

## BREAKTHROUGHS IN IMAGING: ENHANCING EARLY DETECTION OF LARYNGEAL CARCINOMA

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### **Abstract:**

*Throat cancer, primarily squamous cell carcinoma, constitutes a significant portion of head and neck and systemic tumors in China. The prevalence of throat tumors has seen an upward trend in recent years, and it exhibits regional disparities. Traditional risk factors like smoking and alcohol consumption have been strongly associated with throat cancer, characterized by symptoms such as hoarseness, sore throat, foreign body sensation, and swallowing difficulties. However, the landscape of this disease is evolving, with shifting demographics and emerging risk factors. Notably, oropharyngeal human papillomavirus (HPV) infection and gastroesophageal reflux have garnered recognition as critical risk factors in throat tumor development. HPV, particularly high-risk strains like HPV-16 and HPV-18, is increasingly implicated in oral cancers, surpassing the influence of smoking and drinking. A growing body of evidence links HPV infection in the throat to the onset of these tumors. Furthermore, gastroesophageal reflux disease, marked by gastric acid and bile reflux into the throat, has been associated with throat cancer. The refluxed substances erode the protective epithelial layers, induce inflammatory responses, and hinder the growth of throat cells. In this evolving landscape of throat cancer, understanding the role of these emerging risk factors, especially HPV infection and gastroesophageal reflux, is vital for early diagnosis and comprehensive management. Further research is needed to explore these connections and develop strategies for prevention and treatment.*

**Keywords:** throat cancer, squamous cell carcinoma, oropharyngeal HPV infection, gastroesophageal reflux, risk factors

### **1. Preface**

Throat cancer accounts for 13.9 percent of head and neck tumors and 2.1 percent of systemic tumors in China. The main manifestations of tumors are squamous cell carcinoma, with other tumors such as sarcoma and adenocarcinoma occurring less frequently<sup>[1]</sup>. In the recent years, the incidence of throat tumors was increasing year by year in our country and the world with obvious regional difference. There are many causes of throat tumors, the most important of which are smoking and drinking, and smoking and drinking are proportional to the incidence of throat tumors. Its main manifestations are: hoarse voice, sore throat, foreign body sensation, swallowing disorders<sup>[2]</sup>. In recent years, the disease characteristics of the population have changed greatly, and the proportion of smoking and alcohol in the incidence of throat tumors has also changed. In recent years, oropharyngeal HPV infection and gastroesophageal reflux throat tumors have also been recognized as a risk factor that cannot be ignored. Human papillomavirus (HPV) infection is the leading cause of oral cancer, surpassing smoking and drinking, according to a survey. Squamous cells have an "affinity" for HPV, and the human throat is also squamous epithelium, so the infection of HPV in the throat is very closely related to the onset of throat tumors. Data show that HPV-16, 18 two kinds of high-risk HPV, can also cause throat tumors. According to foreign statistics<sup>[3]</sup>, 72% of the HPV test results, and HPV test results are positive, which indicates that HPV infection in the throat cancer diseases, more than alcoholism, smoking, ranked first. The test results of HPV in some parts of our country are not as high as they are abroad, but in the throat tumor, the proportion of HPV testing positive is still one-third. However, the vast majority of oral HPV infections are caused by oral sex, when the patient's mouth, throat, tonsils and throat are exposed to HPV

and eventually become infected. The greater the number of oral sex partners, the higher the risk of HPV infection, and the duration of the disease can be decades. Gastroesophageal reflux disease is a kind of damage to the gastric mucosa caused by gastric reflux, which seriously affects the quality of life of patients. Recent studies have shown that the development of throat tumors is accompanied by gastroesophageal reflux disease. Gastric acid, bile acid and so on by stomach acid, bile acid and so on into the throat, can break the protective layer of throat epithelial cells through the way of "digestion", "remove the dirt", thus causing inflammatory response of throat epithelial cells, thus "aiding in torture" to attack throat epithelial cells, not conducive to the growth of throat epithelial cells [4].

According to the TNM classification standard of UICC 2017, laryngeal cancer can be divided into three types: supraglottic type, glottic type and subglottic type, among which glottic type is the most common, accounting for about 60%. Early laryngeal cancers are those with stages of T<sub>1</sub>, T<sub>2</sub> and no cervical lymph nodes or distant metastasis [5]. Early stage laryngeal cancer has a five-year survival rate of 60-70%, while early stage glottic cancer has a five-year survival rate of more than 90%. Early stage laryngeal cancer has a five-year survival rate of 60-70%, while early stage glottic cancer has a five-year survival rate of more than 90%. In the surgical program for laryngeal tumors, the most important is the precise stage of surgery, which depends on imaging and is combined with clinical and endoscopy. It is of great help for surgical treatment to identify the location, scope, size and surrounding space of the tumor, and the invasion of the tumor by the cartilage tissue forming the laryngeal skeleton [6].

## **2. Examination of laryngeal cancer**

### **2.1 Imaging examinations related to laryngeal cancer**

In recent years, the continuous progress of imaging technology makes it possible to accurately judge the location of the tumor, the extent of involvement, whether there is lymph node metastasis, whether there is systemic distal metastasis, etc. Imaging can easily understand the invasion of the tumor, especially in the preepiglottis, near the portal, and under the glottis, and can be a good judge of whether the cartilage has been invaded, and whether it has been seriously damaged. It also has certain value on the relationship between the tumor and the surrounding tissues, whether there are lymph nodes, whether there are distant metastasis, and what route the metastasis follows. It also plays an important role in the evaluation of postoperative and post-radiotherapy effect. Our previous work has shown that MRI is clearer and more sensitive than CT, and it is easier to find the glottic area and the subportal area. However, both CT and MRI have certain limitations, unable to give a clear description of the lesions on the surface of the pharyngeal cavity, and may be affected by the subjective judgment of the radiologist [7].

#### **2.1.1 CT**

Application of CT examination the most common T<sub>1</sub> laryngeal cancer is glottic cancer, and the lesions are few. If the lesions are small, CT can show normal, which may be because the lesions themselves are small and limited to the mucosa, or because the preoperative biopsy was performed before the lesions. The T<sub>2</sub> neoplasms invaded two subregions of the larynx, including the anterior and posterior joint glottic tumors, and the superior and inferior glottic tumors. Whether T<sub>1</sub> and T<sub>2</sub> laryngeal cancer is invaded in CT stage has a great influence on its occurrence and development. Normally, the anterior union is not more than 2mm thick and may be considered for tumor invasion when its thickness increases [8]. However, due to local edema and bleeding, it can also lead to a thickening of the anterior union, which can easily be misdiagnosed as tumor invasion. CT can well reflect whether supraglottic carcinoma has invaded the vocal cord, and can well reflect whether supraglottic carcinoma has invaded the vocal cord, but the sensitivity of CT to the true vocal cord is not high, and it is easy to appear false anteroposterior cross.

#### **2.1.2 Application of MRI examination**

MR Imaging has many advantages over CT imaging and is not affected by motion-related artifacts such as breathing, swallowing, pulse, etc. MRI can perform multiple parameter analysis (T<sub>1</sub>-weighted, T<sub>2</sub>-weighted, DWI, and post-contrast data). This method can effectively improve the contrast resolution of the image. However, MRI is costly, time-consuming, and not absolutely feasible for patients (compliance is poor, and claustrophobic patients are prohibited from using it). Through the search of relevant literature at home and abroad, most scholars believe that MRI has higher diagnostic sensitivity than CT. At present, many scholars have conducted relevant studies on the

application of MR In early laryngeal cancer<sup>[9]</sup>. Conclusion: MRI can better reflect the location, morphology and degree of invasion of laryngeal cancer, and has high clinical application value for T stage and histological grade of laryngeal cancer. Studies have shown that M R I is consistent with pathological results in the diagnosis of anterior joint infiltration, subglottic spread, preepiglottic space invasion, cartilage destruction, etc. However, there are still high false positivity in the evaluation of paratrophal space infiltration, and it is easy to misdiagnose some T2 stage lesions as T3 stage, which is related to inflammatory response, edema, fibrosis and other factors around the lesion. MRI can enhance the distinction between neoplastic cartilage invasion and peritumoral inflammation. Coronal MRI can clearly show the muscle group and thyroid process in the larynx. Plain and enhanced T1WI can clearly show the extent of cancer invasion.

## **2.2 Application of endoscopy in the diagnosis of laryngeal cancer**

Because it is non-invasive, can be used repeatedly after sterilization, and has a high detection rate for early pharyngeal tumors, it has been playing an important role in the diagnosis of pharyngeal tumors. General white light endoscopy is difficult to find small lesions of early laryngeal cancer to a large extent. In recent years, the emergence and development of various gastroscopy techniques have further expanded the function of gastroscopy on the basis of improving the specificity and sensitivity<sup>[10]</sup>. Internationally, NBI is the most commonly used type. MRI showed that the tumor presented high T2WI, equal or low signal on T1WI, and significantly enhanced after enhancement. DW I sequence showed that the A DC value of early laryngeal cancer was significantly higher than that of late stage, which is of great significance for guiding its staging. Moreover, the auxiliary image effect of MRI is better, which can be used to optimize the patient's data, expand the patient's indications, and achieve thorough treatment, even the maximum protection of the patient. Gastroscopy is helpful for understanding the gastrointestinal tract, but there are certain limitations in evaluating the scope and depth of gastrointestinal lesions, soft tissue infiltration and subglottic expansion<sup>[11]</sup>. Imaging can clearly reflect the depth and depth of tumor and the degree of soft tissue invasion. Therefore, imaging can provide more imaging data for endoscopy and clinic.

## **3. Treatment of laryngeal cancer**

The treatment of laryngeal cancer is mainly open surgery, including multiple laryngectomy, near-total laryngectomy, total laryngectomy, etc., which can provide a clear surgical field of vision, and can also be combined with radiotherapy, chemotherapy, neoadjuvant chemotherapy and other treatments. In recent years, due to the rapid development of endoscopic, microscopic and minimally invasive technologies, some laryngeal cancers can be achieved by personalized minimally invasive surgery such as CO<sub>2</sub> laser, low temperature plasma radiofrequency ablation and transoral robot<sup>[12]</sup>. Compared with open surgery, minimally invasive treatment can carry out personalized fine operations based on the size of the lesion range. On the premise of ensuring no residual scars in the neck, it can also reduce intraoperative blood loss, operation time and average length of hospital stay. Intraoperative tracheotomy is not required, and postoperative gastric tube and nasal feeding diet are not required. It has good retention effect in patient voice therapy, but it has high selectivity for tumor range. Minimally invasive therapy combined with radiotherapy and chemotherapy in the early stage of upper laryngeal tumors can reduce the mortality of specific types of tumors and the overall mortality.

### **3.1 Types of minimally invasive surgery for laryngeal cancer**

#### **3.1.1 Transoral CO<sub>2</sub> Laser Resection (TLM)**

In 1961, the first ophthalmic use was redstone laser, which was used to treat peeling retinas. In 1965, Polanyi and Kaplan used the CO<sub>2</sub> laser, the first optical scalpel. Since then, CO<sub>2</sub> lasers have gradually been used in various medical fields. CO<sub>2</sub> lasers were first used to treat early glottic cancer in the 1970s. CO<sub>2</sub> laser has the advantages of high monochromatic color, high brightness, high coherence and high energy conversion rate, and has little damage to the periphery of the lesion, so it can achieve accurate excision. By excising the diseased tissue at high temperature, its vaporization can cause the volume of the target tissue to increase, and then the target tissue will undergo solid phase transformation during the boiling process to generate water vapor, thus achieving the effect of coagulation and hemostasis for the blood vessels in the surrounding tissue<sup>[13]</sup>.

### **3.1.2 Low Temperature Plasma Radiofrequency Ablation (TLP-RFA)**

Cryoplasma radiofrequency ablation is a new key technology with independent intellectual property rights. Since the FDA approved its application in the world, it has been gradually used in the field of otolaryngology, head and neck surgery. In recent years, this potentially applied technology has been gradually developed in our country<sup>[14]</sup>. The principle of low temperature plasma radiofrequency ablation is as follows: The energy generated by bipolar radio frequency converts the electrolyte between the cutter and the tissue into a layer of thin plasma. Under the action of electric field, the charged particles in the plasma will be accelerated and the energy will be transferred to the tissue, thus destroying the molecules in the cells in the targeted tissue, resulting in the disintegration of the cells in the targeted tissue and their transformation into carbohydrates and oxides. Lead to tissue coagulation and necrosis in the targeted tissue; The necrotic tissue is shed or scarred again so that it can be reduced or removed. VRF maintains low power consumption during operation and only acts on the tissue surface, which can effectively reduce the heat damage of surrounding tissues under the low temperature environment of 40°-70°C. Plasma radiofrequency ablation technology is a relatively popular treatment method in the world, which is performed at a low temperature and has the functions of ablation, hemostasis and suction.

### **3.1.3 Oral Robotic Surgery (TORS)**

Since 1985, robots have operated through the mouth and are used in neurosurgery. After years of development, it has been widely used in urology, gynecology, orthopedics, thoracic surgery, general surgery, head and neck surgery and other professional fields. In 2005, WEINSTEIN<sup>[15]</sup> et al. introduced TORS technology into head and neck surgery, and reported its application for the first time in 2007. This method has been widely used in clinic, especially in the treatment of pharyngeal cancer, and has become an effective treatment method. The TORS have a magnified three-dimensional view, can mimic the natural movements of the hand and sew in deep structures. During the TORS operation, the surgeon can use the mouth opener to expose his oropharynx and put the endoscopic arm and instrument arm into it. At the same time, an assistant can help at the bedside, and the surgeon can sit in front of the operating table and perform the operation. With the help of a robot, he can visualize the diseased area and put free flaps into it in a minimally invasive manner.

### **3.1.4 Comparison between minimally invasive surgery and open surgery**

Compared with open surgery, minimally invasive surgery has the advantages of small damage, good effect, reusable, high safety, short hospital stay, less bleeding, clear vision, no need for tracheotomy, no need for nasal feeding and diet, can maintain complete throat function, improve the quality of life of patients. There is no scar on the neck and it is acceptable to most patients. For early, intermediate, and intermediate supraglottic tumors, the minimally invasive approach is performed faster than conventional open surgery. Of course, there's a downside to this, because it means there's a lot more selectivity in the size of the tumor than there is in open surgery. If the surgical field of vision is not good enough, it may cause the recurrence of the residual tumor. The low-temperature plasma knife is too thick to cut through the lesion accurately, but if it was a straight line, it would likely result in residual tumor. Oral interventional therapy has not been popularized because of expensive equipment, high production cost, high maintenance and management cost.

### **3.2 Traditional open surgery**

Because the throat has the characteristic of embryonic development, its lymphatic excretion and anatomical structure have the unique characteristics, the correct surgical method is the key to ensure the normal function of the throat, can not only improve the quality of life of the patient, but also can prolong the life of the patient. At present, many surgical methods such as laryngeal dilatation and laryngectomy and laryngectomy are used clinically. Although the tumor can be effectively removed, there are many surgical methods, large damage, slow recovery and other problems, which cannot meet the clinical needs<sup>[16]</sup>.

Laryngeal dehiscence vocal cord resection has simple operation, short operation time, small scope of laryngeal mucosa resection, less blood loss, can better protect laryngeal function of patients with laryngeal cancer, increase the success rate of postoperative extubation of patients, and contribute to the recovery of respiratory function of



patients. At the same time, because only a small amount of laryngeal tissue is removed, it will not cause great damage to important blood vessels and nerves, so it can reduce the impact on patients' swallowing and speech communication, and realize the recovery of laryngeal function, which is conducive to the improvement of patients' speech and swallowing ability. Because the procedure is less damaging to the larynx, the wound can be properly treated during the operation, thus reducing the incidence of complications.

### **3.3 Simple radiotherapy**

In recent years, with the continuous progress of medical technology, the treatment of laryngeal tumors has changed from simply obtaining better curative effect to better functional prognosis. Currently, radiotherapy (radiotherapy (RT) has become the standard treatment for early throat cancer. The American Society of Clinical Oncology Guidelines for Laryngeal Cancer (ASCO) points out that the survival outcome of T1 and T2 laryngeal cancer can be similar to that of surgical treatment through radical radiotherapy. For early throat tumors, a single dose of radiotherapy can achieve better results, with no significant effect on vocalization. The therapeutic dose of T1 and T2 laryngeal carcinoma was (60 ~ 70) Gy, (2 ~ 2.25) Gy / f, and studies have shown that larger therapeutic doses may be more beneficial. MNEJJA<sup>[17]</sup> et al. retrospectively analyzed 1050 laryngeal carcinoma cells of T1/T2 type, and most of them (52%) were at stage T1a. The local control rate of tumor within 5 years and 10 years after T1 radiotherapy was 92%, and the local control rate within 10 years was 90%. The 5-year and 10-year office control rates of T2 patients were 78%, and the 10-year office control rates were 72%. The laryngeal function retention rate of all patients after 10 years was 88%. Dinapoli et al<sup>[18]</sup>. compared surgical and radiation outcomes in patients with T1 glottic neoplasms. There was no significant difference in overall vital status between the two groups, even when patients were further divided into stage T1a and stage T1b. But the speech function of the radiotherapy group was significantly better than that of the surgical group. ChUNG et al<sup>[19]</sup>. found in their study of radiation exposure range that in patients with stage T1a glottic cancer, the local control rate reached 96.8% after 5 years of exposure to vocal cords alone, and the articulation function was good after treatment. Some scholars believe that thorough radiotherapy for early laryngeal cancer can achieve 84% local control, and salvage surgery can be performed even if radiotherapy is unsuccessful. Conclusion: Radiotherapy has a good protective effect on the larynx function while ensuring the curative effect.

### **3.4 CCRT**

CCRT is combined with chemotherapy at the time of radiotherapy, and can also be combined with IC+ CCRT, targeted therapy + CCRT and other therapies. Radiation therapy can enhance the absorption of chemotherapeutic drugs in tumor, promote apoptosis, and enhance radiation sensitivity. Radiotherapy (CCRT) is the most effective treatment for middle and advanced laryngeal cancer, but its efficacy remains controversial.

### **3.5 IC**

IC refers to improving the sensitivity of radiotherapy, thereby improving the efficacy of radiotherapy, or shortening the duration of radiotherapy through chemotherapy before radiotherapy. This method is suitable for aggressive tumor tissue, difficult surgery, and induction chemotherapy prior to radiotherapy to improve the sensitivity of the tumor to radiation and thus improve patient survival.

### **3.6 Biological therapy**

It has been reported that VEGF and EGF are closely related to the occurrence and development of tumors. In recent years, monoclonal antibodies against VEGF, as a new type of anti-VEGF drugs, can effectively inhibit the formation of tumor neovascularization, thus delaying the progression of tumor. In previous clinical trials, it was found that bevacizumab could specifically bind to VEGF, thereby reducing its biological effect, improving patients' progression-free survival rate and delaying disease development.

The purpose of laryngeal cancer treatment is to obtain the best survival time on the premise of guaranteeing laryngeal function. For early laryngeal cancer, radical radiation and surgery are the main methods. In contrast, radiation therapy is recommended as the first choice for early laryngeal cancer due to its better protective effect on organs. Relatively speaking, the treatment of the middle and late period is more complex, previously are based on

surgical resection, auxiliary radiotherapy. With the progress of medical technology, various therapeutic methods, such as induction chemotherapy, radiotherapy and biological therapy, have been effective in the treatment of tumors to varying degrees. However, the jury is still out on which protocol is more appropriate for intermediate and advanced laryngeal cancer.

#### **4. Prognosis and prevention of laryngeal carcinoma**

The overall prognosis of laryngeal cancer is good, with 5-year survival rates of over 90% in the early stage, 50-80% in the middle stage and 30-40% in the late stage. There were significant differences in treatment methods, efficacy, quality of life, survival rate and recurrence rate in early, middle and late two years. In the early stage of laryngeal cancer, total laryngectomy is usually not performed, mainly through radiation (or synchronous chemotherapeutic radiation) or laser local excision surgery to maximize the preservation of swallowing and voice. If, at a later stage, the cancer has spread to surrounding tissues and lymph nodes in the neck, then a total laryngectomy is required to completely remove all the tumor, without preserving the larynx, because the patient loses the ability to speak, loses the sense of smell, needs to use air to cut holes to breathe, and after a long period of rehabilitation, In order to use the artificial microphone to produce the sound.

Early detection, early diagnosis and early treatment are of great significance for improving the quality of life of patients with laryngeal cancer. However, the early manifestation of laryngeal cancer is more hidden, mainly manifested as hoarseness, dry climate in autumn and winter, will lead to laryngitis recurrence. The main manifestation of pharyngitis is hoarseness, foreign body sensation, swallowing difficulty, easy to be mistaken for a cold or chronic pharyngitis, many people do not take it to heart, just drink some herbal tea or take some lozenges, so as to miss the best treatment time.

It is important to note that hoarseness can be a precursor to throat tumors. Hoarseness caused by throat tumors will gradually disappear as the inflammation goes away, while hoarseness caused by throat tumors will gradually worsen. Patients should pay attention to the duration and degree of hoarseness, and whether there is any inducement at the time of onset. For men aged 40 and over, with high risk factors, detailed throat examination should be carried out.

#### **5. Conclusion**

In a word, the early manifestations of laryngeal cancer are not obvious, if early detection and treatment, will increase the survival rate and quality of life of patients. Endoscopy can better observe the morphology of mucous membranes, and is easy to find small lesions that are difficult to be found by CT and MR. Therefore, for patients suspected of early laryngeal cancer, endoscopy should be performed if it has certain diagnostic value. CT and MRI are the main diagnostic methods for early laryngeal cancer, and the sensitivity of M, R and I is higher than that of CT, which has a great advantage in the diagnosis of peripheral paralaryngeal space invasion, cartilage invasion and advanced laryngeal cancer, and will not be affected by any radiation. However, its disadvantage is that some patients are reluctant to receive treatment, and the cost is high. Therefore, endoscopy and imaging are of great reference value for the diagnosis of laryngeal cancer. In terms of treatment, attention should be paid to the application of comprehensive therapy to achieve better curative effect and better prognosis. This article provides theoretical basis for the diagnosis and treatment of laryngeal cancer through the analysis of related imaging examination and treatment methods.

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