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· 专题研究 ·

## 腹腔镜下射频消融治疗小肝癌的临床疗效分析

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### 摘要

**目的:** 探讨腹腔镜下射频消融(LRFA)治疗原发性小肝癌的临床效果。

**方法:** 回顾性分析2011年8月—2013年10月南昌大学第二附属医院行LRFA治疗的30例小肝癌患者(LRFA组)以及同期行经皮射频消融(PRFA, PRFA组)和手术切除(手术切除组)各30例的小肝癌患者临床资料。比较3组患者的相关临床指标。

**结果:** 3组患者术前一般资料具有可比性, 所有患者均顺利完成手术。术后, 3组AFP水平均较术前明显降低(均 $P<0.05$ ), 但3组间AFP水平无统计学差异( $P>0.05$ ); 3组肝功能指标均较术前明显升高(均 $P<0.05$ ), 但手术切除组较另两组升高程度大、恢复慢(均 $P<0.05$ )。在手术时间、术中出血量、围手术期并发症、住院时间方面, LRFA组与PRFA组均优于手术切除组(均 $P<0.05$ ), 而LRFA组手术时间长于PRFA组(80.7 min vs. 45.2 min,  $P<0.05$ ), 并发症发生率低于PRFA组(6.7% vs. 26.7%,  $P<0.05$ ); 术后1个月, LRFA组和手术切除组肿瘤完全清除率均为100%, 而PRFA组为86.7%, 两组间差异有统计学意义( $P<0.05$ )。LRFA组、PRFA组、手术切除组3年复发率分别为33.3%、60.0%、26.7%; 3年无瘤生存率分别为66.7%、40.0%、73.3%; 3年总生存率分别为86.7%、76.7%、90.0%, 其中, PRFA组的3年无瘤生存率明显低于另两个组, 复发率明显高于另两组(均 $P<0.05$ ), 而LRFA组和手术切除组之间无瘤生存率及复发率差异无统计学意义(均 $P>0.05$ ); 3组患者3年总生存率差异无统计学意义( $P=0.302$ )。

**结论:** 对于原发性小肝癌, LRFA较PRFA消融率高, 且远期疗效与开腹手术相当, 同时具有微创、术后恢复快的优点, 可作为小肝癌的首选治疗手段之一。

### 关键词

癌, 肝细胞; 导管消融术; 腹腔镜; 预后

中图分类号: R735.7

## Clinical efficacy of laparoscopic radiofrequency ablation in treatment of small primary hepatocellular carcinoma

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### Abstract

**Objective:** To investigate the clinical efficacy of laparoscopic radiofrequency ablation (LRFA) in treatment of small primary hepatocellular carcinoma (HCC).

**Methods:** The clinical data of 30 patients with small HCC undergoing LRFA (LRFA group) during August 2011

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to October 2013 along with 30 patients undergoing percutaneous radiofrequency ablation (PRFA, PRFA group) and 30 patients undergoing surgical resection for small HCC during the same period in the Second Affiliated Hospital of Nanchang University were retrospectively analyzed. The main clinical variables among the three groups of patients were compared.

**Results:** The preoperative data of the three groups of patients were comparable, and operations in all patients were successfully completed. After operation, the AFP levels in all the three groups were significantly decreased compared with their preoperative values (all  $P < 0.05$ ), while AFP levels showed no significant difference among the three groups ( $P > 0.05$ ); the liver function parameters in all the three groups were significantly increased compared with their preoperative values (all  $P < 0.05$ ), but their increasing amplitudes were greatest and recoveries were slowest in surgical resection group than those in the other two groups (all  $P < 0.05$ ). Both LRFA group and PRFA group were superior to surgical resection group in terms of operative time, intraoperative blood loss, perioperative complications and length of hospital stay (all  $P < 0.05$ ), while the operative time was longer and incidence of complications was lower in LRFA group than those in PRFA group (80.7 min vs. 45.2 min; 6.7% vs. 26.7%, both  $P < 0.05$ ). At one month after operation, rate of complete tumor removal in either LRFA group or surgical resection group was 100%, while in PRFA group was 86.7%, and the difference had statistical significance ( $P < 0.05$ ). The 3-year recurrence rates were 33.3%, 60% and 26.7%, the 3-year disease-free survival rates were 66.7%, 40.0% and 73.3%, and the 3-year overall survival rates were 86.7%, 76.7% and 90.0% for LRFA group, PRFA group and surgical resection group, respectively, where, the 3-year disease-free survival rate was lower and the 3-year recurrence rate was higher in PRFA group than those in the other two groups (all  $P < 0.05$ ), but they showed no significant difference between the latter groups (both  $P > 0.05$ ); there was no statistically significant difference in 3-year overall survival rate among the three groups ( $P = 0.302$ ).

**Conclusion:** For small HCC, LRFA has higher ablation rate than that of PRFA, and similar long-term efficacy to surgical resection, and meanwhile has advantages of minimal invasiveness and fast postoperative recovery. So, it can be used as one of the first treatment options for small HCC.

**Key words** Carcinoma, Hepatocellular; Catheter Ablation; Laparoscopes; Prognosis

**CLC number:** R735.7

射频消融 (radiofrequency ablation, RFA) 是继手术切除和肝移植之后小肝癌 (small hepatocellular carcinoma, SHCC) 的又一种根治性治疗手段<sup>[1-3]</sup>, 且具有微创、风险小、可重复性高等特点<sup>[4-6]</sup>, 一般在 CT 引导下经皮射频消融 (percutaneous radiofrequency ablation, PRFA), 但对于特殊部位 (靠近膈顶、胃、胆囊及肝表面等) 的肿瘤往往易出现副损伤或消融不彻底<sup>[7]</sup>, 而腹腔镜下射频消融 (laparoscopic radiofrequency ablation, LRFA) 可有效弥补上述不足。笔者通过比较我院 LRFA、PRFA、手术切除 3 种方式治疗小肝癌的治疗效果、术后恢复情况、3 年复发率、无瘤生存率及总生存率, 评估 LRFA 在小肝癌治疗中的疗效, 现报告如下。

## 1 资料与方法

### 1.1 一般资料

选择 2011 年 8 月—2013 年 10 月南昌大学第二附属医院收治的 90 例原发性肝癌患者 [按卫生部原发性肝癌诊疗规范 (2011 年版) 制定的原发性肝癌诊断标准] 纳入本研究。入选标准: (1) 初发的原发性肝癌, 未接受过任何抗癌治疗; (2) 肿瘤直径  $\leq 5$  cm, 无子灶, 无血管及远处转移; (3) 肝功能 Child-Pugh A 级或 B 级, 或经护肝治疗后达到该标准。排除标准: (1) 有血管或邻近组织器官侵犯; (2) 有淋巴或远处转移; (3) 有凝血功能障碍; (4) 有手术或视频消融的其他禁忌证。90 例患者分别行 LRFA (肿瘤均位于肝脏表面, LRFA 组)、CT 引导 PRFA (PRFA 组)、开腹手术切除 (手术切除组), 每组各 30 例。3 组患者性别、年龄、肿瘤直径等术前一般资料比较, 无统计学差异 (均  $P > 0.05$ ) (表 1)。

表1 患者一般资料 (n=30)

| 资料                             | LRFA组         | PRFA组         | 手术切除组         | P     |
|--------------------------------|---------------|---------------|---------------|-------|
| 年龄 (岁, $\bar{x} \pm s$ )       | 50 ± 16       | 54 ± 12       | 52 ± 13       | 0.517 |
| 性别 [n (%)]                     |               |               |               |       |
| 男                              | 17 (56.7)     | 19 (63.3)     | 20 (66.7)     | 0.718 |
| 女                              | 13 (43.3)     | 11 (36.7)     | 10 (33.3)     |       |
| Child-Pugh 分级 [n (%)]          |               |               |               |       |
| A                              | 29 (96.7)     | 26 (86.7)     | 28 (93.3)     | 0.559 |
| B                              | 1 (3.3)       | 4 (13.3)      | 2 (6.7)       |       |
| 肿瘤直径 (cm, $\bar{x} \pm s$ )    | 3.0 ± 1.1     | 2.6 ± 1.0     | 3.2 ± 1.1     | 0.081 |
| AFP (g/L, $\bar{x} \pm s$ )    | 430.4 ± 273.7 | 493.5 ± 298.1 | 532.7 ± 314.6 | 0.057 |
| 白蛋白 (g/L, $\bar{x} \pm s$ )    | 38.4 ± 4.2    | 36.5 ± 3.1    | 37.6 ± 2.7    | 0.262 |
| ALT (U/L, $\bar{x} \pm s$ )    | 35.1 ± 14.2   | 40.1 ± 16.4   | 36.9 ± 9.3    | 0.247 |
| AST (U/L, $\bar{x} \pm s$ )    | 35.0 ± 17.9   | 36.6 ± 15.8   | 38.1 ± 17.7   | 0.782 |
| TBIL (mol/L, $\bar{x} \pm s$ ) | 17.6 ± 6.3    | 14.7 ± 5.8    | 20.5 ± 11.4   | 0.058 |

## 1.2 治疗方法

LRFA: 全身麻醉, 均采用三孔法。(1) 腹腔镜下先探查腹腔, 确定肿瘤部位及是否转移; (2) 充分显露肿瘤, 必要时游离相应的肝周韧带; (3) 射频电极针 (StarBurstXL/25 cm, RITA公司, 美国) 在腹腔镜直视下穿刺病灶布针, 按说明书操作2~3次、均多方位布针进行消融。消融的范围包含肿瘤和其周边0.5~1.0 cm的肝组织范围。每次消融后常规原针道消融避免出血及肿瘤种植。CT引导下PRFA: 采用腹壁局部麻醉, 常规消毒铺巾, 在CT引导下将电极插入肝脏肿瘤中心, 按说明书操作进行消融, 消融范围同射频消融组。在CT监控下观察肿瘤病灶获完全消融。开腹手术切除: 采用气管插管全身麻醉, 开腹后先探查腹腔, 结合术中B超明确病灶部位及范围, 根据肝功能情况行规则或不规则性肝切除方法行肿瘤根治性切除, 切除范围至少包括肿瘤周围2 cm非瘤肝组织。

## 1.3 观察指标及随访

(1) 术前及术后第1、3、7天肝功能变化; (2) 术前及术后1、2个月AFP的变化; (3) 手术时间; (4) 术中出血量; (5) 围手术期并发症; (6) 住院时间; (7) 肿瘤清除程度: 在治疗后1个月行肝脏增强CT检查, 结合AFP判断肿瘤是否完全清除 (complete response, CR); (8) 复发情况: 所有患者于术后或射频后1个月行肝脏增强CT及血AFP检查, 定期随访, 术后第1年每3个月复查1次B超及血AFP, 术后第2、3年每半年复查1次B超及血AFP; (9) 无瘤生存率和总生存率。

## 1.4 统计学处理

采用SPSS 23.0软件来进行所有的统计分析。对于计量资料, 使用Gaussianity检验来确保数据的同质性, 数据表达为均数 ± 标准差 ( $\bar{x} \pm s$ ), 由单变量ANOVA比较。ANOVA检验的同时, 3组数据的两两比较由LSD或Bonferroni检验实现。对于不符合正态分布的多组样本之间比较采用了Wilcoxon秩和检验。对于定性 (分类) 资料, 采用Pearson  $\chi^2$ 检验。用Kaplan-Meier法计算生存率, Log-rank检验比较无瘤生存率和总生存率。P<0.05为差异有统计学意义。

## 2 结果

### 2.1 术后AFP及肝功能变化

术后1个月3组AFP浓度均明显低于术前 (均P<0.05); 术后2个月AFP浓度均恢复至正常水平; 治疗后3组同期AFP比较, 差异均无统计学意义 (均P>0.05)。术后各组第1、3天肝功能指标均较术前明显升高 (均P<0.05), 术后第7天ALT、AST、TBIL均有所回落, LRFA组和PRFA组与术前比较, 无统计学差异 (均P>0.05), 而手术切除组与术前比较, 差异有统计学意义 (P<0.05)。术后ALT、AST、TBIL同期比较, LRFA组和PRFA组无统计学意义 (均P>0.05), 而手术切除组明显高于其他两组 (均P<0.05) (表2)。

表2 术后各组AFP及肝功能指标比较 (n=30,  $\bar{x} \pm s$ )Table 2 Comparison of postoperative AFP levels and liver function parameters among the 3 groups (n=30,  $\bar{x} \pm s$ )

| 指标           | LRFA组                      | PRFA组                      | 手术切除组        |
|--------------|----------------------------|----------------------------|--------------|
| AFP (g/L)    |                            |                            |              |
| 术后1个月        | 52.6 ± 32.1                | 60.4 ± 34.8                | 58.7 ± 44.5  |
| 术后2个月        | 15.6 ± 7.1                 | 16.4 ± 6.8                 | 18.7 ± 9.5   |
| ALT (U/L)    |                            |                            |              |
| 术后第1天        | 109.6 ± 41.3 <sup>1)</sup> | 90.8 ± 45.6 <sup>1)</sup>  | 150.4 ± 53.7 |
| 术后第3天        | 125.3 ± 36.1 <sup>1)</sup> | 116.2 ± 37.7 <sup>1)</sup> | 219.5 ± 47.6 |
| 术后第7天        | 37.8 ± 10.6 <sup>1)</sup>  | 30.5 ± 9.6 <sup>1)</sup>   | 82.3 ± 32.1  |
| AST (U/L)    |                            |                            |              |
| 术后第1天        | 90.4 ± 32.7 <sup>1)</sup>  | 87.8 ± 36.9 <sup>1)</sup>  | 144.6 ± 51.3 |
| 术后第3天        | 122.3 ± 24.8 <sup>1)</sup> | 117.4 ± 26.5 <sup>1)</sup> | 211.5 ± 45.2 |
| 术后第7天        | 28.6 ± 11.3 <sup>1)</sup>  | 30.7 ± 12.8 <sup>1)</sup>  | 76.3 ± 35.9  |
| TBIL (mol/L) |                            |                            |              |
| 术后第1天        | 19.2 ± 10.9 <sup>1)</sup>  | 17.4 ± 6.7 <sup>1)</sup>   | 80.3 ± 26.7  |
| 术后第3天        | 30.4 ± 8.1 <sup>1)</sup>   | 28.6 ± 7.4 <sup>1)</sup>   | 107.8 ± 21.4 |
| 术后第7天        | 16.8 ± 7.5 <sup>1)</sup>   | 15.3 ± 6.9 <sup>1)</sup>   | 40.6 ± 13.2  |

注: 1) 与手术切除组与同时时间点比较, P<0.05

Note: 1) P<0.05 vs. surgical resection group of the same time point

## 2.2 围手术期并发症及其他结果

LRFA组和PRFA组的手术时间明显短于手术切除组 ( $P=0.024$ )，术中出血明显少于手术切除组 ( $P=0.017$ )，住院时间也明显短于手术切除组 ( $P=0.031$ )。手术切除组术后并发症：胆瘘2例，肺部感染3例，胸腔积液2例，出血1例，腹腔积液1例，切口愈合不良1例；LRFA组术后并发症：发热1例，腹痛1例；PRFA组术后并发症：发热2例，腹痛4例，胸腔积液1例，皮肤灼伤1例。出现并发症患者经对症治疗后均完全缓解。3组间

并发症的发生率差异有统计学意义 ( $P=0.028$ )，LRFA组并发症发生率明显低于PRFA组和手术切除组 ( $P<0.05$ )，而后两者之间差异无统计学意义 ( $P>0.05$ )。术后1个月影像学及AFP结果表明LRFA组和手术切除组60例患者均达到CR，PRFA有4例未达到CR，2例进行了肝动脉栓塞化疗 (TACE)，2例进行了第2次PRFA治疗。PRFA组的肿瘤完全清除率明显低于其他两组，差异有统计学意义 ( $P=0.016$ ) (表3)。

表3 各组围手术期指标比较 ( $n=30$ )

Table 3 Comparison of perioperative variables among the 3 groups ( $n=30$ )

| 组别    | 手术时间<br>(min, $\bar{x}\pm s$ ) | 术中出血量<br>(mL, $\bar{x}\pm s$ ) | 围手术期并发症<br>[n (%)]       | 住院时间<br>(d, $\bar{x}\pm s$ ) | 肿瘤完全清除<br>[n (%)]        |
|-------|--------------------------------|--------------------------------|--------------------------|------------------------------|--------------------------|
| LRFA组 | 80.7 ± 24.6 <sup>1),2)</sup>   | 10.9 ± 8.7                     | 2 (6.7) <sup>1),2)</sup> | 7.1 ± 5.3 <sup>1)</sup>      | 30 (100.0) <sup>2)</sup> |
| PRFA组 | 45.2 ± 9.2 <sup>1)</sup>       | 13.8 ± 11.4                    | 8 (26.7) <sup>1)</sup>   | 6.3 ± 5.6 <sup>1)</sup>      | 26 (86.7) <sup>1)</sup>  |
| 手术切除组 | 172.3 ± 64.5                   | 231.4 ± 153.7                  | 10 (33.3)                | 12.9 ± 6.9                   | 30 (100.0)               |
| P     | 0.024                          | 0.017                          | 0.028                    | 0.031                        | 0.016                    |

注：1) 与手术切除组比较,  $P<0.05$ ; 2) 与PRFA组比较,  $P<0.05$

Note: 1)  $P<0.05$  vs. surgical resection group; 2)  $P<0.05$  vs. PRFA group

## 2.3 无瘤生存率及复发情况

以36个月为随访期限，3组均无失访。LRFA组、PRFA组、手术切除组3年内复发率分别为33.3%、60.0%、26.7%，差异有统计学意义 ( $P=0.021$ )。复发后将综合考虑患者的残余肝脏功能、肿瘤生长形态、大小、位置等方面的因素，选择手术、TACE、局部消融治疗以及姑息性镇痛等治疗。LRFA组、PRFA组、手术切除组的3年无瘤生存率分别为66.7%、40.0%、73.3%。3组的无瘤生存率采用Kaplan-Meier检验有统计学意义 ( $\chi^2=8.480$ ,  $P=0.014$ )，PRFA组的无瘤生存率明显低于其他两组 (图1)。PRFA组

与LRFA组之间差异有统计学意义 ( $\chi^2=3.925$ ,  $P=0.048$ )，同样与手术切除组比较时差异也具有统计学意义 ( $\chi^2=7.265$ ,  $P=0.007$ )，而LRFA组和手术切除组之间差异无统计学意义 ( $\chi^2=0.393$ ,  $P=0.531$ )。

## 2.4 总生存率

在3年随访中，共14例患者死亡。LRFA组、PRFA组、手术切除组的3年总生存率分别为86.7%、76.7%、90.0%。采用Kaplan-Meier检验，3组的总生存率差异无统计学意义 ( $\chi^2=2.396$ ,  $P=0.302$ ) (图2)。

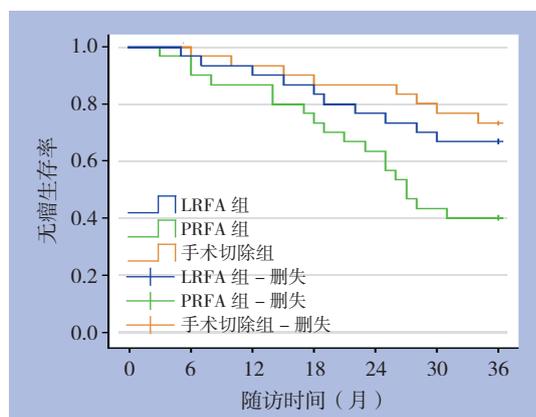


图1 各组3年无瘤生存率曲线

Figure 1 The 3-year disease-free survival curves of the three groups

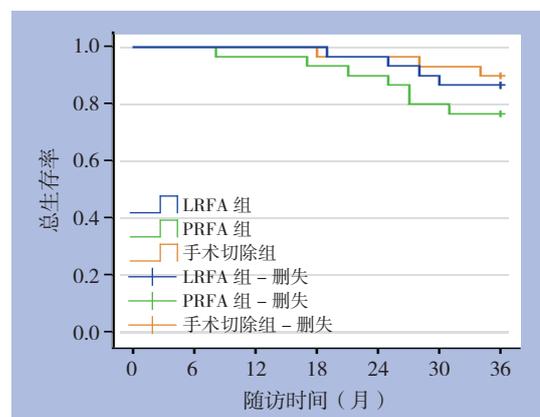


图2 各组的3年总生存率曲线

Figure 2 The 3-year overall survival curves of the three groups

### 3 讨论

肝癌是临床上常见的恶性肿瘤<sup>[8-9]</sup>,目前其主要治疗方式<sup>[10-12]</sup>包括:手术切除、RFA、肝移植、TACE、无水酒精消融术(PEI)等,由于肝移植昂贵的治疗费用以及肝脏供体的短缺,肝移植无法广泛开展<sup>[13-14]</sup>。我国肝癌临床治疗中大多采取手术切除<sup>[15-16]</sup>,且我国绝大部分肝癌患者合并不同程度的肝硬化,因此手术风险大,部分患者不能耐受手术,而射频消融则为此类患者提供了另一种根治性治疗方式。

RFA的直接作用是热毁损肿瘤组织<sup>[17-22]</sup>,同时打破了肿瘤与宿主之间的动态平衡,激活机体局部和整体免疫系统,发挥独特抗肿瘤作用<sup>[23-25]</sup>。有研究<sup>[26-27]</sup>表明,肿瘤患者免疫功能低下和紊乱,而肿瘤细胞可以多种方式逃避免疫系统的监控。研究<sup>[28-30]</sup>表明患者术后免疫功能状况与肿瘤的复发、预后密切相关,射频消融术不仅能够清除病灶,还能够强化患者的免疫功能。因此RFA治疗肝癌,不仅仅是单纯物理性肿瘤消融,还可通过免疫增强获得全身治疗,是局部治疗和全身治疗的统一。由于射频消融毁损范围是以布针点为中心的球形区域,而要治疗体积较大或不规则生长的肿瘤,就需要多次烧灼<sup>[31-33]</sup>。PRFA治疗过程中高温产生蒸气及用二维影像技术的引导,使得其在治疗中很难区分已发生坏死的和残留的癌组织,也很难再精确穿刺定位进行多次消融。因此,传统的PRFA治疗肝肿瘤相对容易毁损不全和病灶残留,这在一定程度上增加了复发的风险<sup>[34]</sup>。相比于PRFA,LRFA可以在直视下进行操作及监测消融范围,准确定位肿瘤,灵活进行多点、多方位布针,达到肿瘤的完全毁损;同时,腹腔镜下可牵开肝脏周围组织及器官,充分暴露肿瘤,减少对周围组织的损伤,有效降低胆囊损伤、胃肠道损伤等并发症;此外,腹腔镜下易于识别和处理穿刺针道出血,清理腹腔内积血,减少腹腔感染。

由于医院当时未引进腹腔镜超声设备,故本次研究中LRFA组纳入的病例均为单发的位于肝脏表面的肝癌患者。本研究结果显示:PRFA组肿瘤完全清除率低于LRFA组,而围手术期并发症、复发率较LRFA高,且差异均具有统计学意义( $P < 0.05$ )。但术中出血量、术后肝功能、住院时间两组比较无统计学差异( $P > 0.05$ )。而LRFA组

与手术切除两组之间复发率、3年无瘤生存率及总生存率之间差异均无统计学意义( $P > 0.05$ ),但手术切除组术中出血量大,手术时间、术后住院时间明显较LRFA组长,患者术后肝功能恢复慢。因此,对于小肝癌治疗,LRFA具有创伤小、肝功能影响小优势,对于一些对于肝功能差、局部肝切除对肝功能打击较大和风险较高的肝癌患者,选择LRFA治疗可减小手术风险,同时又可达到与手术切除相同的根治性效果。

综上所述,本研究表明LRFA不仅具有术后恢复快、出血量少、住院日短等优点,其3年复发率、无瘤生存率及总生存率与手术切除无明显差异,可作为小肝癌的首选治疗方案之一。由于样本量少,随访时间短,还需要更多循证医学证据来进一步研究LRFA对于小肝癌的疗效。

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