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Progress in the study of lymph node metastasis status of squamous cell carcinoma of the oral and maxillofacial region

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Abstract: *Oral and Maxillofacial squamous cell carcinoma is one of the more common malignant tumors of the maxillofacial region, which develops a high lymph node metastasis rate due to the specificity of the site of occurrence and the richness of the lymphatic traffic network in the neck. Its treatment is mainly based on surgery and radiotherapy and chemotherapy. There are various views on the selection of the extent of lymph node dissection during surgery, and the literature reports that the depth of infiltration of cancer cells has a great influence on lymphatic metastasis, and the AJCC released the latest version of the TNM staging with the addition of the DOI index in the T stage, which has set the direction for the extent of lymphatic dissection. The impact of metastatic lymph node ENE on healing and the psychological pressure and burden of life faced by postoperative patients are also of great concern. In this article, we review the findings of oral and maxillofacial SCC in recent years.*

Keywords: *oral and maxillofacial, squamous cell carcinoma, lymph node metastasis*

1. Current status of squamous cell carcinoma of oral and maxillofacial region

Most malignant tumors are characterized by rapid growth, invasiveness, and early metastasis, a disease that affects people's lives. Oral and maxillofacial squamous cell carcinoma (SCC) is a malignant tumor of epithelial tissue origin that occurs in the anatomical region of the head and neck, with a high overall incidence rate, which directly affects the patients' diets, speech functions and normal facial appearance, and it accounts for 6.35% of the systemic malignant tumors [1], and is more common in the age distribution of the age group from 40 to 60 [1,2-4]. The incidence of oral and maxillofacial SCC and the site of incidence are different in different regions, which may be related to the different local races and people's living and eating habits [5-7], but the most common site of incidence is the tongue [1,2,8,9], and the male-to-female ratio is more than that of females, and the ratio of male-to-female patients is gradually decreasing [7,10], which may be related to the increasing proportion of female patients who start smoking and drinking [11], which may be related to the increasing proportion of female patients who start smoking and drinking. This may be related to the fact that the proportion of female patients who started smoking and drinking alcohol increased [11].

2. Treatment

Oral and maxillofacial SCC is difficult to be eradicated, has a high recurrence rate, is prone to early metastasis due to the anatomical site and other reasons, and has a greater impact on the quality of life of patients compared with some other parts of the malignant tumors, so early detection, diagnosis, and treatment is an important goal in the treatment of malignant tumors. In the 1930s to 1970s, oral and maxillofacial head and neck cancers were mainly treated with surgery, radiation, chemical drugs and traditional Chinese medicine [12]. Biological therapy began to appear from the 1980s, which mainly includes gene therapy, immunotherapy, cytokine therapy and molecular targeted therapy [13], but the 5-year survival rate of oral and maxillofacial malignant tumors still has not exceeded 50% to 60% [14-16], which is affected by the growth site of the malignant tumors, their size, tissue origin, degree of differentiation, lymph node metastasis, and the systemic condition of the patients, etc. Among them, the presence or absence of the tumor at the time of initial diagnosis has a significant impact on the survival of the patients. The reasons for this are influenced by the site of malignant tumor growth, size, tissue origin, degree of differentiation, lymph node metastasis, patient's general condition and other factors, of

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which the presence or absence of lymph node metastasis at the time of initial diagnosis has a great impact on the long-term survival rate of patients [14,16-20]. Li XJ[10] and others reported that there was no significant correlation between lymph node metastasis and age and gender. Li XJ[10] reported that the cervical lymphatic metastasis rate of oral and maxillofacial malignant tumors ranged from 34% to 59%, and Braams J W[19] reported that the survival rate of oral and maxillofacial malignant tumors with cervical lymph node metastasis could decrease to 50%. There is also a certain correlation between tumor site and prognosis, with lip cancer having the relatively best prognosis and a 5-year survival rate of 89.5%, while hypopharyngeal cancer has the relatively worst 5-year survival rate of only 31.9% [11]. Especially when head and neck squamous carcinoma metastasis breaks through the deep middle cervical lymph node group to the deep lower cervical lymph node group and/or the posterior triangle of the neck, the five-year survival rate of the patients decreases dramatically [21].

From the anatomical analysis, the head and neck are covered with a rich traffic network of lymphatic vessels, lymphatic organs and lymphatic tissues, etc., with a wide range of drainage for nutrient and oxygen transportation, metabolic waste elimination, immune endocrine, etc., and the flexibility of movement of the maxillofacial structures, which promotes the metastasis of cancer cells to the lymphatic tissues of the neck, an attribute that increases the difficulty of treatment and prognosis of oral cancer. Cancer cells settle in the arriving lymph nodes to infiltrate and grow, making the lymph nodes larger and harder, and then metastasize to the surrounding lymph nodes [22]. The more common lymph node metastasis follows the path of the ducts, but the metastasis of the cervical lymph nodes is not static, but rather diverse, which is related to factors such as individual patient differences and the type of disease. For example, in some patients, the tumor may cross the adjacent lymph nodes to the distant lymph nodes first, which is called jumping metastasis, i.e., metastatic foci appear in zones I and IV, while no lymph node metastasis is seen in zones II and III. The intricate structure of lymphatic vessels may lead to the situation that cancer cells do not metastasize to the next station but to the lymph nodes on the opposite side. Due to the complexity and diversity of the ways of cancer cells metastasizing down the lymphatic channels and the complexity of oral and maxillofacial movements, lymph node metastasis is increased, which makes the clinical diagnosis and treatment more difficult.

Since Crile reported the first systematic elaboration of cervical lymph node dissection for head and neck tumors as early as 1906, lymph node dissection has been improved and perfected in the continuous exploration and summarization of later generations, and many surgical modifications have appeared, from the initial radical treatment without retention to the later modified radical treatment. Radical neck dissection (RND) is the most traditional cervical lymph node dissection, which requires the removal of all lymphatic tissues and adjacent fatty tissues from the unilateral neck and does not emphasize the preservation of adjacent important tissues. Functional neck dissection (FND) is the most traditional neck lymphatic dissection, which requires the removal of all lymphatic tissue and adjacent fat tissue from one side of the neck, and does not emphasize the preservation of adjacent vital tissues. With the deepening of the way of lymph node metastasis and the continuous improvement of surgical methods, selective neck dissection (SND) has been increasingly promoted.

Ebrahimi [23] et al. found that patients with ≥18 cleared lymph nodes had significantly better recurrence-free survival and overall survival than patients with <18 cleared lymph nodes. In the 8th edition of TNM staging of tumours, which was updated and published jointly by the American Joint Committee on Cancer (AJCC) and the Union for International Cancer Control (UICC), the editors recommended that elective cervical lymph node clearance should be ≥10 lymph nodes, whereas standard cervical lymph node dissection should be ≥15 lymph nodes [24].

Although cervical lymph node dissection has improved the survival rate of patients, its complications, such as intracranial blood reflux disorder, shoulder dysfunction, neck deformity, auricular sensory disorders, etc., seriously affect the quality of life of the patients after the operation, in which the increase of cerebral pressure due to the simultaneous bilateral cervical vein ligation of a large number of venous ligations can be a danger to the patient's life. In some cases, no metastasis was found after the clearance operation, which caused additional trauma to the patients and also destroyed the normal immune defense function of the lymphatic tissues in the neck. It is thus clear that standard lymph node dissection is of great significance in improving the survival rate of tumour patients. Precise assessment of the presence of cervical lymph node metastases can help to improve the overall outcome of treatment, as well as reduce the burden on the patient and the risks he or she is exposed to in many ways. Therefore, efforts to reduce the complications of cervical lymph node dissection have been ongoing, and a major milestone has been the introduction of SND, which reduces the operative field and therefore inevitably reduces complications. However, this reduction must be based on a clear pattern of cervical lymph node metastasis; otherwise, it is an increase in the risk of recurrence and a decrease in the therapeutic effect in

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exchange for a reduction in complications, which is not permitted by the principles of surgical oncology.

3. Depth of SCC infiltration and extra-lymph node invasion

The rational treatment plan depends on the staging and grading of the tumor, and the accurate assessment of TNM staging is an important guide for the treatment plan of oral and maxillofacial malignant tumors. Tumors are characterized by three-dimensional growth in multiple directions. However, in previous staging, T stage was mainly calculated based on the maximum diameter of the tumor, and in the mid-1980s, it was noticed that the greater depth of invasion (DOI) suggested a worse prognosis.Melchers LJ [25] and Byers RM [26] suggested that a DOI of 4 mm could be used as a critical value for determining the metastasis of lymph nodes in oral cavity cancer. Li Qun et al found that the cervical lymph node metastasis was as high as 64.29% when the DOI of tongue cancer was >3 mm, while the cervical lymph node metastasis rate was only 5.56% when the DOI was <3 mm. The data of Fukano H et al showed that the cervical lymph node metastasis rate was 5.9% when the DOI was <5 mm, whereas the cervical lymph node metastasis rate was 64.7% when the DOI was >5 mm. The eighth edition updated the T-staging combined with DOI, and 5 mm was used as the threshold point of tumor infiltration depth to predict the risk of lymph node metastasis in oral cancer.

The American Academy of Pathology identified metastatic extranodal extension (ENE) as one of the most important factors of tumor recurrence, affecting healing, and was included in the N staging.The incidence of ENE varies in different regions, which may be related to the differences in sample size, tumor type, and testing methods.The incidence of ENE in the study of Forest [13] was 58%, while Zou Qi and Mao Chi et al reported 43.2%. GB. Snowt [22] and others found that when the diameter of metastatic lymph nodes was < lcm, the incidence of ENE was 15%-25%, and the incidence of ENE in lymph nodes between l and 2cm was 25%-45%, and when the diameter of metastatic lymph nodes was >3cm, the incidence of ENE would reach 75%. It was concluded that ENE increased with the decrease of tumor differentiation, and whether or not it accumulated extraperitoneal metastasis made a significant difference in the five-year survival rate of patients.

4. Postoperative and patient psychology

The diagnosis of malignant tumor itself, as a negative stress, will have an adverse effect on the patient's mood. Some malignant tumors invade the peripheral nerves with spontaneous pain, i.e. cancer pain, and some patients suffer from intolerable pain, which makes it difficult to sleep, and is difficult to be calmed by low-grade and low-dose painkillers. Severe invasion of surrounding normal tissues by malignant tumors often leads to abnormal function of surrounding tissues and organs, and even causes pathological fracture of bone tissues and so on. It is also easy to appear or aggravate dysphagia and speech disorders after treatment, and may also lead to abnormalities in the appearance and function of the face and face, etc., so patients will be accompanied by more psychological problems. The most common postoperative problems associated with oral and maxillofacial SCC patients are oral pain, psychological stress about the change in the shape of the face, worry, nervousness, difficulty in eating, and so on. While receiving treatment, patients also have to face special complex problems such as facial deformity, swallowing difficulties and communication disorders, which make their life stress and psychological burden more serious compared to other types of tumors.

5. Summary and Prospect

Oral and maxillofacial SCC is one of the more common malignant tumors among maxillofacial malignant tumors, and its susceptibility to lymph node metastasis has a great deal to do with the survival rate and healing of patients. Although lymph node dissection improves the survival rate of patients, the complications it brings should not be underestimated, therefore, the determination of the extent of lymph node dissection is and its important scientific research. Many researchers have begun to focus on the relationship between DOI and lymph node metastasis as well as ENE and healing. There is less information on studies related to the relationship between DOI and lymph node metastasis, and between ENE and patient healing, and there are discrepancies between the conclusions reached by various investigators. The psychological stress caused by facial deformity, dysphagia, and communication disorders faced by patients after surgery should also be given increased attention. Therefore, a series of issues such as the surgical plan, the scope of cervical lymphatic dissection, and the psychological health of patients after the healing process of oral and maxillofacial SCC need to be further explored.

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