Management of Advanced Cases of Cancer Larynx and Organ Preservation Protocols Essay

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Submitted in the partial fulfillment of master degree in otolaryngology surgery

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List of Abbreviations

AC	**Anterior Commissure**
AJCC	**American Joint Committee on Cancer**
CF	**Cisplatin / Fluorouracil**
CHEP	**Supracricoid partial laryngectomy with cricohyoidoepiglottopexy**
CHP or CHIP	**Supracricoid partial laryngectomy with cricohyoidopexy**
CT	**Computerized Tomography**
ECOG	**Eastern Cooperative Oncology Group**
FDG PET	**٢-[fluorine-١٨]-fluoro-٢-deoxy-D-glucose positron-emission tomography**
Gy	**Gray: The unit of measure for absorbed dose of radiation therapy.**
HPV	**Human Papiloma Virus**
IMRT	**Intensity-Modulated Radiation Treatment**
MRI	**Magnetic Resonance Imaging**
NAIM	**Nasal Airflow Inducing Maneuver**
ND	**Neck Dissection**
PET	**Positron-Emission Tomography**
RT	**Radiation Therapy**
RTOG	**Radiation Therapy Oncology Group**
SCCA	**Squamous Cell Carcinoma**
SGL	**Supraglottic Laryngectomy**
SND	**Selective Neck Dissection**
SWOG	**Southwestern Oncology Group**
SLP	**Speech-Language Pathologist**
TE	**Tracheo-Esophageal**
TEP	**Tracheo-Esophageal Puncture**
TL	**Total Laryngectomy**
TNM	**Tumor, Node, Metastases**
TVFs	**True Vocal Folds**
type C basis	**There is a widespread consolidated consensus. Randomized trials have not been carried out or have been inadequate, but the issue is settled without major controversy; currently, no further experimental evidence is felt to be needed.**
type ٢ level of evidence	**One or more randomized trials have been completed, but the evidence they provide is**

	not considered definitive (their results are not consistent, and/or they are methodologically unsatisfactory). Some controlled evidence has therefore been provided, but confirmatory trials would be desirable.
US	**United States**
WHO	**World health organization**

Introduction

Laryngeal cancer accounts for ٢ – ٥ % of all cancers, the incidence being higher among males than females. Smoking and alcohol represent the major behavioral risk factors. ***(Licitra et al.,*** ***)***

Several carcinogens, occupations and vitamin deficiencies have been associated with laryngeal cancer. A genetic susceptibility to environmental risk factors and carcinogens is recognized. ***(Licitra et al.,*** ***)***

The treatment of laryngeal cancer has been notable changes during the twentieth century. ***(Lefebvre and Lantigau,*** ***)*** Despite advances in diagnosis and treatment, the prognosis for patients with stage III-laryngeal cancer is not significantly different than it was four decades ago. ***(Strome andWeinman,*** ***)*** This failure to improve survival is multifactorial and is likely linked to controversy surrounding optimal treatment regimens for a heterogeneous patient and tumor population. ***(Strome andWeinman,*** ***)***

Surgery and radiotherapy represent the main therapeutic options. The choice between these two procedures is often controversial. ***(Licitra et al.,*** ***)*** The debate is open between surgery, which is more efficient but mutilating, and radiotherapy, which can preserve the larynx in many instances even though it requires sometimes mutilating surgery for salvage. ***(Lefebvre and Lantigau,*** ***)*** The appearance of platinum-based chemotherapy has updated this discussion. Todate, most of the randomized comparisons of mutilating/nonmutilating approaches have been with induction chemotherapy followed by irradiation if there has been a good clinical response to the chemotherapy. ***(Lefebvre and Lantigau,*** ***)***

For most patients, a total laryngectomy should not be used as the initial treatment for any stage laryngeal tumor. The goal in treating a patient with laryngeal cancer must be not only to cure but also to provide the best functional outcome for the patient. ***(Laramore and Coltrea,*** ***)*** Randomized controlled studies have shown that preservation of the larynx function in patients with advanced respectable laryngeal cancer is possible without compromising survival compared to total laryngectomy. ***(Rudat et al.,*** ***)***

Options for preserving the larynx include function-sparing surgery, radiotherapy alone, induction chemotherapy followed by radiotherapy of responders and concomitant radiochemotherapy. ***(Rudat et al.,)***

Careful monitoring of the conservatively treated patient is mandatory to allow for early salvage of failures to the original therapy. ***(Laramore and Coltrea,)*** Survival following salvage total laryngectomy was not influenced by the initial organ preservation treatment. ***(Weber et al.,)***

Efforts should be made to select patients properly (based on tumor characteristics, clinical aspects, imaging and biology) for the various strategies with the primary goal of curing the patient and secondarily to preserve laryngeal form and function when possible. ***(Lefebvre and Lantigau,)***

It is the physician's responsibility to recommend the best treatment option and to explain the other variable treatment strategies. ***(Strome and Weinman,)*** Clearly, quality-of-life considerations are an integral part of treatment planning and a well-informed patient is necessary to achieve an optimal result. ***(Strome and Weinman,)***

Social and medical support are important factors in improving patients` self-confidence and satisfaction, playing an important role in recovering useful phonation, psychological adjustment, and global quality of life. ***(Ramirez et al.,)***

Aim of The Work

Review of literature dealing with management of advanced cases of cancer larynx and role of organ preservation protocols.

Surgical Anatomy of The larynx

Larynx or **organ of voice** is placed at the upper part of the air passage. It is broad above. Below, it is narrow and cylindrical. It is lined by mucous membrane continuous above with that of the pharynx and below with that of the trachea. ***(Gray,*** ***)***

The skeleton of the Larynx

Consists of a series of single and paired cartilages united by ligaments and membranes.

Cartilages of the Larynx

The cartilages of the larynx are nine in number, three single and three paired, as follows:

- Thyroid.
- Cricoid.
- Two Arytenoid.
- Two Corniculate.
- Two Cuneiform.
- Epiglottis. ***(Gray,*** ***)***

Hyoid Bone

The hyoid bone is a U-shaped bone consisting of the body and paired greater and lesser horns. ***(Cummings et al,*** ***)*** The hypoglossal nerve and lingual artery run close laterally, requiring careful dissection in that area. The hyoid is rarely involved in laryngeal carcinoma. ***(Lai and Weinstein,*** ***)***

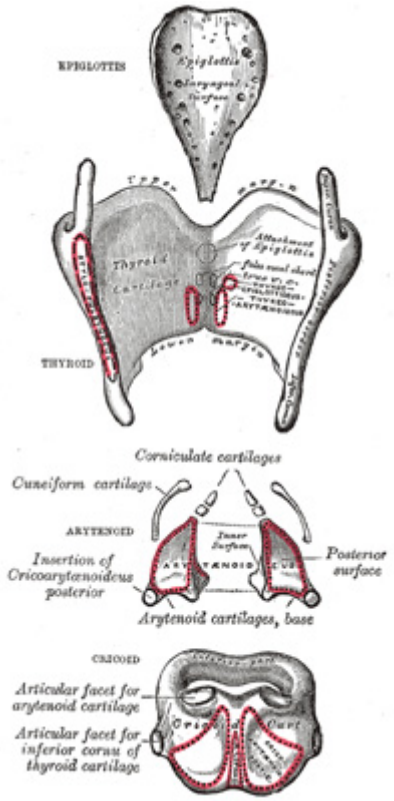
Thyroid Cartilage

This is the largest and most prominent cartilage. Articulations of the inferior horn with facets on the posterior arch of the cricoid form important synovial joints (the cricothyroid joints) that facilitate a hinge motion between the two cartilages. ***(Cummings et al,*** ***)*** Although fenestrations are present in the laminae of the thyroid cartilage, they are not a route for the spread of laryngeal cancer. ***(Lai and Weinstein,*** ***)***

Cricoid Cartilage

The cricoid cartilage is the only complete skeletal ring for the airway. Although these cartilages are composed of hyaline cartilage, they may later calcify. ***(Cummings et al,*** ***)*** Ossification of the cartilaginous framework

is important to consider because cancer has an increased tendency to invade ossified structures rather than cartilage the integrity of the circumference of the cricoid cartilage is necessary to perform organ preservation surgery of the larynx and to decannulate the trachea postoperatively. ***(Lai and Weinstein,*** ***)***



Picture ١. The cartilages of the larynx. Posterior view. ***(Gray,*** ***)***

Epiglottis

The cartilage of the epiglottis is a leaf-like structure composed primarily of elastic cartilage ***(Cummings et al,*** ***)*** Normal structures such as lymphatics, submucosal glands, blood vessels, and nerves cross through the multiple fenestrations present in the epiglottis. These perforations also serve as a route for the spread of supraglottic carcinoma from the surface mucosa into the preepiglottic space. ***(Lai and Weinstein,*** ***)***

Arytenoid Cartilage

Each cartilage is pyramidal in shape. With a base and three surfaces: medial, posterior and antero-lateral. ***(Hiatt and Gartner,***

Corniculate Cartilages

They are two small conical nodules, and are sometimes fused with the arytenoid cartilages. ***(Gray,***

Cuneiform Cartilages

They are placed one on either side, in the aryepiglottic fold. ***(Gray,***

)

Laryngeal compartments

The larynx is divided into three sites and each of these sites is divided into subsites. The current sites and subsites laied down by the International Union Against Cancer (UICC) into

١- Supraglottis	a- Suprahyoid epiglottis (including tip, lingual and laryngeal surface)
	b- Aryepiglottic fold,laryngeal aspect
	c- Arytenoid
	d- Infrahyoid epiglottis
	e- Ventricular bands (false cords)
٢- Glottis	a- Vocal cords
	b- Anterior commissure
	c- Posterior commissure
٣- Subglottis	

(International Union against Cancer, ١٩٩٧)

The larynx also encompasses several spaces, or rather potential spaces, which are important in the spread of disease. These include the pre-epiglottic and paraglottic spaces, Reinke`s spaces and the anterior subglottic wedge. ***(Watkinson et al.,)***

١-The Pre-Epiglottic Space

It is bound superiorly by the hyoepiglottic ligament, posteriorly by the epiglottis and anteriorly by the thyrohyoid ligament. Its apex inferiorly is limited by the attachment of the inferior end of the epiglottic cartilage by a strong fibrous band, the thyroepiglottic ligament, to the posterior surface of the thyroid cartilage below the median notch at the anterior commissure tendon. The epiglottic cartilage has numerous foramina through which carcinoma can pass from its posterior surface into the preepiglottic space. ***(Watkinson et al.,)***

٢-The paraglottic Space

The paraglottic space, or rather potential space, lies lateral to the true and false cords. Medially, it is bounded by the vestibular fold and the quandrangular membrane and more inferiorly by the conus elasticus, which is covered by the mucosa of the subglottic space. Medially, the paraglottic space is continued through the pre-epiglottic space, and superiorly by the vallecula and the aryepiglottic fold. Its lateral relation is the mucosa of the medial wall of the pyriform fossa posteriorly and the thyroid cartilage anteriorly. Inferolaterally, the space is bounded by the cricothyroid ligament. ***(Watkinson et al.,)***

٣-Reinke`s Space

It lies immediately beneath the laryngeal mucosa. i.e. superficial to the vocal ligament, and is bounded superiorly and inferiorly by the junction of the columnar squamous epithelium which represents the superior and inferior arcuate lines. ***(Watkinson et al.,)***

٤-The anterior Subglottic Wedge

It is a triangular-shaped zone with an apex terminating just below the anterior commissure tendon and which is delineated inferiorly by the anterior arch of the cricoid. Anterior commissure tumors commonly spread in a mushroom-like manner to involve this area and then penetrate the cricothyroid ligament. ***(Watkinson et al.,)***

The important tendons and ligaments of the larynx are the vocal ligament, the cricovocal membrane (conus elasticus), the vestibular ligament (the quadrangular membrane) and the anterior commissure tendon. **The cricovocal membrane (conus elasticus)** is attached below the entire border of the arch of the cricoid cartilage running round from one arytenoids facet to the other. Its median part, called the cricothyroid ligament, is tense and strong and triangular in shape. Its apex is inserted into the prominence of the thyroid cartilage at the anterior commissure. The upper edge of the cricovocal membrane extends from this point backwards to be inserted into the inferior border of the vocal process of the arytenoids cartilage. This upper free border is thickened and forms **the vocal ligament** which is the supporting ligament of the vocal cord. **The quadrangular membranes** have as their inferior margin the vestibular folds attached anteriorly to the depression between the two laminae of the thyroid cartilage above the vocal ligament and close to the attachment of the thyroepiglottic ligament. It extends backwards to be inserted into the tubercle on the anterolateral

surface of the arytenoids cartilage. It is composed of elastic fibrous tissue and contains the cuniform cartilages which attach to tha anterolateral surface of the arytenoids cartilages and help to keep the glottis open when the laryngeal muscles are relaxed. Medially, the quadrangular membrane is loosely covered by mucosa and laterally it is bounded by the paraglottic space. Its upper free margin is the aryepiglottic fold. **The anterior commissure tendon** is formed by the fusion of the two vocal ligaments anteriorly to form a tendon inserted into the thyroid cartilage. ***(Watkinson et al.,)***

The supraglottic portion of the larynx is derived from the buccopharyngeal angle (arches III and IV), whereas the glottic and subglottic portions derive from pulmonary angle (arch IV). Thus, each major component has an independent lymphatic circulation, separated into an upper and alower drainagesystem. They are collected together on the posterior wall of the cavity, but are separated laterally and anteriorly by the vocal folds. It is generally said that a vocal fold contains only a few capillary vessels, although some authorities disagree with this. Itis this poverty of lymph drainage which is said to predispose Reinke`s space to accumulation of oedema. The lymph vessels of the upper part pass alongside the superior laryngeal artery, pierce the thyrohyoid membrane and end in the upper deep cervical glands along with the lymph vessels of the pharynx (levels II and III). The efferent vessels from the anterior part of the lower segment of the larynx pierce the cricothyroid ligament and end in the prelaryngeal and pretracheal lymphatic nodal region (level IV) and deep cervical chain (level IV). The efferents from the posterolateral region pierce the cricotracheal membrane and end in the pretracheal (level IV) and lower deep cervical nodes (level IV). ***(Watkinson et al.,)***

The free edge of the vocal cord is coverd by squamous epithelium. Its superior and inferior surfaces are covered by respiratory epithelium and the junction between the respiratory and squamous epithelium above and below is marked by the superior and inferior arcuate lines, respectively. The subglottis can be divided into two parts. The anterior, fixed part is a triangle whose apex lies superiorly at the anterior commissure. Here, the mucosa is tightly bound to the cartilage, which has foramina through which tumour can pass. Laterally, the subglottic mucosa covers the conus elasticus and is mobile. It is clear that there are many different definitions of these two boundaries, which has added to confusion with regards to staging in the past. Some regard the superior border of the glottis as being the superior arcuate

line, whereas others include all the superior surface of the vocal cord and the floor of the vestibule in the glottis. In the past, some authors have placed the lower border of the glottis at the inferior arcuate line, some at the level of the superior border of the cricoid cartilage and other at point ١ cm inferior to the free edge of the vocal cord or ٥ mm inferior to the free edge (at midcord level). In١٩٩٣, the UICC accepted the recommendation by Steiner and Amrosch that ``the inferior border of the glottis is a horizontal plane ١cm inferior to the level of the upper surface of the vocal cord``. ***(Steiner and Ambrosch.***

The strict anatomical definition of the vocal cord is that part of the free edge of the cord, coverd by the squamous epithelium, which has a vertical hight of about ٥mm being bounded superiorly and inferiorly by the superior and inferior arcuate lines. The tissue above and below these lines is now included in the glottis. This means that a tumour may have already spread into this area of richer lymphatic drainage rather than the true vocal cords, so inevitably this change in anatomical classification may dramatically affect reported results. ***(Watkinson et al.,***

The glottis is said to consist of the vocal cords, the space which lies in a horizontal plane ١ cm inferior to the level of the upper surface of the vocal cord, the anterior commissure and posterior commissure but, again, this later two structures are not defined accurately. Strictly speaking commissure means a point, so that the anterior commissure presumably means the point anteriorly where the vocal cords come together. It is clear, however, that many authors regard the anterior commissure as an area from which a tumour can arise. On passing along the vocal cords to the anterior end, the strip of squamous epithelium narrows, so that the anterior end of the cord the strip of squamous epithelium is only about ١mm high. Here, it may join its fellow of the opposite side, or there can be a narrow strip ١-٢mm wide covered with respiratory epithelium passing between the anterior ends of the two vocal cords. Indeed, such an area is necessary on physiological grounds to allow mucus to pass up by ciliary action from the trachea to cross the vocal cords. At this point, the vocal cords are very narrow so that a tumour that crosses the anterior commissure spread readily off the vocal cords, and in particular below the cord into the apex at the anterior part of the subglottic space (anterior subglottic wedge). At this point the mucosa is tightly bound to the thyroid cartilage, which has foramina for the passage of vessels, providing an easy route of escape for cancer into the prelaryngeal tissue. The posterior commissure is not defined, but is taken to comprise the squamous epithelium lining the anterior surface of the arytenoid cartilage. The vocal