·临床研究·

超声引导经皮微波消融治疗老年肾细胞癌患者的疗效评价

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【摘 要】 **目的** 探讨超声引导经皮微波消融治疗老年肾细胞癌患者的疗效。**方法** 回顾性地分析2006年1月至2015年12月在解放军总医院超声介入科接受超声引导经皮水冷微波消融治疗的82例老年肾细胞癌患者,年龄61~87(73.96±7.30)岁,男58例,年龄(74.0±7.3)岁,女24例,年龄(73.8±7.4)岁,共86个肿瘤[平均直径(2.9±0.9)cm]。术后1 d经超声造影或增强CT(MRI)检查评判治疗效果,术后1、3、6个月及以后的每6个月行超声造影和增强CT(MRI)检查随访。**结果** 技术有效率100%(微波消融后1个月增强影像显示完全消融),主要并发症发生率3.7%(3/82)。第1、3、5年局部进展率0.0%,1.9%,5.2%;远处转移率0.0%,1.6%,7.0%;总体生存率98.4%,96.7%,91.3%;无病生存率98.4%,96.6%,83.5%。多因素分析显示年龄、性别、肿瘤大小、部位、消融时间、消融功率等均不影响患者的整体生存率($P>0.05$)。**结论** 微波消融治疗老年肾细胞癌患者安全、有效。

【关键词】 老年人;肾细胞癌;微波消融;超声引导
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Efficacy of ultrasound-guided percutaneous microwave ablation on renal cell carcinoma in the elderly

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【**Abstract**】 **Objective** To investigate the efficacy of ultrasound-guided percutaneous microwave ablation (MWA) on renal cell carcinoma (RCC) in elderly patients. **Methods** Clinical data of 82 RCC patients with 86 lesions [(mean diameter (2.9±0.9)cm] treated with water-cooled MWA under ultrasound guidance in our department from January 2006 to October 2015 were collected and retrospectively analyzed. They were at an age of (73.96±7.30) years (ranging from 61 to 87 years), and 58 males were at an age of (74.0±7.3) years and 24 females at an age (73.8±7.4) years. Enhanced ultrasound and enhanced CT/MRI examination were employed to evaluate the curative effect in 1 d after the treatment, and performed again in 1, 3 and 6 months after operation and every 6 months thereafter. **Results** The effective rate of treatment was 100% (enhanced images showed complete ablation in 1 month after MWA). The major complications were 3.7% (3/82). The local tumor progression rates were 0.0%, 1.9%, and 5.2%, respectively for 1, 3, and 5 years after. The 1-, 3-, and 5-year distant metastatic rates were 0.0%, 1.6% and 7.0%, respectively, the corresponding overall survival rates were 98.4%, 96.7% and 91.3%, respectively, and the corresponding disease-free survival rates were 98.4%, 96.6% and 83.5%, respectively. Multivariate analysis showed that age, sex, tumor size, tumor location, ablation time and ablation power had no effect on the overall survival rate in the patients ($P>0.05$). **Conclusion** Our study shows that MWA is a safe and effective modality for RCC in the elderly patients.

【**Key words**】 aged; renal cell carcinoma; microwave ablation; ultrasound guidance
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肾肿瘤正以每年2%的发病率增长,且发病率和年龄密切相关[1-4]。手术切除依然是治疗的首选,但老年患者大多伴有其他慢性疾病,耐受性差,手术治疗风险高[5,6]。而影像引导下经皮微波消融治疗具有微创、治疗时间短、无放化疗毒副作用等优点,已成功用于肝、肾、肾上腺等部位肿瘤的治疗[7-9]。本研究通过对82例老年肾细胞癌(renal cell carcinoma, RCC)患者微波消融治疗和长期随访观察,探索微波消融治疗老年RCC的安全性和疗效。

1 对象与方法

1.1 研究对象

2006年1月至2015年12月在解放军总医院介入超声科接受微波消融治疗的老年RCC患者82例,年龄(73.96±7.30)岁,其中男58例,年龄(74.0±7.3)岁,女24例,年龄(73.8±7.4)岁。68例(82.9%)患者伴有其他疾病,其中冠心病21例,高血压50例,糖尿病20例,脑梗死4例,伴有其他癌症5例,慢性阻塞性肺疾病6例,慢性肾功能不全4例,再生障碍性贫血1例。40例患者伴有>2种的疾病。

入组标准:年龄>60岁;无肾静脉血栓或肾外转移;凝血酶原时间<25 s;凝血酶原活动度>40%;血小板计数$>40\times10^9$/L;因肾功能中重度损伤而难以耐受其他治疗;术后复发肾肿瘤;患者不愿或拒绝手术且在超声引导下有合适的进针途径。所有患者均签署手术知情同意书,术前经超声引导穿刺活检进行病理诊断。做血、尿常规,血生化,胸片,心电图和超声检查,全面了解患者的身体状况。

1.2 方法

南京康友公司微波消融仪(KY-2000,输出频率为2450 MHz),消融针直径1.9 mm(15G),长18 cm,内置有双通道水循环系统。患者取侧卧位,消毒、铺巾,1%的利多卡因局部麻醉,超声引导下用18G活检针行组织活检穿刺,取2~3条组织。随后将微波消融针沿原切口进入肿瘤内部预定位置。丙泊酚(异丙酚,利康药业,美国威明顿)和克他命(双鹤药业,中国北京)联合进行静脉麻醉,待患者呼吸平稳后开始微波辐射,微波消融输出功率50~60 W,作用时间5~10 min。术中全程监测血氧饱和度、心率、血压。

肿瘤<2 cm的患者放置1根微波针,肿瘤≥2 cm要放置2根微波针,且针距不能>1.8 cm。对于高风险部位肿瘤,要实时监测肿瘤边缘温度、肾毗邻的集合系统和肠道周围的温度。退微波针时要停止水循环,以保证有足够的热量灼烧针道内残留的肿瘤组织,防止针道种植。

1.3 随访

术后1~3 d行超声造影或增强CT(MRI)评估消融效果,如有肿瘤残留则需再次行微波消融治疗,如完全消融则进入随访,治疗后第1、3、6个月复查超声造影、增强CT(MRI),以后每6个月复查1次,随访治疗效果。

1.4 统计学处理

应用SPSS 18.0统计软件,采用Kaplan-Meier生存函数分析无病生存率、总体生存率,两组计量资料比较使用独立样本t检验,多个因素分析采用Cox回归模型。以$P<0.05$为差异有统计学有意义。

2 结 果

2.1 微波消融

82例老年RCC患者86个肿瘤经97次微波消融治疗后完全坏死,其中75个肿瘤经过1次消融,11个肿瘤经过2次消融,技术有效率100%(表1)。消融效果如图1、图2所示。患者术前均通过超声引导下穿刺活检确定了肿瘤病理类型,肾透明细胞癌75例,肾乳头状细胞癌2例,肾嗜酸细胞癌4例,囊性RCC 1例。随访5.2~113.2个月,有11例患者死亡,其中4例死于RCC恶化,7例死于非RCC(分别是胃出血、脑出血、心力衰竭、肺气肿、肝功能衰竭、高血压和冠心病)。第1、3、5年局部进展率分别是0.0%,1.9%,5.2%;远处转移率分别是0.0%,1.6%,7.0%;总体生存率分别是98.4%,96.7%,91.3%;无病生存率分别是98.%,96.6%,83.5%。

2.2 并发症

术中无并发症发生,所有患者顺利完成消融治疗。术后无严重并发症,3例出现主要并发症,1例糖尿病并发紧邻肾集合系统的高危肿瘤引起的尿瘘,经抗感染和糖尿病治疗10 d后治愈;1例肿瘤紧邻结肠引起的肠瘘,经肠造瘘术和抗感染治疗后40 d治愈;1例动静脉瘘,在瘘管处经超声引导皮下注射0.15 ml凝血酶,3 d后出院。由肾周水肿引起其他的较小并发症可药物治疗。微波消融对患者血清尿素氮和肌酐水平无明显影响,肾功能不全患者在消融前经过充分透析,病情未见恶化。

表 1 患者和肿瘤的临床特征

Table 1 Clinical features of patients and tumors

Index	Data
Patient analysis	
Patients number(n)	82
Male[n(%)]	58(70.7)
Female[n(%)]	24(29.3)
One mass ablated[n(%)]	78(95.1)
Two masses ablated[n(%)]	4(4.9)
Age(years,$\bar{x} \pm s$)	73.96 ± 7.3
Male	74.0 ± 7.3
Female	73.8 ± 7.4
Comorbidities[n(%)]	68(82.9)
Tumor analysis	
Tumor number(n)	86
Tumor diameter(cm,$\bar{x} \pm s$)	2.9 ± 0.9
Tumors adjacent to bowel[n(%)]	31(37.9)
Ablation time(min,$\bar{x} \pm s$	8.2 ± 3.1
Ablation power(W,$\bar{x} \pm s$)	50.3 ± 2.5
Ablation sessions[times, medium(range)]	1(1 - 2)
Ablation insertions[number, medium(range)]	2(1 - 4)
Follow-up[months, medium(range)]	38.0 (5.23 - 113.2)

2.3 单因素和多因素分析

单因素和多因素分析显示患者年龄、性别、肿瘤大小、部位、消融时间、消融功率等均不影响患者的整体生存率($P > 0.05$;表 2,表 3)。

3 讨 论

RCC 占所有成人恶性肿瘤的 2% ~3%,是泌尿系统最常见的恶性肿瘤之一[10]。Suen 等[11]通过对 3535 例老人尸检后证实 70 ~75 岁年龄组肾癌发病率最高。目前肾癌的消融治疗主要包括射频消融、冷冻消融和微波消融。和射频消融、冷冻消融相比,微波消融的消融时间短,可形成更大的消融范围和更高的瘤内温度,传输受组织电阻率和炭化的影响小,能最大限度地保护机体免疫功能[12,13],尤其适用于无法耐受手术等其他治疗的老年患者。老年患者这方面治疗的报道较少,Lang 等[14]报道 70 例老年肾癌患者经过冷冻消融治疗,复发率 28.6%,无病生存率 70%。

非老年患者肾癌的治疗也有一些报道,Park 等[15]对 78 例行射频消融治疗,3.2% 患者肿瘤复发,消融技术有效率为 97.4%,整体生存率为 92.3%。Chalasani 等[16]对 19 例肾癌(肿瘤直径 <4 cm)患者行冷冻消融治疗,消融技术有效率为 100%,整体生存率为 94.1%。Yu 等[8]对 98 例肾癌患者行经皮微波消融,技术有效率 100%,局部复发率为 1.0%,5 年整体生存率和肿瘤相关生存率分别为 82.6% 和 97%。本研究微波消融技术有效率为 100%,5 年整体生存率为 91.3%,取得了与上述报道可比的疗效。且年龄、性别、肿瘤大小、部位、消融时间、消融功率等均不影响患者的整体生存率($P > 0.05$)。

老年人主要脏器的生理功能大都减退,且多伴有不同程度的糖尿病、高血压、冠心病、动脉粥样硬

表 2 患者无病生存的单因素分析

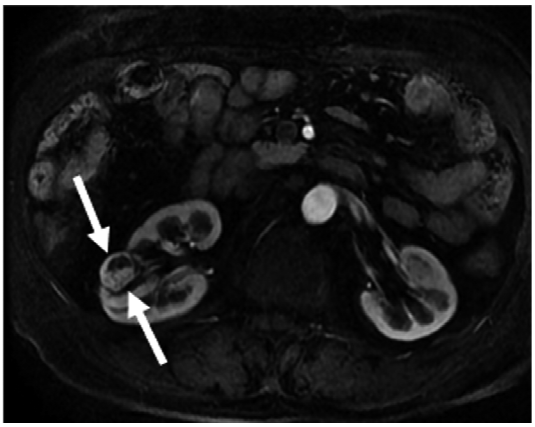
Table 2 Univariate analysis of prognostic factors for disease-free survival

Index	Survival	Recurrence	t/χ^2 value	P value
Gender[n(%)]			0.02	0.967
Male	53(91.4)	5(8.6)		
Female	22(91.7)	2(8.3)		
Age(years,$\bar{x} \pm s$)	73.6 ± 7.3	75.3 ± 7.1	0.331	0.567
Comorbidities[n(%)]			2.033	0.158
Yes	63(92.6)	5(7.4)		
No	12(85.7)	2(14.3)		
Tumor number[n(%)]			1.450	0.232
Single	72(92.3)	6(7.7)		
Multiple	3(75.0)	1(25.0)		
Tumor diameter(cm,$\bar{x} \pm s$)	2.8 ± 0.9	2.6 ± 0.9	0.622	0.433
Tumor location[n(%)]			0.272	0.604
Adjacent to bowel	29(93.5)	2(6.5)		
Not adjacent to bowel	46(90.2)	5(9.8)		
Ablation power(W,$\bar{x} \pm s$)	50.3 ± 2.6	50.0 ± 0.1	0.110	0.741
Ablation time(min,$\bar{x} \pm s$)	8.2 ± 3.2	8.0 ± 2.4	0.017	0.895
Ablation insertions(number,$\bar{x} \pm s$)	2.1 ± 0.8	1.9 ± 0.7	0.605	0.439
Ablation sessions(times,$\bar{x} \pm s$)	1.2 ± 0.4	1.3 ± 0.4	0.531	0.468

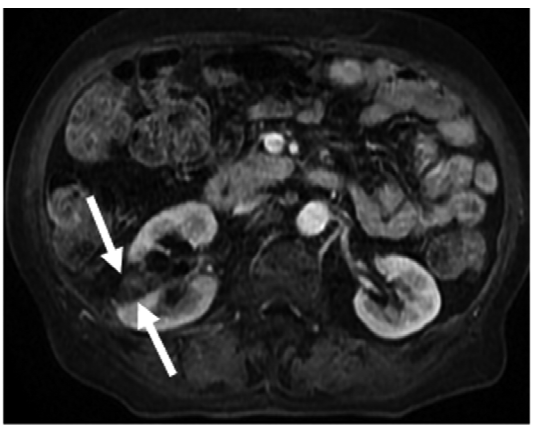
表3 患者预后Cox风险多因素分析

Table 3 Multivariate analysis of prognostic factors with Cox proportional hazards model

Index	Hazard ratio	95% CI	*P* value
Gender	0.51	0.35 – 7.54	0.63
Age	0.91	0.73 – 1.12	0.39
Tumor number	0.04	1.43 – 29.07	0.99
Comorbidities	0.86	0.08 – 9.67	0.89
Tumor diameter	3.83	0.32 – 46.40	0.29
Tumor location	1.25	0.06 – 25.53	0.89
Ablation power	1.19	0.65 – 2.21	0.57
Ablation time	1.13	0.77 – 1.65	0.53
Ablation insertions	0.34	0.02 – 5.17	0.44
Ablation sessions	3.62	0.02 – 673.13	0.63



A

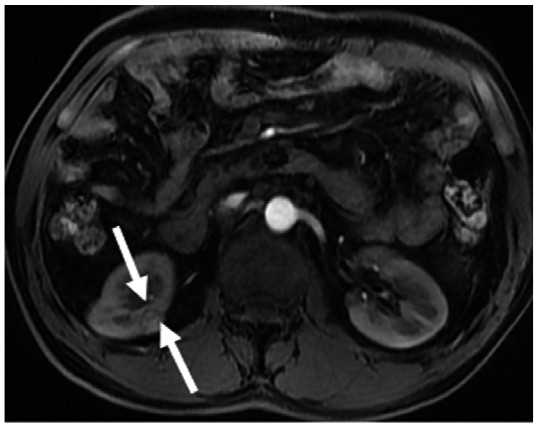


B

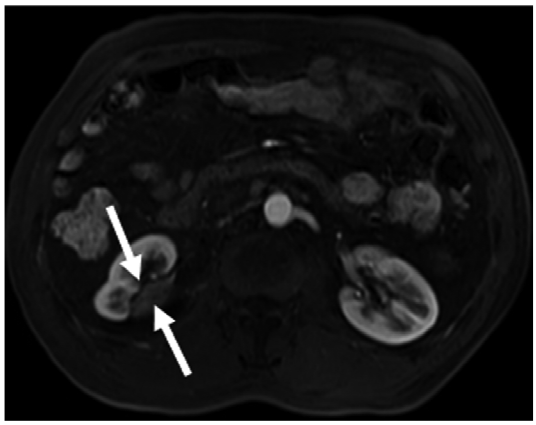
图1 78岁女性右侧肾肿瘤患者,行微波消融治疗前后核磁图像

Figure 1 Contrast-enhanced MRI of a 78 years old female patient with right RCC before and after MWA

A: one 2.5cm×2.0cm hypo-enhancement lesion at T2 before MWA; B: no blood reperfusion six months after MWA. RCC: renal cell carcinoma; MWA: microwave ablation; MRI: magnetic resonance imaging



A



B

图2 61岁男性右侧肾肿瘤患者,行微波消融治疗前后核磁图像

Figure 2 Contrast-enhanced MRI of a 61 years old male patient with right RCC before and after MWA

A: one 1.9 cm×1.6 cm hypo-enhancement lesion at T2 before MWA; B: one slight hypointense one month after MWA, which completely covers the tumor. RCC: renal cell carcinoma; MWA: microwave ablation; MRI: magnetic resonance imaging

化、慢性支气管炎、肺气肿等疾病,因此微波消融治疗老年患者的围手术期处理非常重要。本研究中有82.9%(68/82)的老年RCC患者有合并症,术前需通过药物调整,将血压、血糖、心律、呼吸控制在可耐受静脉麻醉要求范围内,并停用抗凝药>1周,结合MRI(CT)影像资料,超声精准定位,科学制定消融方案;术中注意心电监护、监测血氧饱和度和血气变化;术后继续监测,延长给氧时间,防止肺部感染,对伴有的冠心病、高血压、糖尿病等疾病给予相应处理,控制血糖、血压,保肝,预防应激性溃疡等并发症的发生。本研究中仅有3.7%(3/82)的患者出现主要并发症,其均与老年合并症无明显相关性,低于Lang等[14]报道的老年肾肿瘤冷冻消融的并发症4.3%,Lian等[17]报道的总体人群肾肿瘤射频消融的并发症发生率6.8%~10.2%。

对于邻近肠道、肾盂等危险部位的肿瘤，消融过程中应在瘤周5～10 mm处放置测温针，实时监测消融温度并使用断续式热消融方式，对于无开腹手术史的患者，安全温度设定为54°C，有开腹手术史的患者设定温度为50°C，通过腹腔注入50～100 ml生理盐水，使肾与肠水分离以避免热损伤导致肠粘连。本研究中邻近肠道、肾盂的肿瘤31例(37.8%)，治疗效果满意，随访期内无局部进展病例，仅2例出现远处转移。

综上所述，超声引导经皮微波消融对于老年肾癌患者是安全有效的治疗措施之一，但本研究也存在一定的局限性。回顾性研究阻碍了统一途径的随访，并且病例数较少，对微波消融老年肾癌整体疗效的评估也有局限性。

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