulb is ipsilateral (Fig 10).

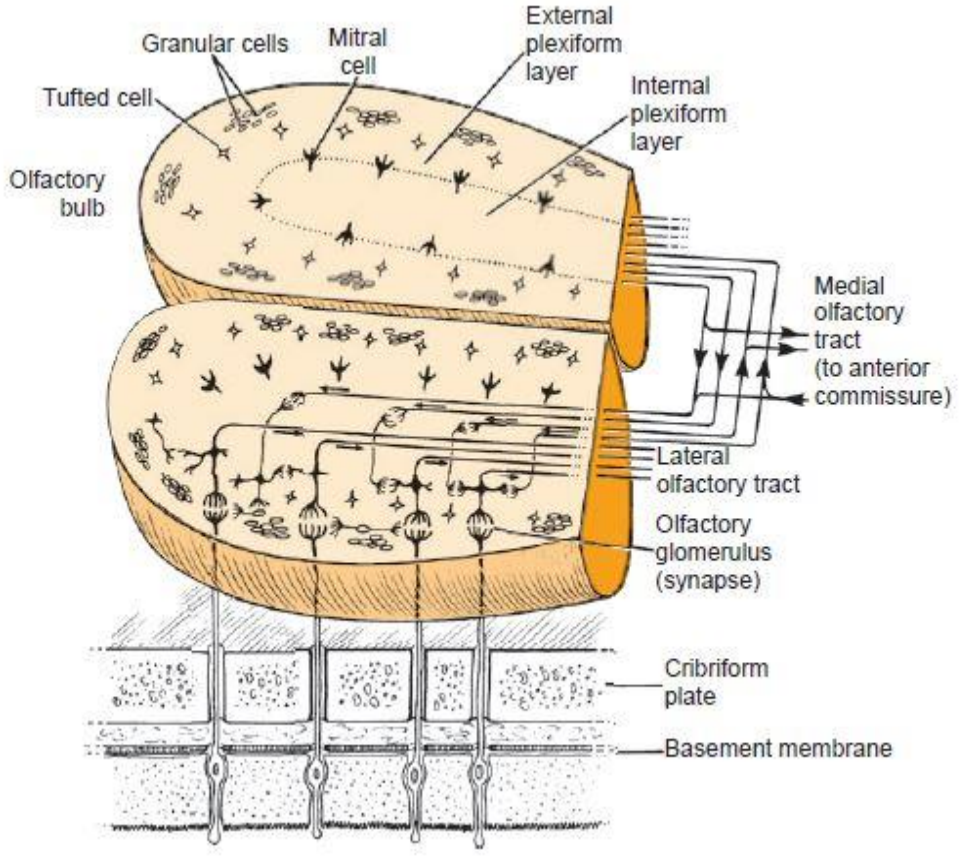

Figure 10 – Olfactory bulb and olfactory tract (Adopted from Cummings Otolaryngology Head and Neck Surgery, 6th edition)

OLFACTORY CORTEX

The olfactory system communicates with the cerebral cortex without relaying with the thalamus unlike the other sensory systems. There are reciprocal relays via the dorsomedial nucleus of the thalamus. It occurs between the primary and secondary olfactory cortical structures. Primary olfactory cortex receives fibers directly from the olfactory bulb. It consists of the following six structures

(1) Anterior olfactory nucleus located in the posterior parts of the olfactory bulb and olfactory tract near the trigone

(2) Olfactory tubercle

(3) Piriform cortex – the major recipient of olfactory bulb output

(4) Anterior cortical nucleus of the amygdala

(5) Periamygdaloid complex and

(6) Rostral entorhinal cortex.

The primary olfactory cortex has rich and reciprocal relations with one another. It also has connections with the hippocampus. The olfactory system has the most direct access to the hippocampus of all other sensory systems in terms of synaptic connections (Fig 11).

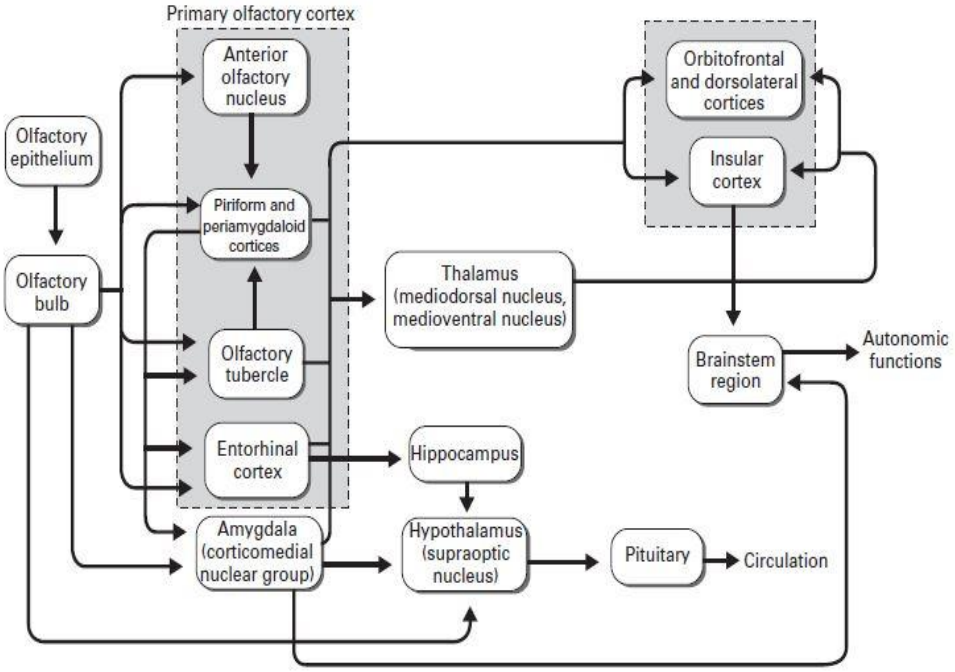

Figure 11 - Olfactory projection (Adopted from The Neurology of Olfaction, 2009)

Lesions of the medial temporal lobe causes disturbances in odour identification and discrimination(100,101). Such observations led to the concept that detection is performed by the bulb. All other tasks, such as identification, discrimination, and memory, are performed by the temporal lobe.

Functional imaging studies have reported greater right than left odour-induced frontal lobe activity even when there was bilateral stimulation, and when there was bilateral activation of the pyriform cortex (102). Another functional imaging study showed that the orbitofrontal cortical activity lateralised depending on the olfactory task.

The act of sniffing, irrespective of presence or absence of odour cause excitation of the piriform cortex of temporal lobe and medial and posterior orbito-frontal gyrus of

the frontal lobe. While a presence of odour irrespective of sniffing causes excitation of the lateral and anterior orbito-frontal gyri of the frontal lobe (103).

Sobel, in his study thus states the distinctive areas of activation in brain during sniff and during presence of odour. He describes the different areas of stimulation during normal olfaction and during olfactory exploration (103).

NERVE SUPPLY TO NOSE

The general somatic nerve supply of the nose is from the branches of the trigeminal nerve (104). Autonomic nerve supply to the nose comes from the sphenopalatine ganglion. The anterior and posterior ethmoid nerves, the branches of the nasociliary nerve (ophthalmic division of V), supply the upper part of the nasal cavity. The posterior part of the nasal cavity is fed by the nasopalatine nerve, a branch of the maxillary nerve (Fig 12).

The free endings of trigeminal nerve, glossopharyngeal nerve and vagus nerve can be stimulated by the odorant particles. They can be perceived as irritation, tickling, burning, warming, cooling or stinging sensation(78) . These are considered as protective mechanism against irritant odours (105) . These somatosensory sensations should not be confused with odours, although they can contribute to the overall appreciation of an odour.

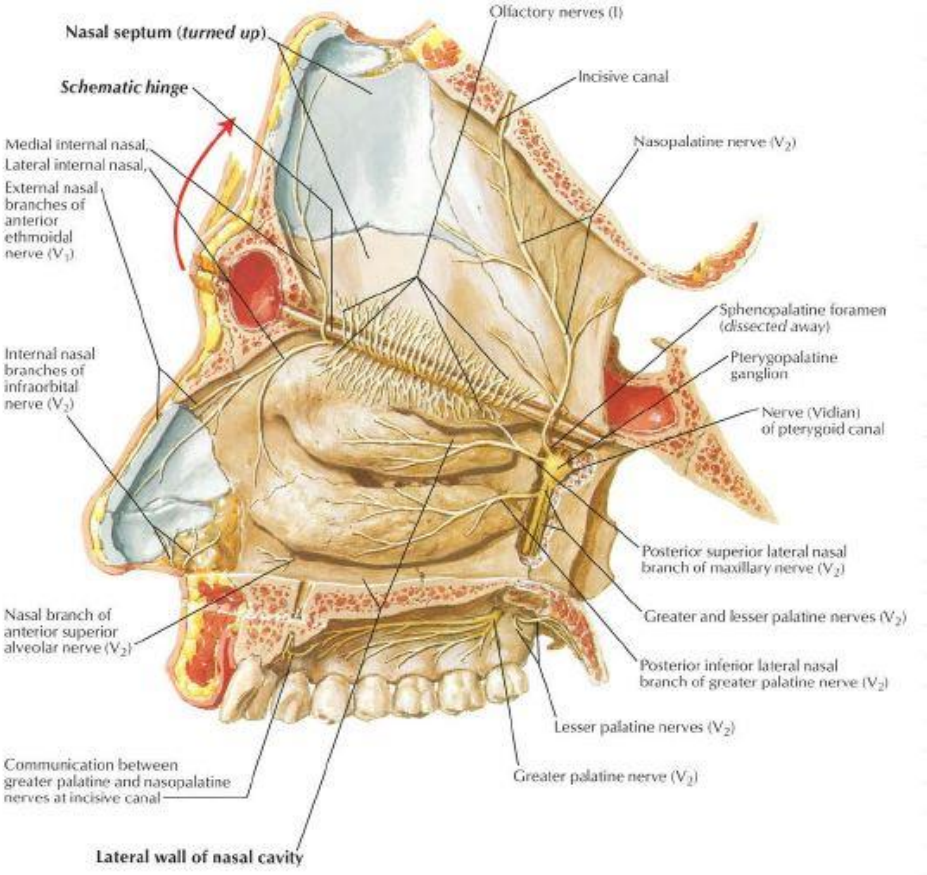

Figure 12 – Nerve supply to the nose (Adopted from Netter's Colour Atlas)

PHYSIOLOGY OF NOSE

The inferior and the middle turbinate are made up of a rich network of tortous veins. Venous engorgement of these veins causes significant alteration in the nasal airway flow. Thus it also affects the amount of odorant particles that reaches the olfactory epithelium that is situated in the roof of the nasal cavity. A moderate distension of these veins causes increased odorant reaching the olfactory epithelium than when markedly engorged (106).

Based on the degree of venous engorgement of the turbinates, thickness of the mucosa, force used for sniffing and the surface area of the nasal valve region, about 5 to 15 % of the inspired air reaches the roof of the nasal cavity reaching the olfactory epithelium(107).

Exercise, hypercapnia, and increased sympathetic tone constrict the turbinate due to reduction in venous engorgement. Cold air, irritants, hypocapnia, and increased parasympathetic tone increase turbinate engorgement (108) .

Between the short repetitive sniffs and the long sustained sniff, the long sustained sniff is considered to be more effective. More inhaled odorant reach the olfactory epithelium during a long sustained sniff and hence has increased olfactory sensitivity (109–112). High nasal airflow favours increased absorption of hydrophilic odorants and low flow rates causes increased absorption of hydrophobic substance (113).

Nasal cycle is caused by the differential engorgement of veins in the turbinates in each nose (114). These cycles are coordinated, and results in a periodic left–right airflow shift. Nasal cycle occurs every 1 to 5 hours in adults and absent in children. 80 percent of the adult population is said to have nasal cycle working in them, though certain studies mention that these numbers are over estimated (115).

ODOUR PROCESSING

Odorants are tiny particles suspended in the air which has hydrophobic and lipophilic molecules in it. This property helps in increasing the binding capacity of the odorant with the mucosa of the olfactory epithelium. The odorant must dissolve in the mucosa of the olfactory epithelium prior to activation of the olfactory receptors. The hydrophobic property helps in dissolving in the liquid medium and activation of the receptors. Odorant binding proteins present in the olfactory surface epithelium helps in transporting the odorant. It binds to the odorant and presents it to the olfactory receptor cells. It also acts as an inhibitor, and helps to filter the amount of odorant reaching the receptors.

Most chemicals even at a very low concentration can be detected by the human nose. Fishy-smelling substance trimethylamine can be detected at a concentration of less than one part per billion.

The information of each odorant, which has to be analysed in the olfactory epithelium is a complex process. Each odorant is recognised by more than one single type of receptor. Even structurally similar odorant molecules will bind to different receptors resulting in a different smell perception. For a particular odour to be perceived, a specific combination of the olfactory receptors is stimulated. This combination of stimulation and odour perception is a complicated process. The information reaches a specific region in the bulbar glomerulus, causing the perception of a particular smell. Hence different smell has been mapped at different regions in the bulbar glomerulus. Interglomerularneural process is thus activated and it causes further activation of second-order neurons occurs (116).

Signal: noise ratio is a process of suppression of background disturbance which can enhance the perception of the needed stimulus. This signal: noise ratio is also present in the olfactory system and is located in the olfactory bulb circuit. This helps in masking the background unnecessary odorant perception and increases the perception of the needed foreground odorants (117,118).

Odour-evoked glomerular spatial pattern is reduced by the activation of D2 dopamine receptor (119). While a reduced dopamine level can lead to increased odour-evoked glomerular spatial pattern (120). Thus, olfactory nerve activity can be controlled by the level of dopamine.

ODOUR ADAPTATION

Odour adaptation means that a repeated presentation of the same stimulus at a high intensity can produce a temporary reduction in perception of the particular odour. It can also cause inhibition in perceiving other odorants, which is termed as cross-adaptation. The duration of the stimulus and the concentration of the odorant decide the degree of adaptation and also the speed of recovery. Adaptation that occurs in one nasal cavity causes adaptation in the other nostril as well. Adaptation process occurs in the anterior olfactory nucleus and the anterior commissure.

Continuous exposure to lemon or orange oil vapours for about 3 minutes can result in almost complete loss of olfactory sensations (121).

ORTHONASAL AND RETRONASAL ROUTES

Airflow through the nasal cavity causes the odorant which is suspended in the air to reach the olfactory epithelium, causing stimulation of the olfactory cilia. Thus the function of olfaction is taking place unconsciously along with breathing. The odorant molecules can reach the desired location by two routes, the Orthonasal and Retronasal routes.

Orthonasal olfaction occurs when the odorant molecules reach the olfactory epithelium via the anterior nares during inspiratory airflow. Retronasal olfaction occurs when these molecules reach the olfactory epithelium through the choanae during expiratory airflow.

The olfactory cilia stimulation is directly proportional to the concentration of the odorant material reaching the olfactory epithelium. Passive orthonasal breathing causes passive smell perception and deep, active orthonasal breathing causes active smell perception (94).

Sniffing, particularly the single sustained sniff causes increased load of odorant to reach the olfactory epithelium and thus increased olfaction sensitivity (122). Olfactory parameters like estimation of odour intensity(123), percentage of correctly recognised odours(77) and magnitude of activated odorant receptors(124) has a positive correlation with the amount of orthonasal airflow.

Retronasal olfaction occurs during expiration and also during swallowing or chewing(125,126). This is very useful in perceiving taste and flavour of the food while chewing (127). Increased chewing causes increased odorant reaching the olfactory epithelium by the retronasal route.

OLFACTION TESTING

Earlier olfaction was tested just by presenting an odour to the patient and asking if he could appreciate the smell or not and identify it. No scores were made or used. More advanced methods of olfaction testing were used in laboratory research. Olfactory testing can be divided into subjective and objective tests. Subjective assessment is done in a conscious patient who is willing to take part in the study. The response of the subject is needed. Objective assessment is tested based on the involuntary response that occurs due to the odorant stimulation. This does not need the subject to respond. The involuntary action like altered electrical or autonomic nervous system activity is recorded and the test interpreted.

Olfactory tests may be classified into two categories

1. Psychophysical
2. Electrophysiological

Combination of electrophysiological and psychophysical tests is always suggested despite the poor reliability for assessment of olfaction disorders (128) .

ODORANT PRESENTATION PROCEDURES

Odorants can be presented by means of glass sniff bottles, plastic squeeze bottles, wooden sticks, felt-tipped pens, draw tube olfatometer, microencapsulated "scratch and sniff" odourised strips etc. to access orthonasal olfactory function (129–136).

Retronasal olfactory function can be assessed by presenting the odorant food items on the tongue (137).

Nakashima et al described odour presentation via intravenous route (138). This helps to determine whether the olfactory receptors are working when there is nasal congestion leading to reduced airflow in the nasal cavity and reduced flow in the olfactory epithelium region (138). Thiamine propyldisulfide is the agent used (139).

PSYCHOPHYSICAL TEST

Psychophysical tests are

1. UPSIT
2. Three-item Quick Smell Identification Test (Q-SIT) (140)
3. 12-item Brief Smell Identification Test (B-SIT) (141)
4. The Smell Diskettes Olfaction Test (142)
5. The T&T Olfactometer and
6. Sniffin' Sticks Test (SST)

This helps in measuring the changes in stimuli with respect to the changes in the psychological sensation of the patient. In these tests a conscious response to the changes in the sensory function is given by the subject, it is psychophysical test. Odour identification, detection, and discrimination correlate with each other, so simple identification tests are used for assessment of olfactory function (143).

Almost all the problems associated with olfaction are bilateral. Hence olfaction testing of each nostril separately helps in identifying the better-functioning side. Thus, unilateral testing should always be done. Total anosmia on one side can be totally masked if a bilateral testing of the nose was done. Non tested nostril has to be occluded during the test of olfaction. Occlusion has to be done in such a way that the nasal valve area is not distorted. Distortion of the nasal valve area can cause eddies which prevents crossing of the inhaled or exhaled hair in the nasopharynx. A piece of Microfoam TM tape is used to

occlude the non-test nostril. It is cut to the needed shape and used to occlude the nostril. The subject is then asked to breathe normally and not to sniff when the odorant is presented.

Odour identification test

Function of smell is mainly assessed by this method. Three common methods are

1. Naming tests
2. yes/no identification tests
3. Multiple-choice identification tests

The naming test has been the test which is widely used by physicians. This test has a choice of no response. Normal individual has difficulty in identifying even familiar odours and hence this test is of lesser accuracy and value. This test is also easy to malinger.

Yes/No identification test is better than the prior test, where the patient is asked to indicate whether the odorant stimuli smells like a particular odour named by the examiner. Two trials per stimulus are given. The first stimulus is provided with the correct odour and the second stimulus is provided with an incorrect one. For example, rose odour is presented and the subject is asked on the first trial whether the odour smells like rose. During the second trial rose odour is presented and asked whether the odour smells like apple.

The patient has to keep the odour memory long enough to compare with the odorant named by the examiner, and this test can be affected by cognitive and memory skills of the individual. Thus repeated trials are needed to get acceptable result.

Olfactory assessment in a clinic setup is usually done by multiple-choice odour identification test. The 40-odorant University of Pennsylvania Smell Identification Test (UPSIT) is one of the popular tests used regularly. It is available in 11 languages and has been administered to about 400,000 patients worldwide (144). Richard L.Doty, a researcher in the field of olfaction from USA is credited with the invention of the UPSIT.

This is a 'scratch and sniff test'. Here 40 different smells are used and the ability of the subject to identify the odour is tested. Four booklets each with 10 microencapsulated odorants are administered to the patient. For each of the smell, the participant must choose an answer from the four given choices. Only one of the options is correct. The odorant is released when microencapsulated odorant is scratched with the tip of a pencil. The test results are expressed as a percentile score relative to age and six matched controls (141). Olfactory function is classified into six categories

1. Normosmia
2. Mild microsmia
3. Moderate microsmia
4. Severe microsmia
5. Anosmia
6. Probable malingering

Chance performance is 10 out of 40, so a very low UPSIT score may suggest malingering. The reliability of this test is high (test – retest r=0.94). The test can be self-administered and takes about 10 to 15 minutes by most patients. A recurrent criticism of the UPSIT is the presence of odorants or response options (e.g. Root beer,skunk etc.) which are unfamiliar to patients outside USA. The various European and Asian versions do not have this problem. The 3 and 12 item versions can be used as screening tests. If dysfunction is found, then more extensive evaluation is advised.

Felt tip pen dispenser are used in SST. These felt tip pens are used to present different odorants for testing (145).16 sticks are used in the identification version, which has 12 odours and 4 blank dispensers. The reliability of this test is much less compared to that of the 40-odour UPSIT. The reliability of this test is comparable with the 12-odour B-SIT (131). A longer version of the SST is available. It combines the identification version with other variables like threshold and discrimination. By addition of these variables the test results in a more reliable ‘‘TDI’’ index. Normative data of the TDI index is obtained by the mean value of the results of several thousand healthy subjects(131,146).

The identification version of the 12-odour SST can be self-administered and is less time consuming (147). A lower value in this test is obtained when an olfactory disturbance is suspected; the extended version can be used. The extended version is time consuming and needs a trained technician to perform this test.

Correlation of the results of UPSIT and screening SST has been compared by the study conducted by Wolfensberger et al and it is reported to have moderate correlation (148).

Odour discrimination tests

The ability of a patient do differentiate two different odours is the principle behind odour discrimination tests. Naming or identification of the odorant is not necessary in this test. For example, the subject has to indicate if the two stimuli presented are same or different. The score is obtained based on the correct number of response in the same-odorant and different-odorant trials(100,149).

Multidimensional scaling (MDS) is another example. It provides a spatial representation of the similarities of odorants presented to the patient. Pair of odour stimuli is presented to the patient. The patient has to respond to the odour stimuli by answering either ‘‘completely different” or “exactly the same’’. These responses are then subjected to an algorithm. The grouping of the odorant is done and is compared with that of a normal subject, thus reflecting the perceptual alteration of the patient.

MDS is not done routinely as it is time consuming (150).

Odour threshold test

Odour threshold test is the second most common test that is used routinely. It is divided into detection threshold, recognition threshold and difference threshold. The lowest threshold that can be correctly detected is the detection threshold. The lowest concentration at which the odour quality is identified is termed as recognition threshold. The difference threshold or the differential threshold is the least amount of change in stimulus that can be identified by the patient to perceive it stronger or weaker. It is also termed as the ‘‘just noticeable difference’’ or JND. Detection threshold is the most commonly used test among the above mentioned three tests. Several of these threshold tests are available. Commercially, these include the T&Tolfactometer, the extended version of the Sniffin' Stickstest, and the Smell Threshold Test (STT). The principle behind all these tests is that the patient is provided with two or more stimuli and asked to indicate which smells stronger. Odour identification is not a part of this test.

This test is thus a type of forced-choice procedure. Thus there is marked reduction in bias and the reliability of the test is high. It can also be used to assess malingering.

Methods of assessment of detection thresholds are

1. Ascending method of limits (AML) and
2. Singlestaircase (SS) procedures.

The odorants are presented sequentially from low to high concentration in case of AML (133). The point of change of response from detection and no detection is estimated.

On contrary, in the SS method, an ascending stimulus series is used initially until the peri-threshold region is reached (151). After this increase in concentration of the stimulus is used if a negative response is obtained and decrease in concentration of stimulus is done in case of a positive response. This test is continued till the final transition point is attained.

SS can take a longer duration to come to the transition point. Variations have been described to reach to the transition point faster and also not affecting the final result. One such example is that initial larger concentration steps are made, till the first reversal occurs. After this peri-threshold is reached smaller steps based on "two down, one up rule" is used. This helps in considerable reduction in time in the initial half of the test.

Two sets of trials are presented under the ''two down, one up rule''. A negative response on two consecutive occasions while reducing the concentration, the next step up is done at a higher concentration. Thus the scores are faster reached.

Maximum-likelihood adaptive staircase is another variant (152). Based on the previous response, an estimate of the threshold is calculated. Stimulation of odorant concentration at the calculated estimate is used. This also results in a drastic reduction in the time taken to reach the threshold value. The threshold values obtained by the above mentioned tests are reported to have marked variability based on the study by Brown et al (153). It is mainly due to different techniques of odour presentation, incorrect instruction to patients and the lack of forced-choice testing.

Signal detection test

Signal detection test (SDT) is based on noise, signalplus noise and the influence of subject expectancies. It measures the olfaction sensory sensitivity and the subject's response decision. It helps in the accurate measurement excluding the bias when there is variation between the olfaction sensitivity and response by the patient. SDT is time consuming and so used rarely.

Odour memory test

The subject is provided with an odour, and after a time delay, has to identify the same stimulus from the others provided. This is the basis of the Odour memory test. A microencapsulated odorant is provided to the subject and asked to keep the odour in memory. After 10, 30, or 60 seconds, he is asked to identify the odour from the choice of four odorants provided. This is a 12 trial test. Total number of correct response gives the score of the test. This test is age and gender specific (154). Also the limitations are that even normal people show reduced memory of the odour during delayed intervals (155,156). Choudhury et al. described odour memory test which are very much similar to odour discrimination tests, with variation of time duration between the initial stimulus and the later stimulus identification (154).

Odour rating and magnitude estimation test

These tests are used to detect the ability of the subject to appreciate changes in odorant quality, intensity, and pleasantness (157). These tests employ the suprathreshold rating scales. Grouping of response in the extreme ends of the scale is one of the limitations. Hence visual symbols along the scales are used. This helps in reducing the limitation (158,159). Cross-modal matching called ‘‘magnitude estimation’’ is another method to reduce the clustering response where numbers are assigned to various smell intensities (160,161).

Bias due to the procedure and due to the subject is possible. A moderate intense odour is considered to be of higher intensity when compared to a weak stimulus than when presented with a stronger stimulus (162). A good odour memory is needed for the correct response. A longer duration between the stimulation may result in loss of odour memory. This provides a subjective bias. A test done too close with each other may result in wrong response due to odour adaptation.

Many of these tests are used in research. Brief identification tests are used in screening tests in clinics and followed up with detailed testing when required.

ELECTROPHYSIOLOGICAL TESTS

A negative potential followed by a rebound potential is generated when the odorant particle excites the olfactory epithelium. These can be measures by placing the electrode on the olfactory membrane or near the surface of the epithelium. The potential generated is termed as electro-olfactogram (EOG).EOG can be measured even after death due to the functioning olfactory epithelial cells. Also it can occur even after pharmacological blocking of axonal transmission. The EOG readings have to be interpreted with caution (163). Damage in the olfactory epithelium is different in different areas of the nose. There can be certain areas of damaged epithelium and certain areas of perfectly normal functioning epithelium. Thus a response from the damaged epithelium can result in an abnormal EOG. This is due to sampling error. EOG measured from other parts of normal olfactory epithelium could still be normal.

Placing an electrode in the roof of the nose in a non-anaesthetised patient is very difficult. Majority of the patients would not co-operate for such placement of electrodes. Hence these tests are not routinely done. Surface electrodes on the dorsum of the nose have been used to record olfactory evoked potential in man. The amplitude of the waves attained is smaller than that to intranasal electrode reading of EOG (164).

Olfactory event-related and evoked potentials

The changes induced in electrical fields generated by the neurons during or immediately after stimulation (sensory or internal psychological event) is termed as Event-related potentials (ERPs). The potential generated in the cortical structures of the brain is termed as Olfactory event-related olfactory potentials (OERPs). These potential can be measured by placement of electrodes over the scalp. Multiple stimulation trial also helps in improving the response graph. The results can further be refined using elaborate olfactometers. This can introduce pulses of odorants into the nose with rapid rise times (<100 ms) without trigeminal co-stimulation (165).

The waves of the OERP are P1, N1 and P2. P1 is the first positive peak which occurs at a latency of 250ms. This is followed by N1 and P2 waves. A stronger stimulus is presented, latency decreases and the amplitude increases(146,166).

The amplitude of the OERP is directly proportional to the number of activated neurons. Factors like increased airflow through the nasal cavity affects the number of odorant reaching the olfactory epithelium, which affects the number of neurons stimulated (167).

GUSTATORY SYSTEM

Gustation occurs when the tastant molecules stimulate the receptors in the taste buds. Taste buds are present on the dorsal surface of the tongue, soft palate, pharynx, larynx, epiglottis or even upto the upper oesophagus (168). Five basic taste sensation have been described : Salt, sour, sweet, bitter and umami(168,169). Gustation is important for nutritional intake, nutritional regulation and protection against external toxins (170).

OLFACTION AND GUSTATION

The perception of flavour of food not only involves the stimulation of taste buds, but also the combination of smell, feel of texture and temperature of food. Odour contributes significantly towards appreciating the flavour of the food (127). Impaired olfaction affects the flavour of the food more than impaired gustation (127). Past memories of smell can lead to aversion or preference of food even before tasting it(171–173).

OLFACTION REHABILITATION AFTER TOTAL LARYNGECTOMY

Various methods have been described for restoring olfaction after permanent discontinuation of upper and lower airway after total laryngectomy. They come in the form of devices which is to be used by the patients or manoeuvres to be performed by the patient.

a) Prosthetic devices :

Bosone was the first to introduce prosthetic device for improving olfaction (174). He used the nipple tube to bring back olfaction after total laryngectomy. Knudson et al described the oral tracheal breathing tube (175). This tube enabled the patient to inhale and exhale through his nose, the working principle being similar to that of larynx bypass.

b) Larynx bypass :

Goktas et al published the efficacy of the larynx bypass device in total laryngectomy patients (176). Their study showed a better improvement in smell with larynx bypass than without an aid. Larynx bypass consists of a plastic tube which connects the sealed tracheostoma to the mouth with the help of the mouthpiece. Negative pressure created by the lungs helps to build up the negative pressure in the nose, thus favouring the orthonasal flow of air and the odorant particles reaching the olfactory epithelium (Fig 13). Though using this device is difficult in day to day life, it has been used as a screening method to exclude anosmia in patient after total laryngectomy.

c) Manoeuvres :

The principle behind the manoeuvres for rehabilitation of olfaction after total laryngectomy is to create airflow through the nose by bringing about changes in the volume in the oral cavity and oropharynx with the lip closed. Examples of these manoeuvres are glossopharyngeal press, buccopharyngeal sniff and buccopharyngeal manoeuvre (77,79) . These manoeuvres have not been used frequently in the rehabilitation of olfaction in total laryngectomy patients. The effectiveness of these manoeuvres has also not been evaluated (80) .

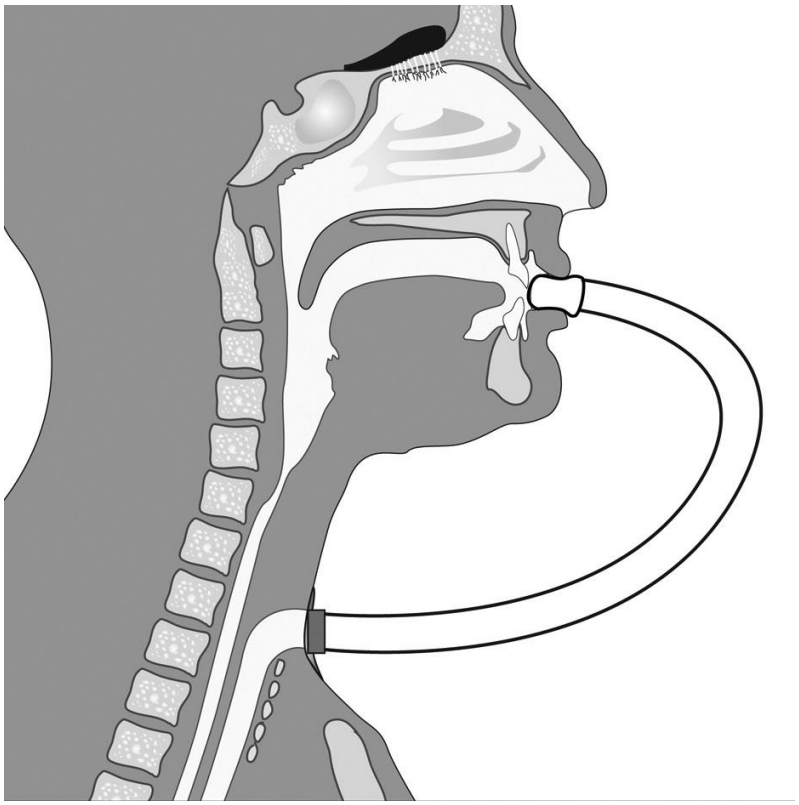

Figure 13 – Larynx bypass (Adopted from Olfaction following total laryngectomy, Journal of Laryngology and Voice, January 2012)

Nasal Airflow Inducing Manoeuvre

Hilgers et al first described the Nasal Airflow Inducing Manoeuvre or the Polite Yawning technique (177). Patients using the facial and neck muscles actively after total laryngectomy had better olfaction perception than the patients who don't use (77,79,178). This observation led Hilgers et al to develop this technique. Negative pressure is created in the oral cavity and oropharynx by asking the patient to yawn with the lips closed and simultaneously lowering the jaw, floor of mouth, base of tongue and soft palate (Fig 14). This manoeuvre is performed in a sequential way, as explained by Hilgers (Fig 15).

- The mandible is lowered, thus bringing the floor of mouth down
- The tongue is simultaneously moved downwards
- The lips remains sealed
- Same movement repeated a couple of times
- Breathing should continue irrespective of the manoeuvre

This induces the orthonasal flow of air. This manoeuvre is rapidly repeated with calm breathing. Breathing has to be independent of the manoeuvre. This helps in increasing the effectiveness of the manoeuvre. Isolated pumping movement of base of tongue without lowering the jaw can be practised as a second step to make the manoeuvre less conspicuous in public. Hilgers et al tried this manoeuvre in 33 laryngectomised patient and had success rate of 46% after a 30 minute training session (177).

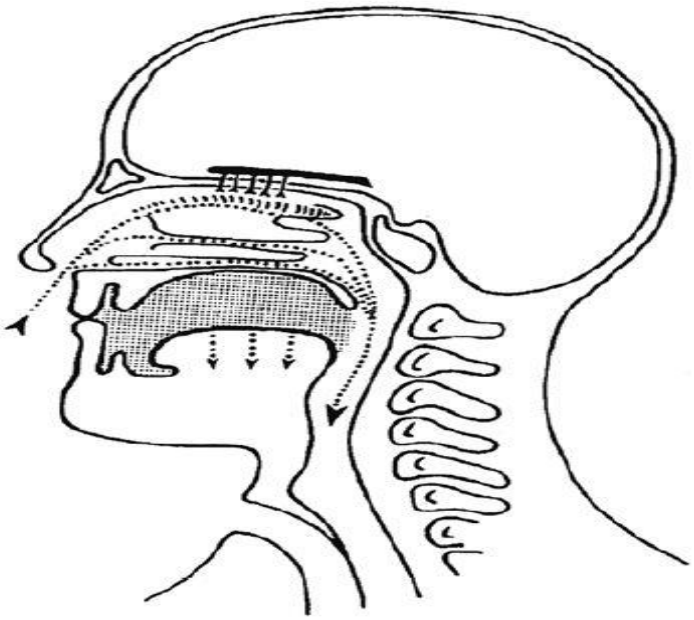

Figure 14 – Polite Yawn Technique (Adopted from BMC Ear Nose Throat Disord. 2009 Jul 29;9:8)

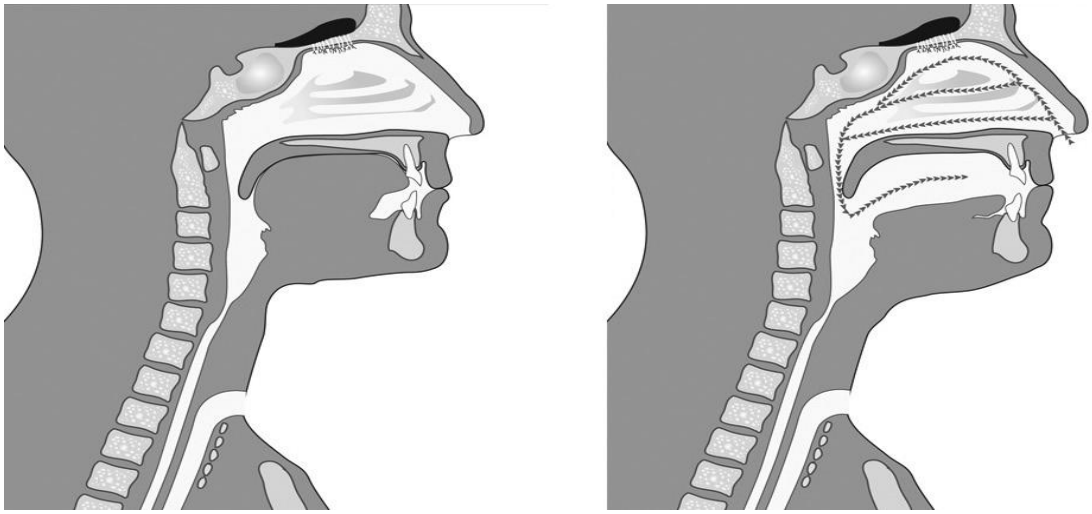

Figure 15 – Steps of Polite yawn technique (Adopted from Olfaction following total laryngectomy, Journal of Laryngology and Voice, January 2012)

QUALITY OF LIFE

Quality of life is defined as satisfaction and wellbeing that an individual experiences on a daily basis (179). Quality of life for patients suffering from malignancy in general and after radical treatment has to be assessed in multiple domains like physical, social, psychological, somatic functioning and general wellbeing (180). Multi domain assessment is done because, after the advent of various treatment options, though the patient may be considered theoretically disease free for 5 years after the treatment, he still would have various hindrances in leading a normal life. Psychosocial factors, change in appearance, social participation limitations and health of these patients could still be affected though he is disease free (181).

After total laryngectomy, the quality of life assessment is done in three domains.

1. Body functions and structures
2. Activities
3. Participation

Body functions refer to the physiological and psychological functions like loss of voice, loss in smell and difficulty in swallowing. Structural domain includes the change in anatomical structure, which is the end tracheostomy in these patients. Activities include the daily activities the patient does and participation includes the involvement in life situations (182).

These changes cause a great impact on the quality of life of the patient; to an extent that organ preservation procedure was used even in advanced stages of the disease (183).

Quality of life assessment in patients after total laryngectomy should include the above mentioned domains. Various tools are available for assessment for head and neck malignancy, like

1. MD Anderson Dysphagia Inventory (MDADI)(184)
2. University of Washington Quality of Life Scale Version 4 (UW QOL v4)(185)
3. Swallowing Quality of Life (SWAL-QOL)(186)
4. European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ C30)(187)
5. European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Head and Neck (EORTC QLQ H&N35)(187)
6. Head and Neck Quality of Life Instrument (HNQOL)(188)

These QOL assessment tools where used for head and neck malignancy in common. Questions specific for total laryngectomy was not present.

Appetite, Hunger and Sensory Perception Questionnaire (AHSP)

AHSP questionnaire was used in the self-assessment of quality of life with respect to appetite, hunger and sensory perception in elderly individuals (189). The questionnaire is divided into five domains.

1. Present taste perception
2. Present smell perception
3. Present smell perception compared to the past
4. Appetite
5. Daily feelings of hunger

These domains have a total of 29 questions with each question having a minimum mark of 1 and maximum mark of 5. A higher score indicates better sensory perception and a lower score implies a low sensory perception. This questionnaire was primarily used to assess the sensory perception loss in a geriatric population (190). The loss of smell, loss of taste, loss of appetite and hunger feelings was assessed in the elderly population. The internal consistency of this questionnaire was satisfactory for the self-assessment. In case of patients undergoing total laryngectomy, the loss of smell occurs. Secondary to the loss of smell, taste dysfunction arises, which results in loss of appetite. Hence, the loss of smell after total laryngectomy, smell before the surgery, appetite, hunger feelings and taste perception can be analyzed in patients undergoing total laryngectomy using this questionnaire

MATERIAL AND METHODS

Olfaction in patients undergoing laryngectomy and the effectiveness of Nasal Airflow Inducing Manoeuvre (NAIM) - Polite Yawn Technique in improving olfaction in laryngectomised patients was studied in a prospectively recruited cohort. This study was conducted in the Department of Otorhinolaryngology, Christian Medical College, Vellore which is a tertiary care referral centre in Tamil Nadu. Approval of the Institutional Review Board (IRB) at Christian Medical College, Vellore was obtained in September 2014. The subjects were briefed about the research project and requested to participate in the study.

Setting

This study was conducted in the ENT department at the Christian Medical College, Vellore.

Study period:

Patients were recruited from September 2014 to July 2015.

Study design:

Prospective Cohort study

Participants

Inclusion criteria:

1. Patients with laryngeal/ hypopharyngeal carcinoma who are planned for total laryngectomy
2. Willing to take part in study

Exclusion criteria:

1. Patients having Acute rhinitis/ sinusitis at the time of evaluation
2. Patients unwilling to participate in the study
3. Patients detected to have any polyps/nasal masses
4. Patients with history of nasal surgeries

Data collection:

Collected data was entered in a proforma and Microsoft excel sheet. Epidata software was used for the data entry.

METHODOLOGY:

All patients recruited for the study were subjected to olfaction testing prior to surgery. Quality of life assessment using Appetite, Hunger, Sensory Perception (AHSP) Questionnaire and repeat olfaction testing were done 2 weeks after surgery. Following this NAIM was taught to these patients and the olfaction testing repeated with NAIM (Fig 16). Olfaction of these patients was assessed based on Butanol threshold test, Odour identification test and Composite score.

METHODOLOGY – ALGORITHM

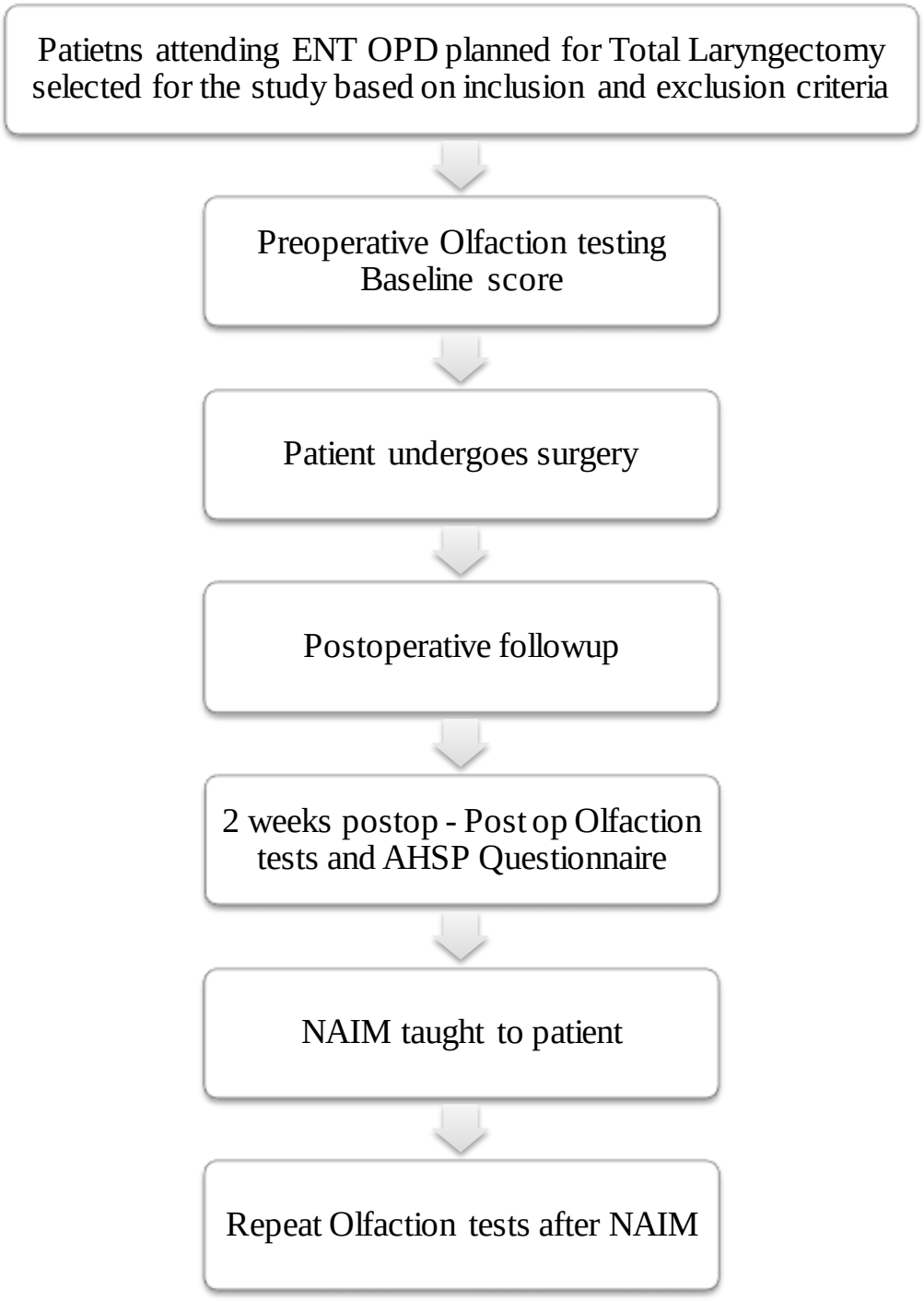

Figure 16 - Methodology

OLFACTION TESTING

1. Butanol threshold test:

Testing was done for each nostril separately by squeeze and sniff technique. Testing was started in the left nostril. The patient was presented with the bottle containing the lowest concentration of Butanol along with a bottle containing distilled water. He was asked to decide which bottle smelt stronger. If incorrect, the next step was done using the next higher concentration of Butanol and compared with a bottle containing distilled water (Fig 17).

Until a correct response was obtained, the test was continued with the next higher concentration of Butanol. When a correct response was obtained, the test was repeated with the same Butanol concentration. Four correct responses in a row led to cessation of the test. The concentration at which this occurred was marked as threshold, which was entered in the proforma as the Butanol threshold score. The same method was used to find the threshold for the right nostril.

Figure 17 – Butanol threshold test

2. Odour identification test:

This test also was started on the left nostril. A jar containing an odour was presented to the patient (Fig 18). Patient was asked to identify the smell and seek its name from the 20-item list provided (Fig 19).

If the patient could not identify the odour, result was marked as "Don't Know" and if the patient could not perceive the odour at all, it was marked as "No sensation". The examiner gave a corrective feedback when the smell was not identified, perceived or incorrectly identified.

The same odour was presented to the patient again randomly. A correct answer at second presentation cancelled the previous wrong one. The answers were marked on the proforma. Each correct response was given one score. The same test was performed on the right nose.

Figure 18 – Odour Identification score

Baby powder	Sandalwood
Chocolate	Vicks
Coffee	Soap
Rose	Burnt Paper
Pepper	Clove / Grampu / Loung
Tobacco	Garlic
Jasmine	Moth balls
Cinnamon / Patta/	Lemon
Asafoetida /Hing / Kayam	Eucalyptus
Tomato	Tea

Figure 19 – Odour names list provided

3. Composite score:

Composite score was calculated by taking the average of the Butanol threshold score and the odour identification score. Butanol threshold has a minimum score of 0 and a maximum score of 6. Odour identification score has a minimum score of 0 and maximum score of 8. The total score of each nostril is calculated separately and divided by two to get the composite score. A minimum score of 0 to a maximum score of 7 can thus be obtained. The patient's olfaction status was classified based on the composite score as follows:

6.0-7.0	NORMOSMIA
5.0-5.75	MILD HYPOSMIA
4.0-4.75	MODERATE HYPOSMIA
2.0-=3.75	SEVERE HYPOSMIA
0-1.75	ANOSMIA

QUALITY OF LIFE (QOL) QUESTIONNAIRE:

Quality of life was assessed using Appetite, Hunger and Sensory Perception (AHSP) questionnaire having 29 multiple-choice questions, addressing the situation both before and after laryngectomy and the present situation. Questions were divided into five sections:

1) Present odour perception (3 items, score range from 3 to 15)

2) Present odour perception compared to the past (3 items, score range from 3 to 15)

3) Present taste perception (8 items, score range from 8 to 40)

4) Appetite (6 items, score range from 6 to 30)

5) Daily feelings of hunger (9 items, score range from 9 to 45).

A low score indicates poor function. It indicates that the perception has deteriorated compared to pre-operative situation. Conversely, a higher score indicates good function or improvement in these domains.

Patients who attended the ENT outpatient clinic and were planned for Total Laryngectomy for laryngeal or hypopharyngeal cancer were recruited in the study. Recruitment was based on inclusion and exclusion criteria.

After obtaining the informed consent, the baseline preoperative olfaction test done. Preoperative olfaction composite score was calculated. Patient was followed up after Total Laryngectomy.

Two weeks after the surgery, patient was subjected to repeat olfaction test. The olfaction score was calculated. Patient was then asked to fill the AHSP questionnaire to assess his quality of life. Patient was then taught NAIM. A repeat olfaction test was done after teaching the patient NAIM. Composite score was then calculated.

The preoperative olfaction score, postoperative pre-NAIM olfaction score and postoperative post-NAIM olfaction score of the patient was entered in the data entry software. Epidata was used for data entry.

The preoperative score was considered as the baseline olfaction of the patient. The postoperative score before teaching NAIM was compared with the baseline score. The postoperative score after teaching NAIM was then used to evaluate the efficacy of the NAIM in improvement of olfaction.

SAMPLE SIZE:

Sample size was calculated based on Single Mean – Paired t-test formula.

Pre-test mean = 8.86

Post-test mean = 10.14

Standard deviation in pre-test = 2.58

Standard deviation in post-test = 3.23

Effect size = 0.440619621342513

Power (%) = 80

Alpha Error (%) = 5

Sided = 2

Required sample size = 42

STATISTICAL METHODS:

Descriptive statistics was presented with mean along with standard deviation for continuous variables, frequencies along with percentages for categorical variable. Paired t test was used to compare pre and post-test measures. Two-sample t test was used for the analysis of olfaction scores based on radiotherapy. Cronbach alpha test was used to analyse the reliability of AHSP questionnaire.

RESULTS

This study was conducted in the department of ENT in Christian Medical College, Vellore. All patients suspected to have malignancy of the larynx or hypopharynx were followed up for biopsy confirmation and staging of the disease, as well as tumour recurrence for those treated with radiotherapy. Patients with advanced stage of the disease for whom total laryngectomy was planned were included in the study based on the inclusion and exclusion criteria and after attaining an informed consent. A total of 28 patients who underwent Total Laryngectomy during the study period (September 2014 to July 2015) were recruited into the study. The baseline characteristics of the study population and the statistical analysis of the scores are described as follows.

BASELINE CHARACTERISTICS OF STUDY POPULATION

Age

The mean age (±SD) of the patients was 55.9(8.5) years (Table 1). All these patients were fit enough to understand and perform the olfaction testing both before surgery and after surgery.

Table 1 – Age of the study population

Variable	Number	Mean (SD)	Minimum	Maximum
Age	28	55.9 (8.5)	37	72

Age of the patients included in the study

Sex distribution

Among the total of 28 patients who were recruited, there was only one female patient who underwent the surgery (Fig 20).

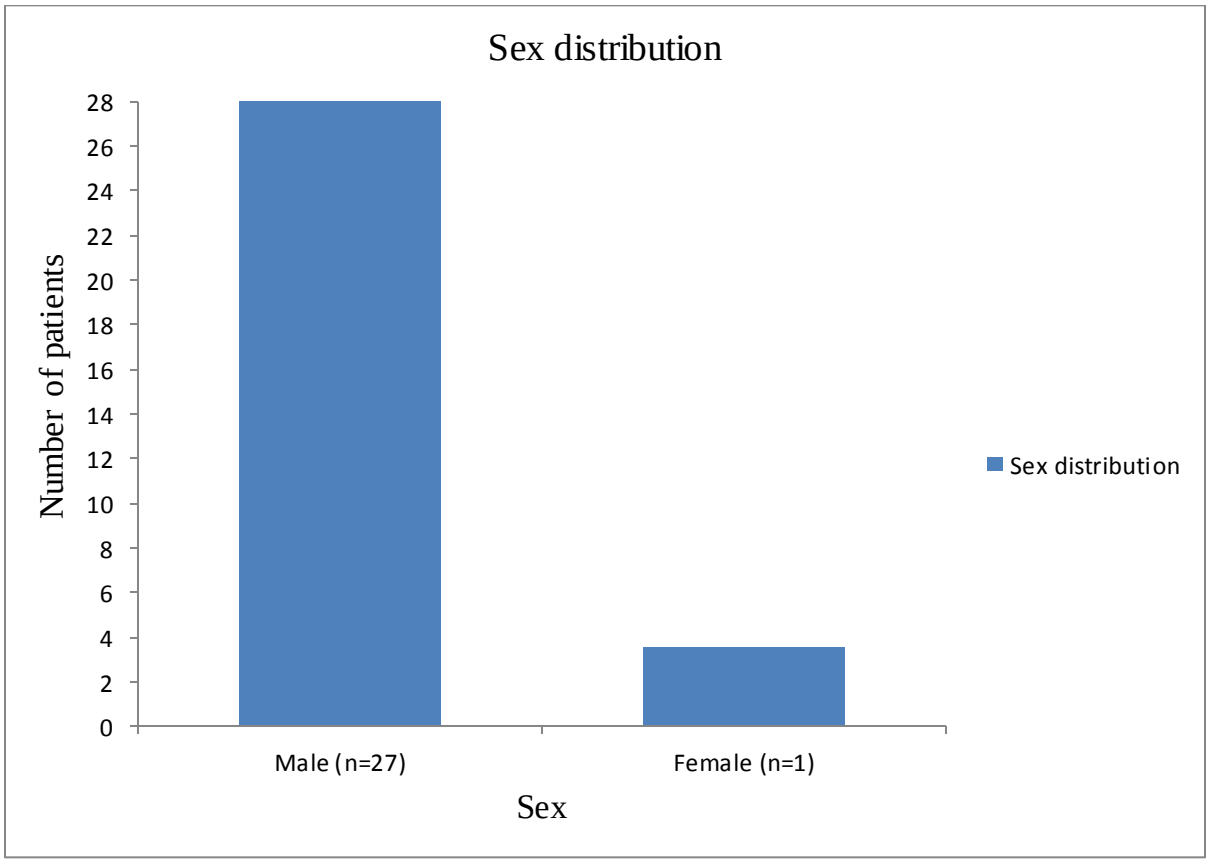

Figure 20 – Sex distribution of the study population

Distribution based on diagnosis

The study group was divided into 4 groups based on the diagnosis made. They were carcinoma glottis, supraglottis, transglottis and hypopharynx (Table 2). 46 percent (n=13) were diagnosed to have carcinoma glottis (Fig 21). There were 6 patients each with carcinoma of hypopharynx and supraglottis. Transglottic carcinoma was the least which was seen in 3 patients.

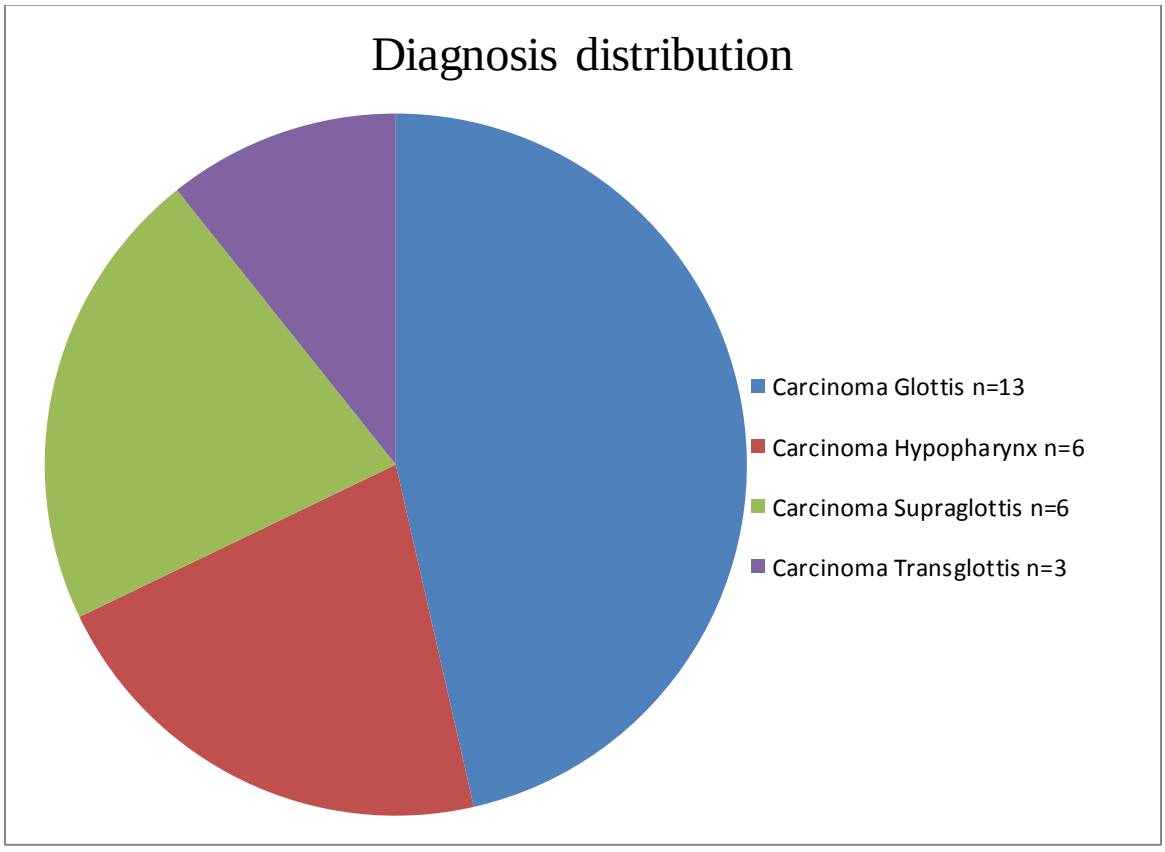

Figure 21 – Diagnosis distribution of study population

Distribution based on radiotherapy

The study population was divided into two groups. One group did not have radiotherapy as treatment prior to the surgery (n=22). The second group had prior radiotherapy done and was planned for surgery due to recurrence of the disease (n=6) (Table 2).

Table 2 – Sex, Diagnosis and distribution based on Radiotherapy

Variable	Number (%)
Sex	
Male	27 (96.4)
Female	1 (3.6)
Diagnosis	
Carcinoma Glottis	13 (46.4)
Carcinoma Hypopharynx	6 (21.4)
Carcinoma Supraglottis	6 (21.4)
Carcinoma Transglotttis	3 (10.7)
Radiotherapy	
No radiotherapy	22 (78.6)
Prior Radiotherapy	6 (21.4)

Sex, diagnosis and radiotherapy

STATISTICAL DATA ANALYSIS

Preoperative olfaction score

All the 28 patients underwent olfaction testing. The scores were obtained for each nostril separately. The mean olfaction score for the right nostril was 4.57 (Fig 22) with a minimum score of 1.00 and maximum score of 6.50. The mean score for the left nostril was 4.54 (Fig 22) with a minimum score of 1.00 and maximum score of 6.50.

Postoperative score after 2 weeks - before Nasal Airflow Inducing Maneuver (NAIM)

As a part of the cohort study, these patients were followed up 2 weeks after the surgery and a repeat olfaction score was done. The mean score of 0.43 in the right nostril and 0.48 in the left nostril (Fig 22) was obtained with a minimum score of 0.00 and a maximum score of 1.50 in both the groups.

Postoperative score after 2 weeks - after Nasal Airflow Inducing Maneuver (NAIM)

The patients were then taught NAIM (Polite yawn technique) and a repeat olfaction testing showed a significant increment in the scores ($p<0.001$). The mean score for the right nostril was 3.57 and left nostril was 3.54 (Fig 22). Both nostrils had a minimum score of 0.50 whereas the maximum score on the right was 5.00 and left was 5.50.

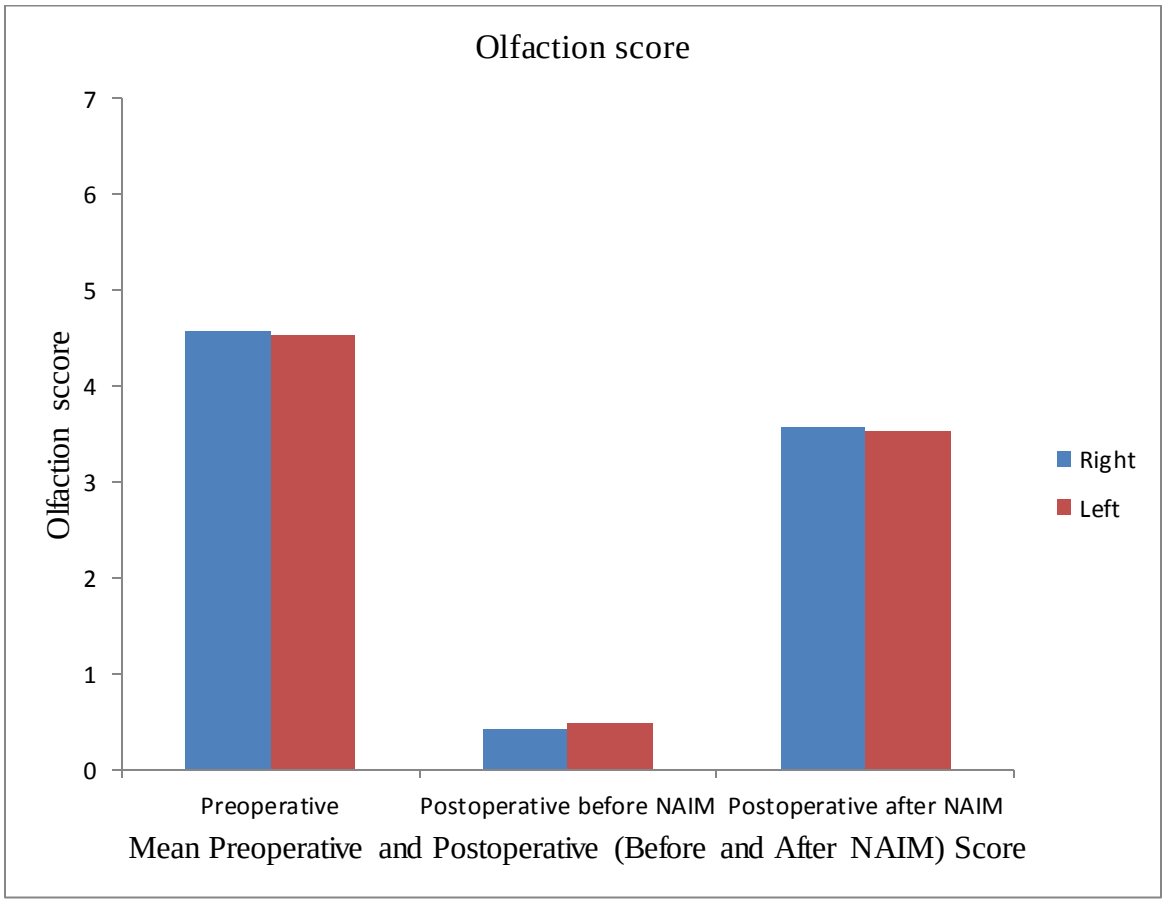

Figure 22 – Mean olfaction scores

Preoperative score vs postoperative before NAIM score

The data obtained were statistically analyzed. Paired t test was used for the analysis. The preoperative scores and the postop before NAIM scores were compared for both the left and the right nostril (Table 3).

There was significant reduction in the olfaction scores in the postoperative scores before NAIM when compared with the baseline values. It was statistically significant, (p value < 0.001) in both right and left nostril.

Postoperative before NAIM vs after NAIM score

The postoperative olfaction scores before NAIM was compared with the postoperative olfaction score after NAIM treatment. Paired t test was used for this statistical analysis (Table 3).

There was statistically significant improvement ($p<0.001$) in the olfaction score following NAIM (Polite yawn technique).

Preoperative score vs postoperative after NAIM score

The baseline olfaction score was compared with the postop after NAIM scores. This was done to assess the effectiveness of the maneuver in bringing back the olfaction score to the baseline level. Paired t test was used for this analysis (Table 3).

The olfaction score after NAIM (Polite yawn technique), had a significant rise. Although the mean score of the olfaction after NAIM did not reach upto the preoperative scores, there was a significant increase in the score ($p<0.001$).

Table 3 – Mean olfaction scores comparison with p value

Variables	Mean (SD)	p-value
Preoperative Right	4.57 (1.32)	
Postoperative Right before NAIM	0.43 (0.47)	< 0.001
Preoperative Left	4.54 (1.37)	
Postoperative Left before NAIM	0.48 (0.52)	< 0.001
Preoperative Right	4.57 (1.32)	
Postoperative Right after NAIM	3.57 (1.27)	< 0.001
Preoperative Left	4.54 (1.37)	
Postoperative Left after NAIM	3.54 (1.20)	< 0.001
Postoperative Right before NAIM	0.43 (0.47)	
Postoperative Right after NAIM	3.57 (1.27)	< 0.001
Postoperative Left before NAIM	0.48 (0.52)	
Postoperative Left after NAIM	3.54 (1.20)	< 0.001

Olfaction score – Paired t test analysis with p value

Comparison based on radiotherapy

The improvement in olfaction score before and after the NAIM – Polite yawn technique was analyzed based on whether the patient has undergone prior radiotherapy or not. Effect of radiotherapy on the effectiveness of polite yawn technique is thus assessed. A two-sided independent t test was used for this analysis (Table 4)

Table 4 – Mean olfaction score comparison based on radiotherapy with p value

Variable	Number	Mean score (SD)	p-value
Right – No Radiotherapy	22	3.14 (1.17)	
Right – After Radiotherapy	6	3.17 (1.50)	0.96
Left – No Radiotherapy	22	3.02 (0.23)	
Left – After Radiotherapy	6	3.17 (0.59)	0.79

With respect to Radiotherapy – Two sample t-test

Both the groups had more or less equal benefit (p = 0.96 and 0.79). Hence radiotherapy did not influence the effectiveness of polite yawn technique.

AHSP questionnaire reliability assessment

The quality of life assessment was done using AHSP questionnaire. It had 29 questions which were subdivided into 5 sections. The domains were Present taste perception, Appetite, Present odour perception, Present odour perception compared to the past and Daily feelings of hunger. The mean scores for each domain and the total score was calculated (Table 5)

The mean score for present taste perception domain was 21.79, with the minimum score of 9 and maximum score of 31. The minimum score in the appetite domain was 9 and maximum score was 23 with a mean of 16.04.

The present odour perception score was 7.86 (mean) with minimum score of 3 and maximum score of 13.

The present odour perception compared to the past mean score was 8.68 with a minimum score of 5 and a maximum score of 41.

Mean score of daily feelings of hunger was 25.21, with a minimum score of 13 and maximum score of 41.

The total mean score was 79.57. The lowest total score attained was 52 and the maximum score was 110.

The reliability of the questionnaire was analyzed based on Cronbach alpha test (Table 5)

Table 5 – Mean AHSP score with Scale reliability coefficient

AHSP score	Number of questions	Mean score (SD)	Scale reliability coefficient *
Present taste perception	8	21.79 (5.2)	0.77
Appetite	6	16.04 (3.8)	0.74
Present odour perception	3	7.86 (2.8)	0.51
Present odour perception compared to the past	3	8.68 (2.0)	0.86
Daily feelings of hunger	9	25.21 (6.8)	0.87
Total	29	79.57 (14.4)	

*AHSP score and Cronbach alpha test

The scale reliability coefficient was calculated. Present taste perception questionnaire had a scale reliability coefficient of 0.77 and appetite questionnaire had 0.74. Present odour perception and present odour perception compared to the past questionnaire had a scale reliability coefficient of 0.51 and 0.86. Daily feelings of hunger questionnaire had a reliability coefficient of 0.87. Hence AHSP questionnaire was a reliable questionnaire which can be used for the assessment of quality of life in patients.

DISCUSSION

Head and neck cancers account for about 30% of all malignancies in India (3). Oral cancer is the commonest followed by laryngeal and hypopharyngeal malignancies. Total laryngectomy is offered as a primary treatment modality for locally advanced laryngeal and hypopharyngeal cancer and also for those who failed the organ preservation treatment of chemoradiation.

The need for rehabilitation of the laryngectomised patient is well recognized. Great attention is paid to voice rehabilitation of these individuals. Prior to the surgery, the patients are counselled regarding voice rehabilitation and various available options including the financial implications are discussed. For pulmonary rehabilitation the expensive heat moisture exchangers or the inexpensive usual stoma care using stomal covers and external humidifiers is considered (191). Swallowing rehabilitation is occasionally required which can be achieved with swallowing exercises which is taught by the speech and language pathologists. About 20% of primary and salvage laryngectomy patients develop dysphagia due to pharyngo-esophageal stricture which requires dilatations or a surgical intervention (191).

Loss of the sense of smell is an inevitable consequence of total laryngectomy as there is a discontinuity between the upper and lower respiratory tract. During respiration that now occurs through the tracheostoma, no air flows to the olfactory epithelium

affecting the passive sense of smell, which in turn affects taste perception too. Loss of olfaction after total laryngectomy and its rehabilitation is not usually addressed.

Not many studies have been conducted to assess olfaction prior to total laryngectomy and also to evaluate the need for olfactory rehabilitation in laryngectomised patients. The effect of Nasal Airflow Inducing Maneuver (NAIM) – the polite yawn technique described by Hilgers et al in improving olfaction in this patient group has not been studied in the India. This study was done to address this deficiency in literature.

Squamous cell carcinoma is the most common cancer of the upper aero-digestive tract. Forty percent of these patients present with advanced disease (192). In our study we included patients with laryngeal and hypopharyngeal malignancies who were planned for total laryngectomy. Of the 28 patient recruited, 27 of them had squamous cell carcinoma and one patient had sarcomatoid carcinoma.

The mean age of the study population was 55 years, with a minimum of 37 years and a maximum of 72 years. This study population was a little younger than those included in the study by Hilgers et al and Risberg et al (177,193). The mean age group of the patient in the study by Hilger et al was 64 years, with a minimum age of 42 and maximum age of 80 years (177). The mean age group of the patients in the study by Risberg was 68 years (193).

In Hilger's study of 44 patients, 34 patients were men and 10 were female (177). Risberg-Berlin in his study recruited 24 patients of which 21 were men and 3 were female (194). The male predominance observed in the above mentioned studies was also seen in this present study.

In our study, a preoperative olfaction score was done. The mean baseline score for the right and left nostril was 4.57 and 4.54 respectively. Various studies conducted to assess olfaction after laryngectomy recruited their subjects after they had undergone laryngectomy (177,193–195). So the status of olfaction before laryngectomy was not available, unlike in our study was a preoperative olfaction score was obtained.

Our subjects were followed up 2 weeks following surgery and an olfaction score (pre therapy olfaction score) was estimated which was 0.43 and 0.48 for the right and left nostril respectively with a significant drop in olfaction score ($p<0.001$). This implied that these patients were not using any technique to augment /enhance their sense of smell. In their study, Van Dam et al noticed that some laryngectomy patient's ability to smell was facilitated by contraction of the facial muscles, floor of the mouth or movement of the jaw (178). This helped develop the nasal airflow inducing manoeuver (NAIM) by Hilgers et al which helped improve olfaction in their subjects (25% to 57% smellers) (177).

NAIM was used in our study in a short single session of 15 minutes, the patient was taught this manoeuver. The patients did not have any difficulty in understanding and learning this skill and reproducing it. The postoperative post therapy score had a significant improvement ($p<0.001$) with the mean scores of 3.57 and 3.54 for the right

and left nostril respectively. This simple exercise can be used to effectively improve the olfaction in our Indian population too, following total laryngectomy. The manoeuver is simple to teach and easy to master.

In Hilger et al study, 44 patients who had undergone laryngectomy with a mean duration of 6 years since surgery, were recruited (177). A short session of 30 minutes was used to teach the maneuver and obtained a success rate of 46 % in converting non-smellers to smellers (177). Hilger also continued the study to analyze the effectiveness of the NAIM on long term follow up. He had followed 41 patients for a mean of 4 months to 2 years and reported a successful rehabilitation in about 50% of the patients (195). He had also mentioned the need for repeated sessions for better rehabilitation.

Risberg-Berlin et al in their study calculated the effectiveness of NAIM after total laryngectomy, where the patients were followed up after 6 months, 1 year and 3 years. Three sessions of training was done within a period of six weeks. After three sessions, percentage of non-smellers reduced from 58% to 17 % and smellers increased from 42% to 83%. At the end of 6 months 87% of the followed up patients were considered smellers. At the end of 1 year 88 % were smellers (193). At the end of 3 years, a successful rehabilitation of 78 % was attained. This showed the effectiveness of the maneuver in aiding olfaction in laryngectomised patients. They suggested including NAIM in the multidisciplinary rehabilitation program after total laryngectomy (196).

Assessment of health-related quality of life (HRQL) is now part of evaluation of cancer treatment and rehabilitation. The assessment of quality of life after laryngectomy

with relation to olfaction, taste and appetite can be done using various available questionnaires. Risberg-Berlin et al in his study used the Questionnaire on Olfaction, Taste and Appetite (QOTA) and European Organization for Research and Treatment of Cancer Quality of life Questionnaire – Head and Neck (EORTC) QLQ-H&N35 questionnaires (193). Bjordal et al in a study to validate (EORTC) QLQ-H&N35 questionnaires mentioned a high compliance rate, but a low internal consistency with respect to special senses (197). Risberg-Berlin in their 3 years follow up study on olfaction and HRQL mentioned a similar problem with the questionnaire. The questionnaire of the sense scale which included "Problems with smell" and Problems with taste" did not have a significant difference between the smellers group and non-smellers group (196). Miwa T et al in their study found that olfactory disturbance caused a significant loss in quality of life (198)

In our study we used the AHSP questionnaire. This questionnaire is very similar to the QOTA questionnaire with 29 questions in 5 groups. High internal consistency was obtained in all 5 groups with an overall total mean score of 79.57. It can thus be used as an effective tool for analysis of quality of life in patients undergoing total laryngectomy.

LIMITATIONS

Our study was not without limitations. A study group of 42 patients was planned for the study. But due to time constraints we could recruit only 28 patients.

A two week follow-up was done for all these patients. So status of olfaction and efficacy of NAIM could be assessed at 2 weeks post laryngectomy. The long term efficacy of the rehabilitation manoeuver can be assessed if these subjects are followed up for a longer period of time.

CONCLUSION

In this study of 28 patients after total laryngectomy, there was a loss in the sense of smell in all the 28 patients, which was tested using Butanol threshold test and Odour identification score. The olfaction score after a 15 minute session of Nasal Airway Inducing Maneuver, the polite yawn technique showed significant improvement.

Quality of life assessment was done using Appetite, Hunger and Sensory Perception questionnaire. The internal coefficient of this questionnaire was high and hence can be used as an effective questionnaire for quality of life assessment in total laryngectomy patients with respect to smell, taste, hunger feelings and appetite.

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APPENDIX

PATIENT INFORMATION SHEET AND CONSENT FORM

You are being requested to participate in a study. In this study we test your olfaction (ability to smell) before and after Total Laryngectomy surgery. Before checking your ability to smell, an examination of your nose will be done using an endoscope to assess your eligibility to participate in the study. We will also be assessing your quality of life after surgery using a questionnaire.

Olfaction testing is done using Butanol test. In this test you will be given a solution at different concentrations and you will be asked at which concentration you can identify the smell. You will also be asked to smell different odours and see if you can differentiate between the different odours and identify each odour.

Quality of life questionnaire has a series of 29 simple questions which you will have to answer. Each question will be given 5 options to choose from.

You will undergo the Butanol test and quality of life assessment questionnaire before and after Total Laryngectomy surgery. After your surgery Nasal Airway Inducing Maneuver (Method to improve olfaction) will be taught and your ability to smell will be tested again. 6 months and 12 months after surgery the olfaction test will be repeated and questionnaire administered again. We are hoping that your sense of smell will improve following this treatment.

What are Butanol test, odour identification and odour discrimination?

Butanol is butyl alcohol (chemical) which is given at different dilutions and you will be asked to smell the different concentrations and tell us at which concentration you can identify the smell. This test is repeated independently in each of the nostrils. In odour identification and discrimination you are asked to smell different odours which we use in our daily life like coffee powder, cinnamon etc., and you are expected to identify each odor and differentiate it from the other one.

Does Butanol test have any side effects?

There are no side effects for this test. This will just help us to identify the extent of your disability

How and where will your nasal examination be done?

Your nasal examination is done using an endoscope. The test is called Rigid nasal endoscopy. It is done in the Endoscopy room in ENT OPD.

Will you have to pay for the nasal examination using an endoscope?

You will not be charged for the nasal examination using the endoscope.

Can you withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way.

What will happen if you develop any study related injury?

We do not expect any injury to occur to you but if you do develop any side effects or problems due to the study, these will be treated at no cost to you. We are unable to provide any monetary compensation, however.

Will you have to pay for the olfaction test and the questionnaire?

You need not pay for the olfaction test and the questionnaire. Any other treatment that you usually take will continue but the usual arrangements that you have with the hospital will decide how much you pay for this.

Will the questionnaire be easy to answer?

The Questionnaire will be easy and answers will be of multiple choices to choose from. A doctor will be with you while answering the questionnaire. Any problem in understanding the questions or difficult to answer will be immediately sorted out by him/her.

Will the answers of questionnaire be kept confidential?

The answers of the questionnaire will not be revealed or published. The questionnaire is used only to quantify the problems pre and post operatively. The results will be reviewed only by people associated with the study.

Will your personal details be kept confidential?

The results of this study will be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

CONSENT FORM

Study Title: Is rehabilitation of Olfaction necessary in patients undergoing total laryngectomy

Study Number:

Subject's Initials:

Subject's Name:

Date of Birth / Age (in years):

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my participation in the study is voluntary and I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected [ ]

(iii) I understand that the investigators of this study, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s). [ ]

(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject

Date:

Signatory's Name: _____

Name & Address of the Witness: _____

Signature (or Thumb impression):

Date:

Study Investigator's Name: _____

Signature of the Investigator:

Date:

CLINICAL RESEARCH FORM

NAME OF PATIENT: | | | | | | | | | | | | | | | | | | | |

AGE OF PATIENT (COMPLETED YEARS): | | |

SEX OF PATIENT ☐ MALE ☐ FEMALE

HOSPITAL NUMBER: | | | | | | | |

STUDY NUMBER: NAIM | | | |

DIAGNOSIS:

TREATMENT PLAN:

DATE OF ADMISSION: | | | | | | | | | (dd/mm/yyyy)

DATE OF SURGERY: | | | | | | | | | (dd/mm/yyyy)

DATE OF DISCHARGE: | | | | | | | | | (dd/mm/yyyy)

SURGEON/ASSISTANT SURGEON:

OLFACTION TESTING (OT)

BUTANOL THRESHOLD TEST

LEFT NOSTRIL				RIGHT NOSTRIL			
11	11	11	11	11	11	11	11
10	10	10	10	10	10	10	10
9	9	9	9	9	9	9	9
8	8	8	8	8	8	8	8
7	7	7	7	7	7	7	7
6	6	6	6	6	6	6	6
5	5	5	5	5	5	5	5
4	4	4	4	4	4	4	4
3	3	3	3	3	3	3	3
2	2	2	2	2	2	2	2
1	1	1	1	1	1	1	1
0	0	0	0	0	0	0	0
BOTTLE				BOTTLE			

ODOR IDENTIFICATION TEST

ODORANT	LEFT NOSTRIL TRIAL 1	LEFT NOSTRIL TRIAL 2	RIGHT NOSTRIL TRIAL 1	RIGHT NOSTRIL TRIAL 2
CINNAMON				
ASAFOETIDA				
COFFEE				
TEA				
PEPPER				
CLOVE OIL				
BABY POWDER				
TOTAL CORRECT				
VICKS/EUCALYPTUS (TRIGEMINAL)				
LEMON				
ROSE				
KEY	✓ CORRECT	NS – NO SENSATION	DK – DON'T KNOW	MISIDENTIFICATION TO BE SPECIFIED

SCORE

	LEFT NOSTRIL	RIGHT NOSTRIL
BUTANOL THRESHOLD		
ODOR IDENTIFICATION		
COMPOSITE SCORE		

APPETITE, HUNGER AND SENSORY PERCEPTION (AHSP) QUESTIONNAIRE

TASTE

In former days I enjoyed food:

[ ] 1 much more than nowadays

[ ] 2 more than nowadays

[ ] 3 the same as nowadays

[ ] 4 less than nowadays

[ ] 5 much less than nowadays

It seems that all foods have the same taste

[ ] 1 totally agree

[ ] 2 agree

[ ] 3 no opinion

[ ] 4 disagree

[ ] 5 totally disagree

It seems that the taste of food

[ ] 1 seriously declined

[ ] 2 declined

[ ] 3 stayed the same

[ ] 4 improved

[ ] 5 seriously improved

I still eat with relish

[ ] 5 totally agree

[ ] 4 agree

[ ] 3 no opinion

[ ] 2 disagree

[ ] 1 totally disagree

In former days, food was

[ ] 1 much more enjoyable than nowadays

[ ] 2 more enjoyable than nowadays

[ ] 3 as enjoyable as nowadays

[ ] 4 less enjoyable than nowadays

[ ] 5 much less enjoyable than nowadays

In general, I find food taste

[ ] 5 very good

[ ] 4 good

[ ] 3 fair

[ ] 2 bad

[ ] 1very bad

In former days I enjoyed eating

[ ] 1 much better than nowadays

[ ] 2better than nowadays

[ ] 3 the same as nowadays

[ ] 4 worse than nowadays

[ ] 5 much worse than nowadays

Nowadays the food is rather tasteless

[ ] 1 totally agree

[ ] 2 agree

[ ] 3 no opinion

[ ] 4 disagree

[ ] 5 totally disagree

APPETITE

Nowadays my appetite is generally

[ ] 5 very good

[ ] 4 good

[ ] 3 fair

[ ] 2 bad

[ ] 1 very bad

Nowadays I donot feel too much like eating

[ ] 1 totally agree

[ ] 2 agree

[ ] 3 no opinion

[ ] 4 disagree

[ ] 5 totally disagree

In former days my appetite was

[ ] 1 much better than nowadays

[ ] 2 better than nowadays

[ ] 3 the same as nowadays

[ ] 4 worse than nowadays

[ ] 5 much worse than nowadays

It seems that my appetite

[ ] 1 seriously declined

[ ] 2 declined

[ ] 3 stayed the same

[ ] 4 improved

[ ] 5 seriously improved

Every day I feel like eating

[ ] 5 totally agree

[ ] 4 agree

[ ] 3 no opinion

[ ] 2 disagree

[ ] 1 totally disagree

I still have a hearty appetite

[ ] 5 totally agree

[ ] 4 agree

[ ] 3 no opinion

[ ] 2 disagree

[ ] 1 totally disagree

SMELL BEFORE

In former days my sense of smell was

[ ] 1much finer than nowadays

[ ] 2finer than nowadays

[ ] 3 as fine as nowadays

[ ] 4 less fine than nowadays

[ ] 5 much less fine than nowadays

In former days, most of foods smelled

[ ] 1 much better than nowadays

[ ] 2 better than nowadays

[ ] 3 the same as nowadays

[ ] 4 worse than nowadays

[ ] 5 much worse than nowadays

It seems that my sense of smell was better in former days than now

[ ] 1 totally agree

[ ] 2 agree

[ ] 3 no opinion

[ ] 4 disagree

[ ] 5 totally disagree

SMELL NOWADAYS

I smell

[ ] 1 very well

[ ] 2 well

[ ] 3 fairly

[ ] 4 badly

[ ] 5 very badly

It seems that everything smells the same

[ ] 1 totally agree

[ ] 2 agree

[ ] 3 no opinion

[ ] 4 disagree

[ ] 5 totally disagree

Nowadays I am not able to identify a lot of odours

[ ] 1 totally agree

[ ] 2 agree

[ ] 3 no opinion

[ ] 4 disagree

[ ] 5 totally disagree

HUNGER FEELINGS

How often do you feel like eating your breakfast?

[ ] 5 daily

[ ] 4 often

[ ] 3 sometimes

[ ] 2 seldom

[ ] 1 never

How often do you feel like eating your lunch?

[ ] 5 daily

[ ] 4 often

[ ] 3 sometimes

[ ] 2 seldom

[ ] 1 never

How often do you feel like eating your dinner?

[ ] 5 daily

[ ] 4 often

[ ] 3 sometimes

[ ] 2 seldom

[ ] 1 never

How often do you feel like eating a snack?

[ ] 5 daily/ several times a day

[ ] 4 often

[ ] 3 sometimes

[ ] 2 seldom

[ ] 1 never

How often do you feel like eating something sweet?

[ ] 5 daily/ several times a day

[ ] 4 often

[ ] 3 sometimes

[ ] 2 seldom

[ ] 1 never

How often do you feel like eating something salty?

[ ] 5 daily/ several times a day

[ ] 4 often

[ ] 3 sometimes

[ ] 2 seldom

[ ] 1 never

How often do you have to force yourself to eat something?

[ ] 1 always

[ ] 2 often

[ ] 3 sometimes

[ ] 4 seldom

[ ] 5 never

How often are you looking forward to the next meal?

[ ] 5 always

[ ] 4 often

[ ] 3 sometimes

[ ] 2 seldom

[ ] 1 never

If you have been snacking, do you still feel like eating your next meal?

[ ] 5 always

[ ] 4 often

[ ] 3 sometimes

[ ] 2 seldom

[ ] 1 never

OLFACTION TESTING	**COMPOSITE SCORE**
OT1 Pre op	
OT2 post op 2 weeks(before NAIM)	
OT3 post op 2 weeks(after NAIM)	

EXCEL DATA SHEET

OLFACTION SCORE

sno	hno	age	sex	diagnosis	rt	surgery	preop	pre_score	pre_score	dos	postop2wk	post_bt_r	post_bt_l	post_at_r	post_at_l
1	963348D	47	M	CA GLOTTIS	POST	TLPP	15-09-2014	6	6	16-09-2014	29-09-2014	0	0	5	5.5
2	043361G	62	M	CA GLOTTIS	PRE	TLPP	16-09-2014	5.5	6.5	17-09-2014	01-10-2014	0	0.5	4	4.5
3	065453G	56	M	CA HYPOPHARYNX	PRE	TLPP	19-10-2014	6	6	20-10-2014	08-11-2014	0	0	5	4
4	055128G	61	M	CA HYPOPHARYNX	PRE	TLPP	12-11-2014	5	5	13-11-2014	26-11-2014	0	0	2.5	3
5	346977F	51	M	CA GLOTTIS	POST	TLPP	03-12-2014	5.5	5	04-12-2014	19-12-2014	1	1	5	4
6	097118G	68	M	CA TRANSGLOTTIS	PRE	TLPP	10-12-2014	4.5	5	10-12-2014	24-12-2014	1.5	1.5	4.5	4.5
7	050599G	55	M	CA GLOTTIS	PRE	TLPP	16-12-2014	5	5	17-12-2014	31-12-2014	0.5	1	4.5	4.5
8	995021C	72	M	CA GLOTTIS	POST	TLPP	17-12-2014	5	5	18-12-2014	31-12-2014	0	0	3.5	3.5
9	937054F	57	M	CA GLOTTIS	PRE	TLPP	16-01-2015	5.5	5	19-01-2015	02-02-2015	0	0	5	5
10	147159G	53	M	CA GLOTTIS	PRE	TLPP	13-02-2015	5.5	5.5	16-02-2015	04-03-2015	0.5	0.5	4	4
11	939096F	56	M	CA GLOTTIS	PRE	TLPP	17-02-2015	4	4	18-02-2015	06-03-2015	0	0	3	3.5
12	119902G	55	M	CA SUPRAGLOTTIS	PRE	TLPP	22-02-2015	5.5	6	23-02-2015	10-03-2015	1	0.5	4.5	4.5
13	842542D	71	M	CA SUPRAGLOTTIS	PRE	TLPP	02-03-2015	6.5	6	03-03-2015	18-03-2015	0	0	4.5	4.5
14	155725G	56	M	CA HYPOPHARYNX	PRE	TLPP	11-03-2015	5.5	5.5	12-03-2015	25-03-2015	0.5	1	4.5	4.5
15	176198G	59	M	CA SUPRAGLOTTIS	PRE	TLPP	11-03-2015	6	6	12-03-2015	25-03-2015	1	1.5	5	5
16	087768G	45	M	CA SUPRAGLOTTIS	POST	TLPP	21-04-2015	4	4.5	22-04-2015	05-05-2015	0	0	3	3
17	199227F	37	M	CA GLOTTIS	POST	TLPP	12-05-2015	1	1	13-05-2015	26-05-2015	0	0	0.5	1
18	177510G	54	M	CA GLOTTIS	PRE	TLPP	13-05-2015	5.5	5	14-05-2015	27-05-2015	1	1.5	4.5	4.5
19	222140G	50	M	CA TRANSGLOTTIS	PRE	TLPP	27-05-2015	4.5	4.5	28-05-2015	10-06-2015	0	0	3.5	4
20	215976G	56	M	CA SUPRAGLOTTIS	PRE	TLPP	03-06-2015	4.5	4	04-06-2015	17-06-2015	0.5	0.5	4	3
21	225869G	64	M	CA HYPOPHARYNX	PRE	TLPP	09-06-2015	1.5	1.5	10-06-2015	23-06-2015	0	0	0.5	0.5
22	233599G	46	M	CA TRANSGLOTTIS	PRE	TLPP	10-06-2015	4	4	11-06-2015	24-06-2015	0.5	0.5	3	2.5
23	231875G	44	M	CA GLOTTIS	POST	TLPP	15-06-2015	5	5	17-06-2015	01-07-2015	1	0.5	4	3.5
24	236984G	53	M	CA HYPOPHARYNX	PRE	TLPP	22-06-2015	3.5	3	24-06-2015	07-07-2015	0.5	0.5	2.5	2.5
25	212255G	53	M	CA GLOTTIS	PRE	TLPP	26-06-2015	3.5	3	29-06-2015	13-07-2015	0	0	2.5	2
26	242256G	69	M	CA HYPOPHARYNX	PRE	TLPP	01-07-2015	3	3	02-07-2015	16-07-2015	1	1	2	2.5
27	251858G	50	F	CA GLOTTIS	PRE	TLPP	14-07-2015	3.5	3	16-07-2015	29-07-2015	0.5	0.5	2.5	2.5
28	242796G	66	M	CA SUPRAGLOTTIS	PRE	TLPP	20-07-2015	3.5	4	22-07-2015	05-08-2015	1	1	3	3

AHSP SCORE

naim	t01	t02	t03	t04	t05	t06	t07	t08	sct	a01	a02	a03	a04	a05	a06	sca
1	3	3	4	4	3	5	4	2	28	4	3	4	4	4	3	22
2	1	2	3	5	3	4	4	5	27	3	4	2	4	4	4	21
3	1	1	1	1	1	2	1	1	9	2	3	1	2	3	2	13
4	2	3	2	2	5	3	4	3	24	3	4	4	1	4	3	19
5	3	3	1	3	5	1	4	2	22	2	5	4	1	5	2	19
6	4	3	2	2	5	1	4	2	23	3	5	5	2	5	3	23
7	3	1	2	1	3	5	1	1	17	2	1	1	1	3	2	10
8	3	5	2	4	2	4	4	5	29	2	1	1	1	3	3	11
9	2	5	2	3	2	3	3	4	24	4	2	2	3	4	4	19
10	3	2	3	1	4	3	3	4	23	3	2	3	2	3	2	15
11	3	2	4	4	3	4	3	3	26	2	3	3	3	2	3	16
12	3	3	4	4	4	3	4	4	29	3	2	2	3	1	3	14
13	3	4	4	5	4	3	4	4	31	4	4	4	3	4	4	23
14	3	3	2	3	2	1	2	3	19	2	2	1	2	1	1	9
15	4	3	4	4	3	4	3	3	28	3	3	4	4	3	2	19
16	3	2	2	3	3	2	2	2	19	3	3	3	2	3	1	15
17	3	3	4	3	4	4	3	2	26	3	3	4	3	2	2	17
18	2	3	3	2	1	2	2	2	17	2	2	1	3	2	3	13
19	2	2	3	2	1	3	3	3	19	2	3	3	2	3	3	16
20	2	2	2	2	3	2	2	2	17	3	2	2	2	2	3	14
21	3	2	1	1	2	1	3	4	17	3	3	3	2	3	2	16
22	2	3	2	2	2	3	2	2	18	3	3	2	3	2	2	15
23	3	3	2	2	2	2	2	2	18	3	3	2	2	2	2	14
24	4	4	4	3	3	3	3	2	26	3	3	3	4	3	4	20
25	3	3	2	2	3	3	2	2	20	3	2	2	3	2	2	14
26	3	2	2	2	2	2	2	2	17	2	2	2	3	3	2	14
27	3	3	2	4	2	3	2	2	21	2	3	3	2	3	3	16
28	3	2	2	2	2	1	2	2	16	2	2	3	1	2	2	12

AHSP SCORE

sb01	sb02	sb03	scsb	sn01	sn02	sn03	scsn	h01	h02	h03	h04	h05	h06	h07	h08	h09	sch	sc
1	1	2	4	4	3	1	8	3	5	3	5	5	3	5	5	5	39	101
1	1	1	3	4	2	1	7	5	4	4	3	5	5	3	3	1	33	91
1	1	1	3	4	2	1	7	4	3	2	2	1	1	3	3	1	20	52
4	4	4	12	3	3	2	8	5	5	5	5	5	3	5	4	4	41	104
3	3	2	8	4	4	1	9	1	1	1	1	1	1	5	1	1	13	71
5	5	3	13	5	5	3	13	1	1	1	3	3	3	4	2	2	20	92
3	3	1	7	2	3	3	8	3	4	4	2	4	4	2	5	3	31	73
2	2	2	6	3	3	4	10	3	3	2	4	4	4	3	3	3	29	85
1	1	1	3	3	5	2	10	5	5	5	3	3	2	5	1	5	34	90
4	2	4	10	4	4	4	12	4	4	4	3	2	2	3	4	4	30	90
3	2	2	7	3	2	2	7	3	3	3	3	3	3	4	2	2	26	82
4	4	3	11	4	4	4	12	4	3	3	4	3	4	4	4	4	33	99
4	4	4	12	5	3	3	11	4	3	5	4	4	3	3	3	4	33	110
2	3	3	8	2	1	2	5	2	3	2	2	3	1	2	3	3	21	62
2	3	2	7	3	3	4	10	2	3	2	4	4	3	2	1	2	23	87
2	2	2	6	3	3	3	9	3	3	3	3	2	3	3	2	3	25	74
3	2	2	7	3	3	3	9	2	3	2	2	2	3	2	2	3	21	80
2	2	3	7	2	2	2	6	2	1	2	1	2	2	2	2	3	17	60
3	3	4	10	3	4	4	11	2	3	3	2	2	1	2	1	1	17	72
3	2	3	8	3	1	2	6	2	3	3	2	2	3	3	2	3	23	68
3	3	3	9	3	3	3	9	2	3	3	2	3	2	3	2	2	22	73
3	3	4	10	3	2	3	8	2	3	3	3	2	2	1	3	2	21	72
2	2	1	5	2	2	4	8	3	3	2	3	3	3	2	3	3	25	70
3	4	3	10	3	3	3	9	3	2	2	3	4	3	3	2	2	24	89
3	2	3	8	3	3	3	9	2	3	3	3	2	2	2	2	2	21	73
3	2	3	8	2	2	2	6	2	3	3	2	2	2	2	2	2	20	65
3	4	4	11	4	3	3	10	2	3	3	2	2	3	2	3	3	23	81
2	3	2	7	2	2	2	6	2	3	2	2	3	2	2	2	3	21	62