Conservation Laryngeal Surgery For Advanced Cancer Larynx

Thesis

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Abstract

Carcinoma of the larynx represents one of the commonest malignant tumors in head and neck region. Although they only represent 2 -5 % of all malignancies worldwide, these cancers have special importance because of their significant effect on voice, breathing, swallowing and quality of life .

Treatment options for these tumors include total laryngectomy and other conservation methods such as radiotherapy , chemotherapy and conservation laryngeal surgery.

In this study , conservation laryngeal surgeries were done for 24 patients with advanced cancer larynx classified as T2b or T3during the period from March 1999 to April 2007 . 17 patients had the operations done during the early years of this study and they were studied retrospectively and 7 cases were done during the last year of the study .

Supraglottic laryngectomy was done for 4 patients , and Supracricoid laryngectomy with cricohyoidopexy or cricohyoidoepiglottopexy was done for 20 patients .

The patients were followed up for a period ranged from 6 months up to 8 years . Follow up data included quality of voice , degree of aspiration , duration of use of the trachestomy , locoregional contol and overall morbidity and mortality.

These data showed that high rate of survival (95 %) , good quality of voice and good locoregeonal control could be gained by these operations .

From this study we conclude that conservation laryngeal surgery is an effective treatment option for advanced cancer larynx as it radically removes the tumor and preserves the patient ability to breath , speak and swallow in a nearly normal way

Key words :

partial laryngectomy , supracricoid laryngectomy , supraglottic laryngectomy , advanced cancer larynx , conservation laryngeal surgery

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List of Abbreviations

AJCC : The American Joint Committee on Cancer staging system for laryngeal carcinoma

CHP : Cricohyoidopexy

CHEP : Cricohyoidoepiglottopexy

CLS :Conservation laryngeal surgery

EGFR : Epidermal growth factor receptor

HPV : Human papilloma virus

PCR : Polymerase chain reaction

SCPL : Supracricoid partial laryngectomy

SGPL :Supraglottic partial laryngectomy

T L : Total laryngectomy

VPL :Vertical partial laryngectomy

INTRODUCTION

Carcinoma of the larynx represents one of the commonest malignant tumors in head and neck region. Although they only represent 2 -5 % of all malignancies worldwide, these cancers have special importance because of their significant effect on voice, breathing, swallowing and quality of life **(Stephen et al ., 2006).**

According to the most recent data released by the American cancer society, approximately 12,000 new cases of laryngeal cancer are diagnosed each year in the united states and 3900 deaths occur yearly as a result of this disease. These cases account for 0.9% of cancers from all sites and 0.8% of all cancer deaths. In Europe about 52,000 new cases are diagnosed per year **(Ferlay et al., 2001) .**

Laryngeal cancer affects men 4 times more frequently than women in the United states. In other countries men are affected up to 10 times more than women. It is also noticed that male to female ratio is higher for glottic tumors than for supraglottic tumors **(Snyder, 2006).**

Aim of the work :

The aim of this work is to review the effectiveness of conservation laryngeal surgery such as supracricoid laryngectomy and supraglottic laryngectomy in treatment of advanced stages of cancer larynx (T2b, T3) with the advantage of preserving laryngeal function as phonation and restoration of normal air way. It is considered now as a good alternative to the other methods of conservation in terms of locoregional control and functional outcomes .

Pathological considerations

Screening and case finding :

No whole population screening program for laryngeal carcinoma has been evaluated and so screening cannot , therefore, be recommended. Narrowing the at risk group down to those exposed to known carcinogens , such as smoking and alcohol is still insufficient to justify screening from a cost- effective view point, even in a high risk sub-population. Preclinical case finding has not been evaluated and cannot therefore be recommended. On the contrary, a diagnostic goal should be to avoid any delay when any suspicious symptoms have been noted **(licitra et al., 2003)**.

Despite the high incidence of second primary cancers developing either in other head and neck sites or the aerodigestive tract, screening methods applied after the first treatment failed to yield a significant reduction in mortalities from these second primaries **(Licitra et al., 2003).**

RISK FACTORS :

Many risk factors are thought to be responsible for the development of laryngeal carcinoma, the most important and the most preventable risk factor is smoking , which is believed to be a direct cause of up to 95% of laryngeal carcinoma. According to a large population based case-control study in southern Europe, over 90% of the present incidence of laryngeal cancer could be prevented by avoiding smoking **(Licitra et al., 2003).**

Alcohol also has a role, rising the risk in non smokers up to 5 times especially for supraglottic carcinoma irrespective of the type of beverage. More importantly, alcohol has been implicated as a synergistic cofactor when combined with smoking. The synergistic risk for smokers who drink is estimated to be 100 times that of individuals who do not smoke or drink **(Tuyns et al., 1988).**

Recently, there are many updated studies which claim a relationship between the development of laryngeal carcinoma and other risk factors. These risk factors

include **Human papilloma virus infection, diet, genetic factor, gastro-oesophageal reflux and immunity.** The method by which these factors share in the development of laryngeal malignancy is still controversery . what is sure is that these factors have a strong share in the development of laryngeal malignancy **(Licitra et al ., 2003).**

Human papilloma virus and laryngeal cancer :

The larynx is among the most significant anatomical sites in terms of Human papilloma virus(HPV)involvement exceeded in clinical importance perhaps only by the genital tract involvement. This causes a clinically significant disease known as recurrent respiratory papillomatosis which is known to be a benign condition. Spontaneous malignant conversion of papillomas is a rare event and the cofactors causing these conversion are not clearly identified yet (**Kashima et al., 1997**).

However, the association between HPV with laryngeal carcinoma was first suggested by detecting typical cytopathic effect of HPV in these lesions. The presence of HPV was confirmed by certain staining techniques that demonstrated the expression of HPV structural proteins in cancer cells **(Sayerjanen et al., 2000).**

The most convincing evidence to implicate HPV to laryngeal cancer is derived from the studies demonstrating HPV DNA in cancer lesions by different hybridization techniques and PCR **(Herrero, 2003).**

HPV serotype 16 seems to be the most common HPV serotype detected in about 25% of cancer lesions with other high risk types being occasionally reported such as serotypes 18, 31 ,33 **(Sayerjanen et al., 2000).**

At the moment, the evidences linking HPV to laryngeal carcinoma should be considered incomplete, it seems highly probable that the highly risky HPV 16 is implicated in the etiology of at least a subset of laryngeal carcinomas, but, a large scale multicenter case-control study with adequate statistical data is mandatory to fully explain this association and to give a comment on the relationship between HPV and other risk factors **(Hobbs and Birchal 2004).**

Hobbs and Birchal (2004) presented several questions about cancer cases related to HPV :

(1) Is HPV DNA screening needed for patients at increased risk for head and neck cancers (such as heavy smokers and drinkers at the age over 40 years) to detect latent HPV infection ?

(2)What is the appropriate treatment for premalignant lesions with HPV infection ?

(3)Should the treatment for HPV associated carcinomas be the same for HPV negative cancers ?

Diet and laryngeal cancer :

Diet may play a role in both development and prevention of laryngeal malignancy. A diet rich in fruits and vegetables can decrease the risk of development of laryngeal cancer. Evidence from many epidemiologic studies suggests that diet rich in vitamins such as carotenoids, retinol and vit C may decrease the risk **(Licitra et al ., 2003).**

Genetic factor and cancer larynx:

Head and neck cancers occur largely in exposed individuals who are susceptible to that exposure. Several factors have to be considered in estimating the true risk for developing cancer. Any factors influencing carcinogen absorption may play a role. For example, metabolic polymorphism of cytochrome P 450, cyp 1a1 gene, glutathione-s transeferase and other genes are under investigation **(Raferty et al., 2001).**

As it is known , tumor arises colonally from cells undergoing specific genetic alterations. A significant proportion of head and neck tumors have been shown to contain alteration of common oncogenes such as p16, p53, PTEN, Rb

or protoncogenes Cyclin D1, p63 and EGFR (epidermal growth factor receptor). In laryngeal cancer, Rb , Cyclin D1 and EGFR may play a role in terms of carcinogenesis. For example, loss of p53 function due to a mutation results in a progression from premalignant lesion to invasive cancer and increases the propability of further genetic progression **(Raferty et al., 2001).**

It is of significance here to mention that genetic modifications can be also used to detect cancer cells in tissues with normal histological appearance. The molecular analysis of cells in the free margins of operated tumors has been shown to predict tumor recurrence early before development of definite lesions **(Brennan et al., 1995).**

Gene therapy, which involves the introduction of genes into the body with the goal of treating a disease, is an exciting new field. Both genetic and acquired disease can be treated theoretically with gene therapy. Gene therapy in the treatment of cancer involves the introduction of genes into cells to direct the production of proteins that target malignant cells. These proteins are released at a specific location within the body to target diseased tissues and minimize toxicity to normal tissues. Gene therapy is still in the experimental stages , but holds promise for the treatment of head and neck cancer **(Snyder, 2006)**

Immunologic aspects of cancer larynx

Squamous cell carcinoma of the head and neck is a tumor where immunosuppresion has been observed for many years, but, is there evidence that the immune system can control cancer? There are several indirect types of observations suggest that it does . First, we commonly see patients who have had a presumptive regression of a primary cancer because they present with a regional lymph node. Second, there are observations of other cancers that seem to regress in the face of immune reactions. Third, there are rare cases of spontaneous regression usually in the face of infection **(Patel et al., 1994).**

A number of authors in 1960, identified a form of systemic immunosupression in the form of delayed hypersensitivity skin testing in a head and neck cancer patient. This cell mediated immune depression appeared to persist as the cancers were unsuccessfully treated, and remain as the single most powerful predictor of successful therapeutic outcome. How can laryngeal cancer contribute to systemic immunosupression ? this still under study, but, dendritic cells may play a role **(Richtsmeier , 2000).**

Dendritic cells have been shown to be the critical antigen processing cells in