Analysis of auxiliary diagnosis, cell survival, angiogenesis and nutritional support in patients with oral cancer
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OBJECTIVE
To investigate the changes and clinical significance of auxiliary diagnosis, cell survival, angiogenesis and nutritional support in patients with oral cancer.

METHODS: 50 patients with oral cancer treated in our hospital from June 2016 to September 2017 were selected as the observation group and 50 healthy people as the control group. The expression levels of auxiliary diagnosis [including secretory immunoglobulin A (SIgA), catalase (CAT)], cell survival [including survivin, focal adhesion kinase (FAK)], angiogenesis [including vascular endothelial growth factor (VEGF), hepatocyte growth (HGF), urokinase-type plasminogen activator (uPA)] and nutritional support [including lead (Pb), magnesium (Mg), calcium (Ca), iron (Fe), zinc (Zn) and copper (Cu)] related indicators in the two groups were observed and compared.

RESULTS: The levels of SIgA [(83.30±6.05) ug/mL], Mg [(1.21±0.17) mmol/L], Fe [(6.75±1.03)mmol/L] and Zn [(87.11±15.31) ug/L] in the observation group were significantly lower than those in the control group (P<0.05), while the levels of CAT [(39.87±9.18) U/mL], survivin [(131.63±10.53) ng/L], FAK [(62.27±5.20) ng/mL], VEGF [(533.73±150.63) ng/L], HGF [(411.32±181.72) ng/L], uPA [(5.12±1.31) mg/L], Pb [(65.55±20.76) μg/L], Ca [(1.55±0.20) mmol/L] and Cu [(14.90±5.30) μmol/L] were significantly higher than that of the control group. The difference was statistically significant (P<0.05).

CONCLUSIONS: Patients with oral cancer, the immune function of salivary mucosa decreased and cell survival was abnormal. Oral cancer patients are easy to regenerate tumor blood vessels. Tumor cells and vascular endothelial cells are active in proliferation, migration and invasion. The expression of trace elements is also abnormal, which is not conducive to the nutritional support of the body. The relevant indicators should be strengthened in clinical practice, so as to provide evidence for early diagnosis and treatment of the disease.

1. Introduction
Oral cancer is a common malignant tumor located in the head and neck, ranking fifth in malignant tumors. The tissue type is mainly squamous cell carcinoma, with high recurrence rate and poor prognosis. The survival rate is low, and more than half of patients with advanced oral cancer survival time is less than one year, and its incidence is also rising and becoming younger. Clinical complications often lead to various complications, such as eating disorders, unclear speech and other parts of the organ function loss[1,2]. Therefore, how to better treat oral cancer is still a difficult problem in the current medical field. This study monitors and analyzes the indicators of assisted diagnosis, cell survival, angiogenesis and nutritional support in patients with oral cancer, in order to provide a better method for clinical treatment of oral cancer.

2. Materials and methods
2.1 Clinical data
50 patients with oral cancer who were treated in our hospital from June 2016 to September 2017 were selected as observation group, including 35 males and 15 females, aged 45-76 years, including...
22 cases of tongue cancers and 19 cases of salivary gland cancer, 9 cases of buccal cancer, 5 cases of carcinoma in situ, 23 cases of high differentiation, 13 cases of high-moderate differentiation, 9 cases of moderate differentiation and poor differentiation; clinical stage according to UICC TNM clinical staging criteria\(^3\), including 18 cases of stage I, 7 cases in stage II, 9 cases in stage III, and 16 cases in stage IV. In addition, 50 healthy subjects underwent physical examination in the same period were selected as the control group, including 33 males and 17 females, aged 44-75 years. There was no significant difference in gender and age between the two groups (\(P>0.05\)), which could be compared and analyzed.

Inclusion criteria: (1) were diagnosed as oral cancer by pathological examination; (2) none of them received surgery, radiotherapy and chemotherapy. Exclusion criteria: (1) exclude those with other systemic malignancies; (2) exclude those with serious diseases such as heart, brain, liver, kidney and endocrine system.

2.2 Methods

Sample collection: All patients with oral cancer were collected 4 mL of non-irritating saliva in the early morning on the 2nd day after admission. The normal control group collected 4 mL of fasting non-irritating saliva in the waiting room. All saliva samples were centrifuged and the supernatant was taken. Store at 80 \(^\circ\)C, to be tested.

Observation indicators: detection of secretory immunoglobulin A (SIgA), survivin, focal adhesion kinase (FAK), vascular endothelial growth factor (VEGF), hepatocyte growth factor (HGF) and urine Kinase-type plasminogen activator (uPA) in saliva by ELISA; detection of catalase (CAT) levels by visible spectrophotometry; detection of blood lead (Pb) levels using BH2100 (2.0) spectrometer, the levels of serum Mg, Ca, Fe, Zn and Cu were measured using BH5100 (2.0) spectrometer.

2.3 Statistical methods

The data were analyzed by SPSS13.0 statistical software. The measurement data were expressed by mean \(\pm\) standard deviation (x+s). The two groups were compared by independent sample t test. When \(P<0.05\), the difference was considered statistically significant.

### 3. Results

#### 3.1 Saliva assisted diagnostic factor levels in both groups

After testing the two groups, the SIgA level in the observation group was \((83.30\pm6.05)\) \(\mu\)g/mL, which was significantly lower than that of the control group \((96.91\pm2.73)\) \(\mu\)g/mL; the CAT level in the observation group was \((39.87\pm9.18)\) U/mL, significantly higher than the control group \((29.15 \pm 9.97)\) U/mL, the difference was statistically significant \((P<0.05)\), see Table 1.

#### 3.2 Cell survival factor levels in both groups

After the two groups were tested, the levels of Survivin and FAK in the observation group were \((131.63\pm10.53)\) ng/L and \((62.27\pm5.20)\) mg/mL, respectively, which were significantly higher than the control group, and the difference was statistically significant \((P<0.05)\) See Table 2.

#### 3.3 Angiogenic factors in both groups

The levels of VEGF, HGF and uPA in the observation group were \((533.73\pm150.63)\) ng/L, \((411.32\pm181.72)\) ng/L and \((5.12\pm1.31)\) mg/L, respectively, which were significantly higher than in the control group, the differences were statistically significant \((P<0.05)\), as shown in Table 3.

#### 3.4 Nutritional support factor levels in both groups

After testing the two groups, the levels of Pb, Ca and Cu in the observation group were \((65.55\pm20.76)\) mg/L, \((1.55\pm0.20)\) mmol/L and \((14.90\pm5.30)\) mmol/L, respectively, which were obviously higher than control group \((P<0.05)\); the levels of Mg, Fe and Zn in the observation group were \((1.21\pm0.17)\) mmol/L, \((6.75\pm1.03)\) mmol/L and \((87.11\pm15.31)\) mmol/L, respectively, which were significantly lower than the control group \((P<0.05)\), see Table 4.

| Table 1. Comparison of saliva assisted diagnostic factors between the two groups. |
|-----------------|-----------------|-----------------|
| Group | n  | SIgA (μg/mL) | CAT (U/mL) |
| Observation group | 50 | 83.30±6.05   | 39.87±9.18 |
| Control group    | 50 | 96.91±2.73   | 29.15±9.97 |
| \(T\)            |    | 14.496       | 5.600       |
| \(P\)            |    | <0.05        | <0.05       |

| Table 2. Comparison of cell survival factor levels between the two groups. |
|-----------------|-----------------|-----------------|
| Group | n  | Survivin (ng/L) | FAK (ng/mL) |
| Observation group | 50 | 131.63±10.53   | 62.27±5.20 |
| Control group    | 50 | 40.91±4.83     | 27.85±2.60 |
| \(T\)            |    | 55.387         | 41.863      |
| \(P\)            |    | <0.05          | <0.05       |
Table 3.
Comparison of angiogenic factor levels between the two groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>VEGF (ng/L)</th>
<th>HGF (ng/L)</th>
<th>uPA (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>50</td>
<td>533.73±150.63</td>
<td>411.32±181.72</td>
<td>5.12±1.31</td>
</tr>
<tr>
<td>Control group</td>
<td>50</td>
<td>150.89±18.87</td>
<td>173.89±33.00</td>
<td>1.56±0.20</td>
</tr>
<tr>
<td>T</td>
<td></td>
<td>17.83</td>
<td>9.090</td>
<td>19.001</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Table 4.
Comparison of nutritional support factor levels between the two groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Pb (μg/L)</th>
<th>Mg (mmol/L)</th>
<th>Ca (mmol/L)</th>
<th>Fe (mmol/L)</th>
<th>Zn (μmol/L)</th>
<th>Cu (μmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>50</td>
<td>65.55±20.76</td>
<td>1.21±0.17</td>
<td>1.55±0.20</td>
<td>6.75±1.03</td>
<td>87.11±15.31</td>
<td>14.90±3.30</td>
</tr>
<tr>
<td>Control group</td>
<td>50</td>
<td>53.54±12.72</td>
<td>1.63±0.14</td>
<td>1.01±0.06</td>
<td>9.03±0.80</td>
<td>97.25±10.67</td>
<td>11.74±3.93</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

4. Discussion

Oral cancer can occur in any part of the mouth. As a common malignant tumor of the head and neck, which accounts for up to 24% of head and neck cancer. It is mainly squamous cell carcinoma, which is invasive and diffuse that has a serious impact on the quality of life of patients with this disease, among which to explore new or more markers also can provide an important basis for the specific diagnosis or prognosis evaluation of oral cancer[1].

Oral cancer has a high local recurrence rate and a poor prognosis. How to interfere with the infiltration of cancer cells into the proliferative phase is the key to solving the problem. The immune status of the body plays an important role in the development of tumors. IgA is the main effector of mucosal response, and its level of change reflects the local immune status of the oral cavity[7-8]. When tumors occur, the increase in expression in oral cancer tissues and the decrease in the expression of adhesion molecules lead to tumor cell shedding, which increases the CAT content in saliva[9,10]. It can be seen that CAT is an important substance in the body to scavenge reactive oxygen species, which is critical for the occurrence and development of tumors[9]. In this study, the level of IgA in patients with oral cancer was significantly lower than that in healthy subjects (P<0.05), and the level of CAT was significantly increased (P<0.05), suggesting that mucosal immunity decreased in oral cancer patients, and CAT was associated with tumor development.

Survivin is a member of the apoptosis inhibitory protein family and is specifically expressed in most tumor tissues, which is closely related to tumorigenesis, development, angiogenesis, metastasis and prognosis evaluation[11,12]. FAK is a non-receptor protein tyrosine kinase that is distributed in cell adhesion sites and regulates cell proliferation, metastasis and survival, and is associated with tumorigenesis, development and metastasis[13,14]. In this study, the levels of survivin and FAK in patients with oral cancer were significantly higher than those in healthy subjects (P<0.05), suggesting that serum survivin and FAK levels may be closely related to the occurrence and progression of oral cancer, and can be used for prognosis evaluation of the disease.

VEGF can strongly induce vascular endothelial cells to undergo mitosis and stimulate vascular invasion, which is associated with angiogenesis in various tumors[15-17]; HGF is involved in the growth, regeneration and remodeling of many organ tissues, and can stimulate cell proliferation. It plays a role in mitogens and morphogens and is closely related to tumor metastasis and invasion[18]; uPA acts as a proteolytic enzyme that binds to fibrinolytic enzymes and degrades extracellular matrix and basement membrane. It has important effect on invasion and metastasis[19,20]. In this study, the levels of VEGF, HGF and uPA in oral cancer patients were significantly increased compared with the control group (P<0.05), suggesting that the proliferation, migration and invasion of tumor cells and vascular endothelial cells were active in oral cancer patients, and the degradation rate of extracellular matrix and basement membrane were fast.

Microelements are nutrients that are rare but essential in the human body. The imbalance of trace elements can lead to malnutrition and even pathological conditions. There is a direct and close relationship between oral and trace element intake and even pathological conditions. There is a direct and close relationship between oral and trace element intake[21]. As a heavy metal element, Pb can change the expression of genes, causing abnormal expression of tumor suppressor genes and causing tumors. Ca is a factor that inhibits tumorigenesis and effectively reduces the incidence of intestinal tumors. Cu participates in the synthesis of various copper-containing active protein, which can bind to DNA and affect the stability of nucleic acid and its obvious abnormal changes can cause a variety of diseases, and cancer may occur; Mg is related to cell metabolism, oral mucosal epithelial cell renewal and repair, magnesium deficiency, leading to oral cavity ulcers, exposure to carcinogens, increase tumor incidence; Fe can stabilize cells, participate in hemoglobin synthesis, lack of iron, affect white
blood cell function, reduce lymphocyte sensitivity and stress
resistance of infection; Zn is related with enzyme composition and
metabolism, direct participation in protein synthesis and nucleic
acid metabolism and plays an critical role in the development of
malignant tumors[22-24]. In this study, the levels of lead, calcium
and copper in patients with oral cancer were significantly increased
(P<0.05), and the contents of magnesium, iron and zinc were
significantly decreased (P<0.05), suggesting that the balance of	race elements in oral cancer patients is imbalanced. There is a
certain correlation with the occurrence of oral cancer.

In summary, oral cancer patients are prone to decreased salivary
mucosal immunity, abnormal cell survival, active vascular
endothelial cell proliferation, imbalance of trace elements in the
body, these clinical indicators detection should be strengthened to
better treat the disease.

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