Changes of CT dynamic contrast-enhanced scan parameters in patients with lung cancer before and after radiofrequency ablation

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Objective: To study the changes of CT dynamic contrast-enhanced scan parameters in patients with lung cancer before and after radiofrequency ablation (RFA) and their correlation with serum tumor markers. Methods: A total of 60 patients who were diagnosed with lung adenocarcinoma in the Second Hospital of Yulin City between May 2015 and January 2017 were selected and randomly divided into the RFA group and control group who received RFA combined with GP chemotherapy and GP chemotherapy alone respectively. Before and after treatment, CT dynamic contrast-enhanced scan was performed to calculate blood perfusion parameters, and serum was collected to determine the contents of cancer cell proliferation activity molecules, angiogenesis molecules and cell invasion molecules. Results: After treatment, BF, BV, MTT and PS levels as well as serum CYFRA21-1, SCC-Ag, TK-1, HE-4, TPS, HDGF, VEGF, PCDGF, bFGF, NGAL, MMP7, MMP9 and OPN contents of both groups of patients were significantly lower than those before treatment, and BF, BV, MTT and PS levels as well as serum CYFRA21-1, SCC-Ag, TK-1, HE-4, TPS, HDGF, VEGF, PCDGF, bFGF, NGAL, MMP7, MMP9 and OPN contents of RFA group after treatment were significantly lower than those of control group. Conclusions: The changes of CT dynamic contrast-enhanced scan parameters in patients with lung cancer before and after radiofrequency ablation suggest that the blood perfusion significantly reduces and is closely related to cancer cell proliferation and invasion as well as angiogenesis.

1. Introduction

Lung cancer is the malignant tumor with the highest incidence worldwide, and the incidence of lung cancer in China has been increasing year by year. As early lung cancer lacks specific clinical symptoms and is difficult to diagnose, most patients have been at advanced stage when diagnosed, and some patients have even missed the chance of surgical resection. Intravenous chemotherapy is the main therapy for advanced lung cancer, but under the influence of adverse reactions, chemotherapy resistance and other factors, the curative effect of chemotherapy for advanced lung cancer is not ideal. Radiofrequency ablation (RFA) is a newly developed technology of minimally invasive treatment of solid tumors, which uses 460-500 kHz of radiofrequency current to make local tumor tissue temperature elevate, and then cause coagulation necrosis of tumor tissue[1,2]. CT dynamic contrast-enhanced scan can reflect the blood perfusion in tumor lesions, and then provide a basis for evaluation of tumor malignancy[3,4]. In the following study, in order to define the value of radiofrequency ablation for advanced lung cancer treatment, the changes of CT dynamic contrast-enhanced scan parameters in patients with lung cancer before and after radiofrequency ablation and their correlation with serum tumor markers were analyzed.

2. Materials and research methods

2.1. General case information

A total of 60 patients who were diagnosed with lung adenocarcinoma in the Second Hospital of Yulin City between May 2015 and January 2017 were selected. All patients were diagnosed by pathological biopsy, and patients being allergic to contrast agent and those combined with heart, liver and kidney insufficiency were excluded. The 60 patients were randomly divided into RFA group and control group, with 30 cases in each group. RFA group included 12 male cases and 18 female cases that were 45-65 years old; control group included 13 male cases and 17 female cases that were 43-66 years old. There was no statistically significant difference between the two groups ($P>$0.05).
2.2. Therapy

Both groups underwent chemotherapy according to GP regimen with 21 d as one cycle, for at least 2 cycles and no more than 6 cycles. RFA group received radiofrequency ablation in the process of GP chemotherapy, and the specific methods were as follows: they received intramuscular injection of diazepam injection (10 mg) and fentanyl injection (0.1 mg) before treatment; the CT scan was conducted to locate tumor lesion and identify the puncture point, puncture path and distance; puncture area was given 2% lidocaine for anesthesia, then puncture and needle arrangement were done; single radio frequency temperature was 95 ℃, the time was 10-15 min, and the range included 0.5-1.0 cm outside the tumor edge.

2.3. CT dynamic contrast-enhanced scan parameter detection

Before treatment and 2-4 cycles after treatment, CT dynamic contrast-enhanced scan was conducted, non-ionic contrast agent 45 mL was injected at a speed of 5 mL/s via cubital vein with double high-pressure syringe, and then 30 mL saline was injected at a speed of 5 mL/s; after injection of contrast agent, the CT perfusion scan was performed on the lesion site, and the blood flow (BF), blood volume (BV), mean transit time (MTT), permeability surface (PS) and other parameters were calculated after the image was obtained.

2.4. Serum index detection methods

Before treatment and 2-4 cycles after treatment, 5-6 mL cubital venous peripheral blood was collected from two groups of patients and centrifuged to separate serum, and enzyme-linked immunosorbent assay kit was used to determine CYFRA21-1, SCC-Ag, TK-1, HE-4, TPS, HDGF, VEGF, PCDGF, bFGF, NGAL, MMP7, MMP9 and OPN contents.

2.5. Statistical methods

SPSS 20.0 software was used to input data, t test was conducted and P<0.05 indicated statistical significance in differences.

3. Results

3.1. CT dynamic contrast-enhanced scan parameters of two groups of patients

Before and after treatment, analysis of CT dynamic contrast-enhanced scan parameters BF (mL/100 mL·min), BV (mL/100 mL), MTT (s) and PS between two groups of patients was as follows: BF, BV, MTT and PS levels were not significantly different between two groups of patients before treatment (P>0.05); after treatment, BF, BV, MTT and PS levels of both groups of patients were significantly lower than those before treatment, and BF, BV, MTT and PS levels of RFA group after treatment were significantly lower than those of control group. Differences in BF, BV, MTT and PS levels were statistically significant within group before and after treatment as well as between groups after treatment (P<0.05), shown in Table 1.

3.2. Serum cancer cell proliferation activity molecule contents in two groups of patients

Before and after treatment, analysis of serum cancer cell proliferation activity molecules CYFRA21-1 (ng/mL), SCC-Ag (ng/mL), TK-1 (pmol/L), HE-4 (pmol/L) and TPS (U/L) contents between two groups of patients was as follows: serum CYFRA21-1, SCC-Ag, TK-1, HE-4 and TPS contents were not significantly different between two groups of patients before treatment (P>0.05); after treatment, serum CYFRA21-1, SCC-Ag, TK-1, HE-4 and TPS contents of both groups of patients were significantly lower than those before treatment, and serum CYFRA21-1, SCC-Ag, TK-1, HE-4 and TPS contents of RFA group after treatment were significantly lower than those of control group. Differences in serum CYFRA21-1, SCC-Ag, TK-1, HE-4 and TPS contents were statistically significant within group before and after treatment as well as between groups after treatment (P<0.05), shown in Table 2.

3.3. Serum angiogenesis molecule contents in two groups of patients

Before and after treatment, analysis of serum angiogenesis molecules HDGF, VEGF, PCDGF (ng/mL) and bFGF (pg/mL) contents between two groups of patients was as follows: serum HDGF, VEGF, PCDGF and bFGF contents were not significantly different between two groups of patients before treatment (P>0.05);

Table 1.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>BF (mL/100 mL·min)</th>
<th>BV (mL/100 mL)</th>
<th>MTT (s)</th>
<th>PS</th>
</tr>
</thead>
<tbody>
<tr>
<td>RFA group</td>
<td>30</td>
<td>Before treatment</td>
<td>55.12±7.76</td>
<td>7.61±0.93</td>
<td>11.31±1.47</td>
<td>14.68±1.86</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>17.64±2.25</td>
<td>2.51±0.36</td>
<td>7.69±0.93</td>
<td>6.97±0.94</td>
</tr>
<tr>
<td>Control group</td>
<td>30</td>
<td>Before treatment</td>
<td>54.89±7.25</td>
<td>7.70±0.89</td>
<td>11.46±1.72</td>
<td>14.81±1.81</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>29.31±4.59</td>
<td>4.26±0.79</td>
<td>9.31±1.05</td>
<td>9.21±1.05</td>
</tr>
</tbody>
</table>

*: comparison between RFA group and control group, P<0.05; #: comparison between before and after treatment, P>0.05.

Table 2.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>CYFRA21-1 (ng/mL)</th>
<th>SCC-Ag (ng/mL)</th>
<th>TK-1 (pmol/L)</th>
<th>HE-4 (pmol/L)</th>
<th>TPS (U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RFA group</td>
<td>30</td>
<td>Before treatment</td>
<td>12.58±1.67</td>
<td>3.28±0.46</td>
<td>3.86±0.62</td>
<td>163.37±20.32</td>
<td>232.65±33.27</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>2.95±0.42</td>
<td>1.04±0.12</td>
<td>1.77±0.22</td>
<td>99.73±10.28</td>
<td>93.51±1.25</td>
</tr>
<tr>
<td>Control group</td>
<td>30</td>
<td>Before treatment</td>
<td>12.77±1.87</td>
<td>3.32±0.48</td>
<td>3.91±0.58</td>
<td>166.21±19.35</td>
<td>233.73±35.25</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>5.02±0.78</td>
<td>1.65±0.22</td>
<td>2.52±0.35</td>
<td>124.25±17.85</td>
<td>152.42±18.97</td>
</tr>
</tbody>
</table>

*: comparison between RFA group and control group, P<0.05; #: comparison between before and after treatment, P>0.05.
between groups after treatment (P<0.05), differences in serum HDGF, VEGF, PCDGF and bFGF contents of RFA group after treatment were significantly lower than those of control group. Differences in serum HDGF, VEGF, PCDGF and bFGF contents were statistically significant within group before and after treatment as well as between groups after treatment (P<0.05), shown in Table 3.

Table 3.
Comparison of serum angiogenesis molecules before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>HDGF (ng/mL)</th>
<th>VEGF (ng/mL)</th>
<th>PCDGF (ng/mL)</th>
<th>bFGF (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RFA group</td>
<td>30</td>
<td>Before</td>
<td>289.76±34.12</td>
<td>179.76±20.34</td>
<td>22.31±2.26</td>
<td>242.52±28.94</td>
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<tr>
<td></td>
<td></td>
<td>After</td>
<td>138.68±19.25a</td>
<td>97.75±10.25a</td>
<td>10.28±1.56a</td>
<td>152.39±18.95a</td>
</tr>
<tr>
<td>Control</td>
<td>30</td>
<td>Before</td>
<td>291.21±33.27</td>
<td>181.14±19.45</td>
<td>22.80±3.77</td>
<td>245.2±29.34</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After</td>
<td>195.63±22.58a</td>
<td>132.68±17.84a</td>
<td>17.53±2.26a</td>
<td>194.57±22.46</td>
</tr>
</tbody>
</table>

*: comparison between RFA group and control group, P<0.05; #: comparison between before and after treatment, P<0.05.

3.4. Serum cell invasion molecule contents in two groups of patients

Before and after treatment, analysis of serum cell invasion molecules NGAL, MMP7, MMP9 and OPN contents of both groups of patients were significantly lower than before treatment, and serum HDGF, VEGF, PCDGF and bFGF contents of RFA group after treatment were significantly lower than those of control group. Differences in serum HDGF, VEGF, PCDGF and bFGF contents were statistically significant within group before and after treatment as well as between groups after treatment (P<0.05), shown in Table 4.

Table 4.
Comparison of serum cell invasion molecules before and after treatment (ng/mL).

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>NGAL</th>
<th>MMP7</th>
<th>MMP9</th>
<th>OPN</th>
</tr>
</thead>
<tbody>
<tr>
<td>RFA group</td>
<td>30</td>
<td>Before</td>
<td>68.95±9.24</td>
<td>0.98±0.11</td>
<td>351.93±44.67</td>
<td>67.69±9.24</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After</td>
<td>26.53±4.46</td>
<td>0.35±0.07</td>
<td>190.23±22.62</td>
<td>26.53±3.57</td>
</tr>
<tr>
<td>Control</td>
<td>30</td>
<td>Before</td>
<td>69.11±9.84</td>
<td>0.96±0.12</td>
<td>554.4±49.24</td>
<td>69.11±9.58</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After</td>
<td>38.59±5.42</td>
<td>0.57±0.08</td>
<td>275.94±36.72</td>
<td>40.28±6.68</td>
</tr>
</tbody>
</table>

*: comparison between RFA group and control group, P<0.05; #: comparison between before and after treatment, P<0.05.

4. Discussion

The goal of advanced lung cancer treatment is to prolong survival and improve the quality of life. Intravenous chemotherapy is the most widely used therapy for advanced lung cancer, which can effectively kill tumor cells and inhibit the growth of tumor cells by combined use of different chemotherapies. However, the overall effect of intravenous chemotherapy is not satisfactory under the influence of adverse reactions of chemotherapy, chemotherapy drug resistance and other factors. Radiofrequency ablation (RFA) has been a therapy for malignant solid tumor in recent years, then makes tumor cell necrosis and damages blood supply; at the same time, the heat effect of local tissue can also increase the sensitivity of cancer cells to chemotherapy drugs[5,6]. Dynamic contrast-enhanced CT is the auxiliary examination that has been widely used in the diagnosis of malignant solid tumors and the assessment of the malignant degree in recent years; it uses contrast agents to reflect the blood perfusion in tumor lesions and determine related parameters, and it can directly reflect the blood supply of tumor, and indirectly reflect the tumor proliferation and invasion activity[7,8]. In the study, in order to clarify the value of RFA for advanced lung cancer treatment, the CT dynamic contrast-enhanced scan parameters were analyzed before and after treatment, and the results showed that BF, BV, MTT and PS levels of both groups of patients after treatment were significantly lower than those before treatment, and BF, BV, MTT and PS levels of RFA group after treatment were significantly lower than those of control group. This indicates that both conventional intravenous chemotherapy and RFA combined with intravenous chemotherapy can effectively reduce the blood supply of lung cancer and inhibit the growth of the lesion; the treatment effect of RFA combined with intravenous chemotherapy is significantly better than that of chemotherapy alone.

Serum tumor markers are important indicators to determine the proliferation activity of lung cancer cells. CYFRA21-1 is a shedding fragment of keratin CK19, the expression of CK19 is increased in the process of epithelial cell carcinogenesis, and the shedding CYFRA21-1 is also increased accordingly; SCC-Ag is the antigen of squamous epithelial cells, and its generation significantly increases in the course of lung cancer[9]; Tk-1 is a key enzyme that catalyzes the salvage synthesis of DNA in cells and can promote the synthesis of DNA and the process of cell cycle salvage synthesis of DNA in cells and can promote the synthesis of DNA and the process of cell cycle; HE-4 and TPS are the newly discovered tumor markers, which have high sensitivity to lung cancer diagnosis[11,12]. In the study, analysis of serum contents of cancer cell proliferation activity molecules before and after treatment showed that serum CYFRA21-1, SCC-Ag, TK-1, HE-4 and TPS contents of both groups of patients after treatment were significantly lower than those before treatment, and serum CYFRA21-1, SCC-Ag, TK-1, HE-4 and TPS contents of both groups of patients after treatment were significantly lower than those of control group. This shows that both conventional intravenous chemotherapy and RFA combined with intravenous chemotherapy can effectively kill cancer cells, and the combination of RFA and intravenous chemotherapy is better than chemotherapy alone. Further analysis of the correlation between CT dynamic contrast-enhanced scan parameters and serum cancer cell proliferation activity molecule levels indicated that the BF, BV, MTT and PS levels were positively correlated with CYFRA21-1, SCC-Ag, TK-1, HE-4 and TPS levels. This indicates that blood perfusion of lung cancer lesions is closely associated with the proliferation vitality of cancer cells, and dynamic contrast-enhanced CT scan can measure blood perfusion parameters to reflect the proliferation activity of cancer cells within the lesion.

The proliferation of cancer cells in lung cancer lesions requires the nutrition from new blood vessels, while angiogenesis involves the
abnormal expression and secretion of multiple growth factors. VEGF is the most powerful pro-angiogenesis cytokine, which can promote the proliferation of endothelial cells and develop the vascular structure[13]. HDGF can induce the expression of VEGF and enhance the pro-angiogenesis effect mediated by VEGF[14]. PCDGF can not only directly promote endothelial cell proliferation, but also promote angiogenesis by increasing the expression of VEGF; bFGF is a mitogen with broad pro-proliferation effects[15]. In the study, analysis of serum contents of angiogenic molecules before and after treatment showed that serum HDGF, VEGF, PCDGF and bFGF contents of both groups of patients after treatment were significantly lower than those before treatment, and serum HDGF, VEGF, PCDGF and bFGF contents of RFA group after treatment were significantly lower than those of control group. This indicates that both conventional intravenous chemotheraphy and RFA combined with intravenous chemotheraphy can effectively inhibit angiogenesis, and the combined use of RFA and intravenous chemotherapy has stronger inhibitory effects on angiogenesis than chemotherapy alone. Further analysis of the correlation between CT dynamic contrast-enhanced scan parameters and serum angiogenesis molecule contents showed that BF, BV, MTT and PS levels were positively correlated with HDGF, VEGF, PCDGF and bFGF contents. This suggests that the blood perfusion of lung cancer lesions is closely related to the vitality of angiogenesis, and the dynamic contrast-enhanced CT scan can reflect the angiogenesis extent in the lesion by measuring the blood perfusion parameters.

Lung cancer cells show infiltrative growth on the basis of enhanced cancer cell proliferation activity and increased angiogenesis. NGAL has a moderating effect on the activity of various MMPs, which can form complexes with MMP and antagonize TIMP's inhibitory effect on MMP[16]; MMP7 and MMP9 are members of MMP family, which can degrade the collagen, laminin, elastin and so on in the extracellular matrix and cellular basal membrane to promote cell invasion[17]; OPN is a kind of secreted calcium-binding protein, which can promote the infiltrative growth of cells after combined with integrin receptor and CD44 receptor[18]. In the study, analysis of serum contents of cell invasion molecules before and after treatment showed that serum NGAL, MMP7, MMP9 and OPN contents of both groups of patients after treatment were significantly lower than those before treatment, and serum NGAL, MMP7, MMP9 and OPN contents of RFA group after treatment were significantly lower than those of control group. This indicates that both conventional intravenous chemotheraphy and RFA combined with intravenous chemotheraphy can effectively inhibit angiogenesis and the combination of RFA and intravenous chemotherapy has stronger inhibitory effects on angiogenesis than chemotherapy alone. Further analysis of the correlation between CT dynamic contrast-enhanced scan parameters and serum invasion molecule contents showed that BF, BV, MTT and PS levels were positively correlated with HDGF, VEGF, PCDGF and bFGF contents. This indicates that blood perfusion of lung cancer lesions is closely associated with cell invasion process, and dynamic contrast-enhanced CT scan can measure blood perfusion parameters to reflect the invasive growth extent of the cells within the lesion.

The efficacy of RFA combined with intravenous chemotheraphy for lung cancer is better than that of intravenous chemotheraphy alone; the changes of dynamic contrast-enhanced CT scan parameters before and after radiofrequency ablation indicate that blood perfusion of tumor lesions significantly reduces, and the changes of these blood perfusion parameters are closely related to the cancer cell proliferation, invasion and angiogenesis.

References