Objective: To explore the correlation of TI-RADS grading with oncogene and invasion molecule expression in thyroid cancer lesions. Methods: Patients who were diagnosed with thyroid cancer in this hospital between January 2017 and January 2018 were divided into TI-RADS grade 4 group (n=54) and TI-RADS grade 5 group (n=56) according to TI-RADS grading. 50 patients who underwent surgery and were diagnosed with thyroid adenoma in this hospital during the same period were chosen as benign thyroid group. The differences in the expression of oncogenes and invasion molecules in lesion tissues were compared among the three groups. Results: Proto-oncogenes c-myc, c-erbB-2, RET and TRK mRNA expression in lesions of TI-RADS grade 4 group and TI-RADS grade 5 group were higher than those of benign thyroid group whereas tumor suppressor genes DPC4, p53, PTEN and HBB mRNA expression were lower than those of benign thyroid group; invasion molecules BCORL1, BRD4, STAT3, CD151, SATB1 and CXCR4 mRNA expression were higher than those of benign thyroid group whereas ST7L mRNA expression were lower than that of thyroid benign group. With the increase of TI-RADS grading, the changes in the expression of oncogenes and invasion molecules were aggravated. Conclusion: The changes in oncogene and invasion molecule expression were aggravated with the increase of TI-RADS grading of thyroid cancer, and the specific TI-RADS grading was positively correlated with tumor malignancy.

1. Introduction

Thyroid cancer is the most common clinical malignant tumor disease, and to define the tumor nature and malignancy is very important for the follow-up therapy establishment[1,2]. Ultrasound is the main means to screen for thyroid diseases, foreign scholars put forward the thyroid imaging reporting and data system (TI-RADS) concept to standardize the thyroid imaging image evaluation, the thyroid tumors at TI-RADS grade 3 and below are the mostly benign tumors, and with the increase of TI-RADS grading, the malignant risk of tumors increases[3,4]. The role of TI-RADS grading in the evaluation of thyroid tumor properties has been recognized, but there is not much research on its intrinsic relationship with the specific tumor malignancy. In this research, the TI-RADS grading is referred to group the patients with thyroid cancer, the malignant molecule expression levels in various tumor lesions were further tested, and the relationship between TI-RADS grading and tumor malignancy was evaluated, which is elaborated as follows.

2. General information and research methods

2.1 Case information

A total of 110 patients who were diagnosed with thyroid cancer in this hospital between January 2017 and January 2018 were divided into the TI-RADS grade 4 group (n=54) and the TI-RADS grade 5 group (n=56) according to the TI-RADS grading. 50 patients who underwent surgery and were diagnosed with thyroid adenoma in this hospital during the same period were selected as the benign thyroid group. There were 25 males and 29 females in the TI-RADS grade 4 group, and they were 26-71 years old; there were 30 males and 26 females in the TI-RADS grade 5 group, and they were 25-68 years old; there were 25 males and 25 females in the benign thyroid group, and they were 27-70 years old. There was no significant
difference in the gender or age distribution among the three groups, and the follow-up research plan was approved by the hospital ethics committee.

2.2 Inclusion criteria

(1) The nature of thyroid tumor was confirmed by pathological examination; (2) patients were without history of thyroid surgery; (3) the patients signed the informed consent.

2.3 Exclusion criteria

(1) Combined with thyroid disorders such as hyperthyroidism, hypothyroidism and Hashimoto's thyroiditis; (2) combined with the malignant tumors diseases of other tissue viscera; (3) pregnant or breast-feeding women.

2.4 Oncogene and invasion molecule expression

Thyroid tumor tissue samples were collected during operation, the fluorescence quantitative PCR method was used to detect the expression of oncogenes and invasion molecules in them, oncogenes included c-myc, c-erbB-2, RET, TRK, DPC4, p53, PTEN and HBB, and invasion molecules included BCORL1, BRD4, STAT3, CD151, SATB1, ST7L and CXCR4.

2.5 Statistical processing

Oncogene and invasion molecule mRNA expression were all expressed as mean ± standard deviation and input in SPSS 24.0 to calculate the statistic P, and there was statistical significance in the differences if \( P < 0.05 \).

Table 1.

Comparison of proto-oncogene expression in lesions among the three groups of patients.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>c-myc</th>
<th>c-erbB-2</th>
<th>RET</th>
<th>TRK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign thyroid group</td>
<td>50</td>
<td>94.39±10.15</td>
<td>80.18±8.54</td>
<td>101.39±13.52</td>
<td>75.43±8.19</td>
</tr>
<tr>
<td>TI-RADS grade 4 group</td>
<td>54</td>
<td>118.45±13.26</td>
<td>91.33±9.57</td>
<td>115.48±12.96</td>
<td>87.09±9.15</td>
</tr>
<tr>
<td>TI-RADS grade 5 group</td>
<td>56</td>
<td>137.09±15.74</td>
<td>114.95±13.28</td>
<td>148.56±17.21</td>
<td>98.53±10.18</td>
</tr>
<tr>
<td>( F )</td>
<td></td>
<td>15.329</td>
<td>9.183</td>
<td>12.056</td>
<td>10.761</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>
</tr>
</tbody>
</table>

Table 2.

Comparison of tumor suppressor gene expression in lesions among the three groups of patients.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>DPC4</th>
<th>p53</th>
<th>PTEN</th>
<th>HBB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign thyroid group</td>
<td>50</td>
<td>77.25±8.91</td>
<td>85.76±9.54</td>
<td>90.11±9.67</td>
<td>92.07±9.12</td>
</tr>
<tr>
<td>TI-RADS grade 4 group</td>
<td>54</td>
<td>60.19±7.53</td>
<td>76.22±8.19</td>
<td>81.05±8.63</td>
<td>80.35±8.69</td>
</tr>
<tr>
<td>TI-RADS grade 5 group</td>
<td>56</td>
<td>45.23±5.19*</td>
<td>59.34±6.06*</td>
<td>62.18±5.55*</td>
<td>62.19±6.57*</td>
</tr>
<tr>
<td>( F )</td>
<td></td>
<td>12.048</td>
<td>13.746</td>
<td>10.194</td>
<td>9.284</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>
</tr>
</tbody>
</table>

Note: compared with benign thyroid group, \( *p<0.05 \); compared with TI-RADS grade 4 group, \( *p<0.05 \).

Table 3.

Comparison of invasion molecule expression in lesions among the three groups of patients.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>BCORL1</th>
<th>BRD4</th>
<th>STAT3</th>
<th>CD151</th>
<th>SATB1</th>
<th>ST7L</th>
<th>CXCR4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign thyroid group</td>
<td>50</td>
<td>80.84±8.91</td>
<td>72.35±8.19</td>
<td>95.37±10.18</td>
<td>86.42±9.18</td>
<td>65.39±7.14</td>
<td>114.28±13.74</td>
<td>75.38±8.19</td>
</tr>
<tr>
<td>TI-RADS grade 4 group</td>
<td>54</td>
<td>92.61±9.06*</td>
<td>86.09±9.12*</td>
<td>114.95±12.41*</td>
<td>95.11±9.85*</td>
<td>80.12±8.65*</td>
<td>90.55±9.67*</td>
<td>92.16±9.23*</td>
</tr>
<tr>
<td>TI-RADS grade 5 group</td>
<td>56</td>
<td>113.50±14.28*</td>
<td>97.48±10.06*</td>
<td>143.01±16.88*</td>
<td>116.23±19.82*</td>
<td>97.63±10.70*</td>
<td>71.63±7.82*</td>
<td>132.48±15.19*</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>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Note: compared with benign thyroid group, \( *p<0.05 \); compared with TI-RADS grade 4 group, \( *p<0.05 \).
4. Discussion

TI-RADS grading is a qualitative assessment of thyroid imaging therapy, and the malignant possibility of thyroid tumors with TIRADS grade 4 and above is high[5,6]. At present, there is less research about TI-RADS grading on evaluating the specific malignancy of thyroid carcinoma, the patients who were diagnosed with thyroid cancer in the research were grouped according to TI-RADS grading, and the differences in malignant tumor molecule expression between thyroid cancer patients with different TI-RADS grades were further evaluated in order to clarify the significance of TI-RADS grading in quantitatively assessing the malignant degree of thyroid carcinoma.

The expression imbalance of proto-oncogene and tumor suppressor gene is directly involved in the occurrence and development of thyroid cancer and specific expression of each gene can objectively reflect the malignant degree of tumor. The activation of c-myc gene is related to the occurrence of multiple malignancies such as colon cancer, breast cancer and lung cancer[7,8]. The protein encoded by c-erbB-2 has the activity of tyrosine protein kinase, and can participate in other gene regulation and promote the proliferation of malignant tumor cells[9,10]. RET is a proto-oncogene discovered in recent years, it has been found to be unusually highly expressed in many malignant tumor tissues, and abnormally silencing its expression can effectively inhibit the proliferation activity of tumor cells[11]. The activated TRK gene becomes the oncogene related to PTC, and it can directly stimulate the proliferation of cancer cells and increase tumor malignancy[12,13]. DPC4 is a tumor suppressor gene, is the hub of intracellular signal transduction, and can regulate cell proliferation and apoptosis, and the DPC4 gene expression reduction and even deletion can promote the proliferation activity of tumor cells[14]. p53 is the gene that is currently known to be closest related to human tumorigenesis, p53 may prevent the damaged DNA replication, and p53 inactivation or mutation will cause the infinite DNA proliferation and tumorigenesis[15]. PTEN regulates cell proliferation, differentiation and apoptosis, is the tumor suppressor gene with phosphatase activity, and negatively regulates tumor via PI-3K pathway[16]. HBB is generally expressed in all tissue organs of the human body, and its expression deletion is discovered in lowly differentiated and undifferentiated tumor tissues[17]. The results of the research showed that above proto-oncogenes c-myc, c-erbB-2, RET and TRK mRNA expression in thyroid cancer tissues were higher than those of benign thyroid group whereas tumor suppressor genes DPC4, p53, PTEN and HBB mRNA expression were lower than those of benign thyroid group; with the increase of TI-RADS grading, the change trend of above gene expression increased in thyroid cancer tissues, which shows that TI-RADS grading is directly related to thyroid cancer cell proliferation activity, and can reflect the malignant degree of thyroid carcinoma.

Abnormal proliferation gene expression results in rapid thyroid cancer cell proliferation and increased tumor volume, and the abnormal expression of invasion molecules causes the distant metastasis of the cancer cells, and is the core cause of increased tumor malignancy and adverse outcome. BCORL1 is a transcriptional co-inhibitory factor that promotes cancer cell invasion and metastasis by binding to E-cadherin promoter[18]. BRD4 is a member of the BET family, and cytological studies have shown that the proliferation and invasion activity of thyroid papillary carcinoma cells decrease after the BRD4 expression is silenced[19]. STAT3 is an important member of the signal transducer family, and its excessive activation can cause the cells to grow infinitely and resist apoptosis, also induce the synthesis of a variety of matrix metalloproteinases, accelerate extracellular matrix degradation and promote cell invasion and metastasis[20,21]. CD151 is the only oncogene in TM4SF family. In vitro experiments have confirmed that this gene promotes the proliferation of endothelial cells, and can accelerate the tumor angiogenesis and cell adhesion[22]. SATB1 can increase the expression of matrix metalloproteinase, and promote the invasion and metastasis of tumor cells through the PI3K/Akt signaling pathway[23]. ST7L is a gene that plays an anti-cancer role in a variety of malignant tumors, and it can inhibit tumor cell invasion ability and induce its apoptosis[24]. CXCR4 is the SDF-1 receptor known at present, and it has been confirmed that the combination of the two can increase the invasion vitality of breast cancer, thyroid cancer, colorectal cancer and other cancer cells[25]. The results of this study showed that BCORL1, BRD4, STAT3, CD151, SATB1 and CXCR4 mRNA expression in thyroid cancer tissues were higher than those of benign thyroid group whereas ST7L mRNA expression were lower than that of thyroid benign group; with the increase of TI-RADS grading, the change trend of above gene expression increased in thyroid cancer tissues, which shows that TI-RADS grading is directly related to thyroid cancer cells invasion vitality, and can reflect the malignant degree of thyroid carcinoma.

In conclusion, the higher the TI-RADS grading, the higher the proliferation and invasion vitality of thyroid cancer cells; there is a direct correlation between TI-RADS grading and thyroid cancer malignancy.

References


