Relationship between tumor location and intraprocedural pain during ultrasound-guided percutaneous radiofrequency ablation of hepatocellular carcinomas under local anesthesia

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Abstract: Objective: To investigate the relationship between tumor location and intraprocedural pain in ultrasound-guided percutaneous radiofrequency ablation (RFA) of hepatocellular carcinomas (HCC) under local anesthesia. Methods: Twenty-three patients with 31 HCCs received ultrasound-guided percutaneous RFA under local anesthesia. According to the distance that tumor was away from liver capsule or branch of the portal vein, lesions were classified into group 1 (the distance that tumor was away from liver capsule or branch of the portal vein was less than 5 mm) and group 2 (The distance that tumor was away from liver capsule or branch of the portal vein was more than 5 mm). Pain was scored using the relative visual analog scale (VAS) which was calculated by the highest VAS score during RFA minus the VAS score during local anesthesia at the puncture site. The highest RFA power used was also recorded. The difference of relative visual analog scale and highest RFA power between group 1 and group 2 were compared. Results: The highest VAS score during ultrasound-guided RFA, the VAS score during local anesthesia at the puncture site and the relative VAS were 3 (0-6), 8 (2-10), 5 (1-7) for group 1 and 3(1-5), 6(2-8), 3 (0-5) for group 2. The relative VAS in group 1 was much higher than that in group 2 (P=0.001, Z=-3.490). So the HCC in group 1 caused more severe pain than that in group 2. The median of the highest RFA power in group 1 and group 2 were 140W (70-200) and 150W (100-200), no significant difference was found (P=0.639, Z=-0.505) between the two groups. Conclusion: HCC adjacent to liver capsule or portal vein would cause more severe pain in ultrasound-guided percutaneous RFA under local anesthesia.

KEYWORDS: Ultrasonography; Hepatic neoplasms; Ultrasound-guided; Radiofrequency ablation; Visual analogue scale; Pain

Ultrasound-guided radiofrequency ablation (radiofrequency ablation, RFA) has become commonly used in clinical liver cancer treatment due to the small surgical trauma, local anesthesia without the risks of general anesthesia and short postoperative recovery time as well as other characteristics. However, some liver cancer patients cannot tolerate the pain caused by radiofrequency ablation treatment, which affects the smooth progress of the treatment. In recent years, foreign studies[1-2] found that, in radiofrequency ablation treatment, there are quite big differences in pain caused by different lesion locations in the liver, and there is some correlation between the degree of pain and tumor location as well as ablation time. However, there is few related research reported in the litera-
ture, and there is no domestic report.

Carlsson and Bodian [3-5] have employed a visual analog scale (visual analogue scale, VAS) to quantitatively assess the degree of the sensation of pain for patients. They used a ruler with a scale (set the scale to represent the size of pain severity), and asked their patients to point out the appropriate degree corresponding to the intraoperative pain on the scale. The physician could judge and assess patients with pain scores according to the ruler readings to visualize the extent of the patient's pain for a quantitative assessment. Currently, the visual analog scale has been widely recognized in clinical practice. In this study, visual analog scale was applied for quantitative evaluation and comparison of the degree of pain in radiofrequency ablation of 23 liver cancer patient cases (lesions near and away from the liver capsule or branch of portal vein above the liver segment). This study provided a reference for liver cancer patients' intraoperative anesthesia methods and medication options in radiofrequency ablation.

Materials and Methods

1. Objects

23 Patients were admitted to our hospital from December 2009 to December 2010 with liver cancer after pathological or clinical diagnosis, and were in line with ultrasound-guided percutaneous radiofrequency ablation treatment under local anesthesia after clinical assessment, 16 males and 7 females, age 32 to 74, average (51.4 ± 11.7) years old. There were 21 cases of primary liver cancer (27 lesions) and 2 cases (4 lesions) of cancer recurrence after liver transplantation. There were 16 cases of one lesion by preoperative ultrasound, 4 cases of 2 lesions, 2 cases of 3 lesions and 1 cases of 4 lesions, with lesion diameters 8 to 35 mm, average (18.5 ± 5.7) mm.

2. Instruments and methods

(1) United States Radionics Cool-tipTM RF ablation system and the cold cycle electrode needle were used for Radiofrequency ablation. The ultrasound guide system uses Italy Yum Mylab 90 Color Doppler ultrasonography. The abdominal CA431 probe is equipped with piercing guide tube, with the probe frequency 1 to 8 MHz.

(2) Grouping and radiofrequency ablation method: 23 Cases of patients were grouped according to the lesion locations from preoperative ultrasound and were treated with ultrasound-guided percutaneous radiofrequency ablation under local anesthesia. For the group with lesion near the liver capsule, the distance that tumor was away from liver capsule or branch of the portal vein was ≤5 mm. For the group with lesion away from the liver capsule, the distance that tumor was away from liver capsule or branch of the portal vein was >5 mm. Conventional prepped and draped, local anesthesia was applied by the use of 1% lidocaine along the puncture path line. With automatic transmission, the starting power was 80W, and was gradually increased to the maximum power within 2 min, or up to the maximum power that patients could tolerate. The maximum power value was recorded. When patients had both lesions near and away from the liver capsule group, the lesion near the liver capsule group was first ablated followed by ablation of the lesion away from the liver capsule group. The ablation interval for different lesions was more than 15 minutes. RF needle with exposed side of a 3cm was selected. Liver tumors with diameter ≤1.5 cm were ablated once during operation and numerous ablation for liver lesions with diameter> 1.5 cm. According to literature specification requirements, the radiofrequency ablation of liver tumors covers the tumor and its surrounding normal liver tissue at least 5 mm away [2,6-10]. The ultrasound real-time observation of the lesion was used to determine whether the ablation was completely.

(3) Intraoperative VAS quantitative scoring method: A 10 cm long ruler with 0 to 10 scale was used. Before surgery, the patients were informed of the course of treatment and method of expressing the pain, which is to point out the degree of their own level of pain on the ruler during the treatment. 0 means painless and 10 shows that the pain cannot be tolerated. The VAS score under local anesthesia was treated as the basic VAS scores, and the VAS score when the ablation power raised to the highest value which patients can tolerate was used as the intraoperative VAS score. Therefore, the relative VAS score = intraoperative VAS score - basic VAS scores. When the relative VAS score is negative, the record is zero for result analysis. After treatment of 23 cases of hepatocellular carcinoma patients with radiofrequency ablation, VAS scores were summarized and analyzed. Follow-up reviews with ultrasound, CT or MRI were carried out for the two groups of patients after treatment.

3. Statistical analysis

SPSS13.0 software package was used for data analysis. The various VAS scores of patients and the maximum ablation power that patients can tolerate were expressed as median. The comparison of the relative VAS scores between the near and away from liver capsule groups, and the comparison of maximum power patients can tolerate during ablation were subject to Wilcoxon rank sum test. When P <0.05, it was considered statistically significant.

Results
1. VAS score results of radiofrequency ablation surgery in 23 cases of liver cancer patients

Two groups of patients with 31 liver lesions completed ultrasound-guided radiofrequency ablation and basic VAS scores, intraoperative VAS score as well as the maximum power patients can tolerate during ablation were obtained to calculate relative VAS scores.

(1) In the group with lesion near the liver capsule, there were 15 cases with 19 liver cancer lesions, lesion diameter (19.6 ± 5.6) mm. There were 5 lesions near the portal vein branch (Figure 1), 14 near the liver capsule. The median VAS scores in radiofrequency ablation were basic score 3 (0-6), intraoperative VAS score 8 (2-10) and relative VAS score 5 (1-7). The median maximum power patients can tolerate in ablation was 140 (70-200) W.

(2) In the group with lesion away from the liver capsule, there were eight cases of 12 liver lesions (Figure 2), lesion diameter (16.8 ± 5.5) mm. Comparison with adjacent liver capsule group showed no statistical significance (P = 0.101, and Z= -1.649) of lesion diameter difference between the two groups. The Median VAS score in radiofrequency ablation were basic VAS score 3 (1-5), intraoperative VAS score 6 (2-8) and relative VAS score 3 (0-5). The median maximum power patients can tolerate in ablation was 150 (100-200) W.

(3) In 23 cases, 4 cases (4/23) of 2 lesions were near the liver capsule and away from the liver capsule. When the maximum power was similar in ablation treatment, in three cases (3/23), the relative VAS scores of lesions near the liver capsule were higher than those of the lesions away from the liver capsule. The remaining 1 patient (1/23) had the same relative VAS score for lesions near the liver capsule and away from the liver capsule.

2. The comparison of relative VAS scores and the maximum power between two groups of patients with hepatocellular carcinoma radiofrequency ablation treatment

In the 23 cases of hepatocellular carcinoma patients with radiofrequency ablation, the relative VAS scores of lesions near the liver capsule 5 (1-7) were higher than those of lesions away from the liver capsule group 3 (0-5). The difference was statistically significant (P = 0.001, Z =-3.490). That is, near the liver capsule group of patients had pain more severe than patients away from the liver capsule in ablation therapy. There was no significant difference between the two groups of patients for the maximum power that can be tolerated during ablation therapy (P=0.639 · Z=-0.505 · table 1).

Table 1 – Comparison of IL-27 and IL-17 levels in serum of AR group and control group (±s) pg/ml

<table>
<thead>
<tr>
<th></th>
<th>IL-27 (pg/ml)</th>
<th>IL-17 (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AR group (n=18)</td>
<td>21.69±12.62</td>
<td>672.82±63.45</td>
</tr>
<tr>
<td>control group (n=10)</td>
<td>53.10±12.55</td>
<td>576.62±22.81</td>
</tr>
</tbody>
</table>

1) compared with control group, P < 0.01 ; 2) compared with control group. P < 0.01

Table 2 The correlation analysis of IL-27 level with Th17 cell percentage and IL-17 level in peripheral blood

<table>
<thead>
<tr>
<th>Correlation coefficient</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-27 and Th17cell</td>
<td>-0.361</td>
</tr>
<tr>
<td>IL-27 and IL-17</td>
<td>-0.435</td>
</tr>
</tbody>
</table>

Figure 1. Th17 cells flow cytometry diagram (a: AR group b: control group)
Table 1: Comparison of relative VAS scores and the maximum power between two groups of patients with hepatocellular carcinoma radiofrequency ablation treatment

<table>
<thead>
<tr>
<th>Groups</th>
<th>Number of cases</th>
<th>HCC lesions (个)</th>
<th>Basic VAS score (points)</th>
<th>Intraoperative VAS score (points)</th>
<th>Relative VAS score (points)</th>
<th>Maximum power patients can tolerate during ablation (W)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Away from the liver capsule group</td>
<td>8</td>
<td>12</td>
<td>3 (1~5)</td>
<td>6 (2~8)</td>
<td>3 (0~5)</td>
<td>140 (70~200)</td>
</tr>
<tr>
<td>near the liver capsule group</td>
<td>15</td>
<td>19</td>
<td>3 (0~6)</td>
<td>8 (2~10)</td>
<td>5 (1~7)</td>
<td>150 (100~200)</td>
</tr>
</tbody>
</table>

Note: * compared with the away from liver capsule group  p<0.05

3. The comparison of relative VAS scores with different grouping of lesions in ablation of patients with cancer recurrence after liver transplantation

There were two cases liver cancer recurrence (2/23, 4 recurrent tumors) in 23 cases of liver transplantation. Two lesions were near the liver capsule (one near the liver capsule, another one near the branch of the portal vein, the relative VAS score positive), and two were away from the liver capsule (relative VAS score negative).

Discussion

Radiofrequency ablation of hepatocellular carcinomas is minimally invasive, more effective with few complications, and is commonly used clinically to treat small hepatocellular carcinoma or liver cancer recurrence in patients with poor liver function[11-12]. Most of the treatment employs ultrasound-guided percutaneous radiofrequency ablation, and patients experience rapid postoperative recovery and shorter hospital stay. However, due to big differences between the patients with pain tolerance, some patients are unable to tolerate the pain caused by radiofrequency ablation, and with the increasing RF power, the pain can get worse, which affects the ablation power to maximum in order to achieve the ablation effect. If we can predict the tolerance of patients with pain before operation, the appropriate method of anesthesia and the dose can be chosen to avoid the change of anesthesia in the ablation. Foreign studies have shown that there is some correlation between the pain in ablation and the lesion location, time of ablation as well as ablation power[1-2]. This study used VAS scores for quantitative assessment of the pain. When there is no significant difference of the maximum power patients can tolerate in the ablation, the pain in patients with lesion near the liver capsule or portal vein was significantly greater than patients with lesion away from the liver capsule or portal vein (P <0.05). Different from previous studies, this study did not use the absolute VAS score [2], but the pain score under local anesthesia as the basis, and used relative VAS scores for analysis to reduce the error due to the different pain threshold of patients. When the lesion ablation power is the same in the group of four cases of liver cancer patients with lesions near the liver capsule and away from the liver capsule, the pain score of patients with lesion near the liver capsule is higher than lesion away from the of the liver capsule. This indicated lesion near the liver capsule is an important factor for pain ablation.

The different degrees of pain from the radiofrequency ablation of liver tumors near the liver capsule or away are related to liver sensory nerve distributions. The cell body of the liver sensory nerve fibers is located in the posterior horn of the spinal cord, and peripheral pain receptors are distributed in the liver surface membrane, distributed along the portal vein through the first hepatic portal; while liver parenchyma nerve is from the bottom of the hepatic plexus, containing sympathetic and parasympathetic nerves. Therefore, it is not sensitive to pain perception [13-16]. After liver transplantation, all patients’ sensory nerves in liver are cut, so patients seldom produce pain towards heat stimulation, mechanical stimulation and traction. The relative VAS scores in RF ablation of three cases of this group of patients after liver transplantation were negative; for another case with lesion near the liver capsule, the VAS score in liver cancer recurrence lesion ablation was positive. This is because sensory nerves within peritoneal surrounding liver are not affected by the surgery, which would still have caused significant pain. The statistical analysis were still
statistically significant for the two cases of transplant patients in this group of patients, a total of four lesions, after the merger with the lesions of non-liver transplant recipients. It did not significantly affect the evaluation results. Therefore, pain tolerance of patients during radiofrequency ablation can be predicted according to whether liver lesions are near the liver capsule or portal vein branch, which benefits preliminary judgment to choose a more appropriate preoperative anesthesia method. For lesions near the liver capsule or portal vein, before ablation treatment we can use multi-point full anesthesia for the adjacent liver capsule, and appropriately increase the analgesic sedative dose, while paying attention to the reasonable control of the ablation power. For lesion near the portal vein lesions, we can choose anesthesia and anesthetic with better analgesic effect, thereby reducing the impact of pain in patients for the treatment in ablation therapy.

Ablation time can impact the VAS too, and with increasing ablation time, patients feel more severe pain[2]. Four cases of patients in this group of patients have both lesions near the liver capsule and away from the liver capsule. To minimize the impact of the first ablation lesion to the VAS score from later ablation lesion, we chose lesions near the liver capsule first for ablation, followed by lesions away from the liver capsule group, and the interval was greater than 15min. If under the circumstance the lesion away from the liver capsule group was the later ablation lesion, two groups of pain was still statistically significant, it would better explain that lesion ablation near the liver capsule group leads to more severe pain. At the same time, the diameters of the two groups of lesions are not statistically significant, while ablation time is directly related to the diameter of the lesions, so the ablation time will not affect the evaluation of the result for this group of patients.

In summary, the pain in patients is more severe for lesion near the liver capsule and the portal vein in ultrasound-guided percutaneous radiofrequency ablation of hepatocellular carcinomas under local anesthesia. The information from the preoperative ultrasound as to whether liver lesions close to or away from the liver capsule and portal vein can provide a basis for the clinical selection of different anesthesia methods and medications.

REFERENCES