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## 经皮椎体成形术联合射频消融治疗脊柱转移瘤的临床疗效及术后预后的影响因素分析 \*

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**摘要 目的:**观察经皮椎体成形术(PVP)联合射频消融(RFA)治疗脊柱转移瘤的临床疗效,并分析术后预后的影响因素。**方法:**回顾性分析2016年5月~2019年5月期间广州中医药大学第一附属医院和广州中医药大学第三附属医院的60例脊柱转移瘤患者的临床资料。在60例患者中,行PVP治疗的患者28例纳为PVP组,行PVP联合RFA治疗的患者32例纳为联合组。术前、术后6个月采用视觉疼痛模拟评分(VAS)、ODI指数、卡式功能(KPS)评分评价患者的疼痛、运动功能、生活质量。统计患者生存情况,对脊柱转移瘤患者的术后预后进行单因素分析,并进行COX多因素分析,观察影响预后的危险因素。**结果:**联合组术后6个月VAS、ODI评分低于PVP组,KPS评分高于PVP组( $P<0.05$ )。联合组骨水泥总外渗率、术后6个月肿瘤复发率均低于PVP组( $P<0.05$ )。Kaplan-Meier生存曲线显示,两组术后生存率比较无显著性差异( $P>0.05$ ),两组随访患者术后生存时间基本一致。经单因素分析表明,术后局部放疗、脊柱外骨转移、内脏转移、原发肿瘤性质及确诊至转移时间在两组间的对比,差异有统计学意义( $P<0.05$ )。COX回归模型分析结果显示影响脊柱转移瘤患者术后预后的危险因素包括确诊至转移时间≤20个月、术后无局部放疗、原发肿瘤进展迅速、脊柱外骨转移、有内脏转移( $P<0.05$ )。**结论:**PVP联合RFA治疗脊柱转移瘤患者,可有效提高患者运动功能及生活质量,减轻疼痛。但其术后预后受多种因素影响,需采取针对性预防措施。

**关键词:**经皮椎体成形术;射频消融;脊柱转移瘤;临床疗效;术后预后;影响因素

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## Clinical Efficacy and Postoperative Prognostic Influencing Factors Analysis of Percutaneous Vertebroplasty Combined with Radiofrequency Ablation in the Treatment of Spinal Metastases\*

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**ABSTRACT Objective:** To observe the clinical efficacy of percutaneous vertebroplasty (PVP) combined with radiofrequency ablation (RFA) in the treatment of spinal metastases, and to analyze the postoperative prognostic influencing factors. **Methods:** The clinical data of 60 patients with spinal metastases in the The First Affiliated Hospital of Guangzhou University of Traditional Chinese Medicine and the The Third Affiliated Hospital of Guangzhou University of Traditional Chinese Medicine from May 2016 to May 2019 were retrospectively analyzed. Among the 60 patients, 28 patients receiving PVP treatment were enrolled in the PVP group, and 32 patients receiving PVP combined with RFA were enrolled in the combined group. Visual pain analog scale (VAS), ODI index and card function (KPS) score were used to evaluate the pain, motor function and quality of life of the patients before operation and 6 months after operation. The survival of patients was counted, the postoperative prognostic of patients with spinal metastases was analyzed by univariate analysis, and Cox multivariate analysis, and the risk factors affecting prognosis were observed. **Results:** 6 months after operation, the VAS and ODI scores of the combined group were lower than those of the PVP group, and the KPS score was higher than that of the PVP group ( $P<0.05$ ). The total extravasation rate of bone cement and tumor recurrence rate at 6 months after operation of the combined group were lower than those of the PVP group( $P<0.05$ ). Kaplan-Meier survival curve showed that there was no significant difference in the postoperative survival rate between the two groups ( $P>0.05$ ), and the postoperative survival time of patients in the two groups was basically the same. Univariate analysis showed that there were statistically significant differences between the two groups in postoperative local radiotherapy, extraspinal bone metastasis, visceral metastasis, primary tumor nature and time from diagnosis to metastasis( $P<0.05$ ). The results of COX regression model showed that the main risk factors affecting the postoperative prognosis of patients with time from diagnosis to

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metastasis  $\leq 20$  months, there were no local radiotherapy, rapid progression of primary tumor, extraspinal bone metastasis, visceral metastasis ( $P < 0.05$ ). **Conclusion:** PVP combined with RFA in the treatment of patients with spinal metastatic tumor can effectively improve the patients' motor function and quality of life, and relieve pain. However, the postoperative prognosis is affected by many factors, and targeted preventive measures should be taken.

**Key words:** Percutaneous vertebroplasty; Radiofrequency ablation; Spinal metastases; Clinical efficacy; Postoperative prognostic; Influence factor

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## 前言

随着经济的发展,生活方式的变化,恶性肿瘤的发生率也在升高。恶性肿瘤极易发生远处转移,脊柱是恶性肿瘤转移的好发部位,临床调查显示脊柱转移瘤约占全身转移性瘤的20%<sup>[1]</sup>。原发性肿瘤转移到脊柱后,肿瘤细胞可慢慢破坏脊柱椎体骨质,导致生物力学结构受损;同时,若是肿瘤细胞累及神经根、脊髓,还会引起持续的脊柱疼痛和神经功能障碍<sup>[2-4]</sup>。目前临床多采用经皮椎体成形术(PVP)治疗脊柱转移瘤,可以快速地对受压迫的神经组织进行减压,并有效稳定脊柱<sup>[5-6]</sup>。但也存在肿瘤控制不佳、骨水泥渗漏、截瘫等不足。射频消融(RFA)是一种新兴的微创热疗技术,最初用于心脏介入治疗,后来不断有研究发现RFA的有效热凝固可定点破坏肿瘤组织,受到医学界的广泛关注<sup>[7-9]</sup>。然而,脊柱转移瘤处于肿瘤晚期,病情复杂、预期生存时间短,因此,探讨患者术后预后的影响因素对指导治疗方式具有重要意义。本研究通过观察PVP联合RFA治疗脊柱转移瘤的临床疗效,并分析术后预后的影响因素,旨在为临床诊疗提供数据支持。

## 1 资料与方法

### 1.1 临床资料

回顾性分析2016年5月~2019年5月期间广州中医药大学第一附属医院和广州中医药大学第三附属医院的60例脊柱转移瘤患者的临床资料。在60例患者中,行PVP治疗的患者28例纳为PVP组,行PVP联合RFA治疗的患者32例纳为联合组。其中PVP组:男性患者17例,女性患者11例,年龄介于43~69岁,平均( $54.92 \pm 3.84$ )岁。联合组:男性患者20例,女性患者12例,年龄介于41~70岁,平均( $55.38 \pm 4.02$ )岁。两组一

般资料对比无明显差异( $P > 0.05$ ),具有可比性。

### 1.2 纳入排除标准

纳入标准:(1)①患者具有骨骼疼痛、局部恶变质等症状,②骨扫描显像脊椎有病灶,③磁共振成像(MRI)、X线或电子计算机断层扫描(CT)等影像学诊断为脊柱转移,符合≥2个即可确诊;(2)两组患者均经双磷酸盐、抗炎止痛等药物保守治疗无效后,同意接受手术治疗;(3)病例资料齐全;(4)预期寿命>6个月;(5)签署知情同意书。排除标准:(1)合并认知功能障碍、精神障碍,无法配合研究者;(2)原发肿瘤诊断不明确;(3)合并两种及以上的恶性肿瘤;(4)骨髓炎或凝血功能障碍者。

### 1.3 治疗方法

1.3.1 术前准备 术前了解病史,完善血/尿/便三大常规,行X光、螺旋CT扫描、MRI扫描及体格检查等,并观察患者凝血功能、电解质及肝肾功能等,观察患者有无异常。

1.3.2 手术方法 PVP组:取俯卧位,常规消毒、铺巾,局部麻醉,在数字血管减影机DSA(Siemens Axiom Artis, Germany)透视下,自椎弓根影外上缘开始,直至椎体前中1/3交界处,穿入15G穿刺活检针(山东冠龙医疗用品有限公司),采用PVP螺旋推进器(山东冠龙医疗用品有限公司)将已经调配好的糊状聚甲基丙烯酸甲酯骨水泥(Howmedica, 美国)注入,一般1个椎体4~6mL,当骨水泥至椎体边缘时,立即停止注入。联合组:给予PVP联合RFA治疗,先给予RFA治疗,术前CT、MRI检查肿瘤位置确定穿刺路径和角度,将电极片置于双侧大腿或小腿内侧,经椎弓根将骨穿刺针(Cook公司,美国)穿刺到目标部位,拔出针芯,穿入射频电极针,RFA参数:温度70°C,功率150W,持续时间约10~15 min。结束RFA后直接行PVP。典型病例图见图1、图2。

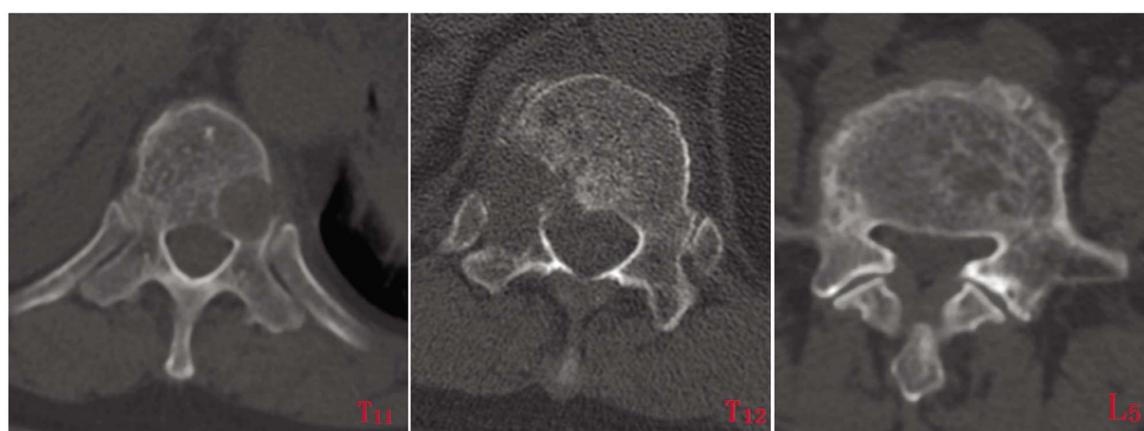


图1 术前T<sub>11</sub>、T<sub>12</sub>、L<sub>5</sub> CT图  
Fig.1 CT images of T<sub>11</sub>, T<sub>12</sub>, L<sub>5</sub> before operation

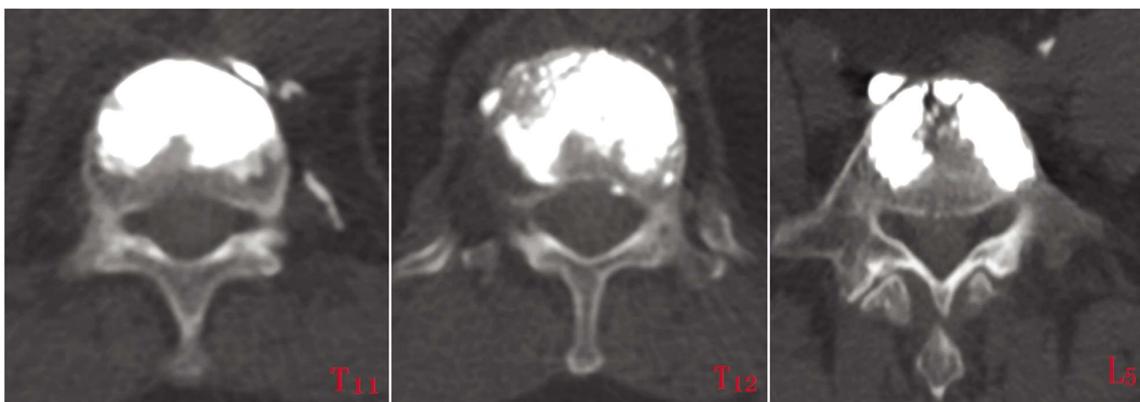


图 2 术后 T<sub>11</sub>、T<sub>12</sub>、L<sub>5</sub> CT 图  
Fig.2 CT images of T<sub>11</sub>, T<sub>12</sub> and L<sub>5</sub> after operation

**1.3.3 术后处理** 术后避免脊柱过度旋转、弯曲及剧烈运动，均常规应用抗生素 24 h 预防感染，卧床休息。

#### 1.4 资料搜集

指定统一的调查问卷，调查所有患者的性别、年龄、累及椎体个数(1 个, ≥ 2 个)、有无脊柱外骨转移、原发肿瘤(结直肠癌、肺癌、乳腺癌、其他)、有无合并基础疾病(包括糖尿病、高血压、高血脂)、有无术后并发症、有无内脏转移、原发肿瘤性质(缓慢、中等、迅速)、有无术后局部放疗、确诊至转移时间(>20 个月, ≤ 20 个月)。

#### 1.5 观察指标

术前、术后 6 个月采用视觉疼痛模拟评分 (VAS)<sup>[10]</sup>、ODI 指数<sup>[11]</sup>、卡式功能(KPS)<sup>[12]</sup>评分评价患者的疼痛、运动功能、生活质量。其中 ODI 指数评分总分 100 分，分值越高，功能障碍越严重。VAS 评分总分 10 分，分值越高，疼痛感越强。KPS 评分总分 100 分，分值越高，健康状况越好。记录两组患者术后 6 个月肿瘤复发率以及骨水泥外渗情况。对两组患者进行术后 2 年的随访，统计生存情况，随访方式可为门诊复查或电话 / 微

信等电子通信方式，以随访期截止或患者死亡为终点。此外，对脊柱转移瘤患者的术后预后进行单因素分析及多因素分析。

#### 1.6 统计学方法

采用 SPSS 22.0 软件进行统计学分析。术后预后单因素等计数资料使用频数表示，两两比较使用卡方检验。计量资料使用均数± 标准差表示，行组内比较(配对 t 检验)、组间比较(独立样本 t 检验)。采用 COX 多因素分析脊柱转移瘤患者术后预后的危险因素。随访生存资料，建立 Kaplan-Meier 乘积限模型，并行两组生存率比较(Logrank 检验)。以 P<0.05 为差异有统计学意义。

## 2 结果

### 2.1 两组相关量表评分对比

两组患者术后 6 个月 VAS、ODI 评分下降，KPS 评分升高 (P<0.05)。联合组术后 6 个月 VAS、ODI 评分低于 PVP 组，KPS 评分高于 PVP 组 (P<0.05)。详见表 1。

表 1 两组 VAS、ODI、KPS 评分对比( $\bar{x} \pm s$ )

Table 1 Comparison of VAS, ODI and KPS scores between the two groups ( $\bar{x} \pm s$ )

Groups	Time points	VAS(scores)	ODI(scores)	KPS(scores)
PVP group(n=28)	Before operation	4.81± 0.63	63.45± 7.91	53.62± 6.58
	6 months after operation	2.64± 0.47	48.23± 6.38	71.67± 7.93
	D-value	-2.17± 0.49	-15.22± 13.02	18.05± 1.48
	Paired test t, P	23.434, 0.000	6.186, 0.000	64.535, 0.000
Combined group(n=32)	Before operation	4.87± 0.72	63.67± 7.53	53.15± 9.31
	6 months after operation	1.72± 0.54	29.49± 4.57	84.29± 8.46
	D-value	-3.15± 0.67	-34.18± 9.25	31.14± 4.36
	Paired test t, P	26.596, 0.000	20.903, 0.000	40.402, 0.000
Comparison between the two groups(Unit test t, P)	Before operation	0.341, 0.734	0.110, 0.913	0.223, 0.824
	6 months after operation	6.990, 0.000	13.197, 0.000	5.935, 0.000

### 2.2 两组患者骨水泥外渗情况、术后 6 个月肿瘤复发率情况对比

联合组骨水泥总外渗率、术后 6 个月肿瘤复发率均低于

PVP 组 (P<0.05)，详见表 2。

### 2.3 两组患者生存情况对比

所有患者随访 2 年，共失访 2 例，死亡 45 例，其中 PVP 组

1例于术后8个月失访,死亡22例,联合组1例于术后7个月失访,死亡23例,Kaplan-Meier生存曲线显示,两组术后生存

率比较无显著性差异( $P>0.05$ ),两组随访患者术后生存时间基本一致,详见表3、图3。

表2 两组患者骨水泥外渗情况、术后6个月肿瘤复发率情况对比[例(%)]

Table 2 Comparison of bone cement extravasation and tumor recurrence rate at 6 months after operation between the two groups [n(%)]

Groups	Bone cement extravasation					Tumor recurrence rate at 6 months after operation	
	Paravertebral leakage	Intervertebral disc leakage	Spinal canal leakage	Vertebral arch leakage	Mixed leakage		
PVP group (n=28)	4	2	1	2	3	12(42.86)	7(25.00)
Combined group (n=32)	1	1	1	0	1	4(12.50)	1(3.13)
$\chi^2$						7.037	4.436
P						0.008	0.035

表3 两组患者生存情况对比

Table 3 Comparison of survival between the two groups

Groups	n	Survival data			Logrank test	
		1 year survival rate n(%)	2 year survival rate n(%)	Median survival (month)	$\chi^2$	P
PVP group	27	18(66.67)	5(18.52)	13(6,21)	0.354	0.552
Combined group	31	20(64.52)	8(25.81)	14(7,22)		

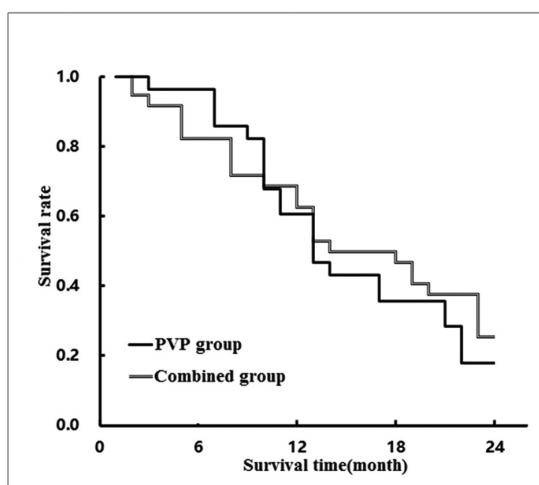


图3 两组患者的Kaplan-Meier生存率曲线

Fig.3 Kaplan Meier survival curve of two groups

#### 2.4 脊柱转移瘤患者术后预后的单因素分析

根据预后情况分为存活组( $n=13$ )和死亡组( $n=45$ ),经单因素分析表明,内脏转移、脊柱外骨转移、术后局部放疗、原发肿瘤性质及确诊至转移时间在两组间的对比有差异( $P<0.05$ )。累及椎体个数、术后并发症、性别、原发肿瘤、年龄、合并基础疾病在两组间的对比无差异( $P>0.05$ )。见表4。

#### 2.5 脊柱转移瘤患者术后预后的多因素分析

以前述单因素分析中有统计学差异的因素为自变量,以脊柱转移瘤患者术后预后状况为应变量,赋值0=生存,1=死亡,建立COX比例风险回归模型。回归过程采用逐步后退法,设定 $\alpha$ 入选=0.05, $\alpha$ 剔除=0.10。回归结果表明:影响脊柱转移

瘤患者术后预后的危险因素主要有脊柱外骨转移、术后无局部放疗、确诊至转移时间≤20个月、有内脏转移、原发肿瘤进展迅速( $P<0.05$ )。见表5。

### 3 讨论

脊柱在恶性肿瘤常见的转移部位中居第3位,仅次于肺和肝脏转移,肿瘤细胞主要通过血行播散,少数通过淋巴转移,以胸椎受累最为常见,其次为腰椎<sup>[1]</sup>。临床针对脊柱转移瘤的治疗原则为增加止痛效果,控制肿瘤生长,增加骨稳定性,预防神经症状的发生发展,最早的开放性手术创伤较大,且对患者整体身体状况要求较高,术后恢复缓慢。针对开放手术面临的问题,微创技术因其创伤小、术后恢复快等优势在脊柱转移瘤中得到了重视。

PVP、RFA均是治疗脊柱转移瘤的常用术式,PVP是指通过注射骨水泥至目标椎体,从而促使椎体稳定的一种手术方式<sup>[13-15]</sup>。王松等人<sup>[16]</sup>研究认为,病变椎体经骨水泥注射后,可促进椎体高度恢复,防止塌陷。此外,骨水泥在椎体内的固化过程中产热,产生的热能可导致肿瘤细胞变性坏死,从而产生阻止肿瘤疾病进展的效果<sup>[17-19]</sup>。尽管如此,PVP仍存在以下不足:骨水泥在注射过程中,可能存在移动肿瘤组织碎片的风险,引起继发转移;骨水泥固化所产生的热量,仍然处于一个较低的水平,且维持时间不超过30 min,不足以彻底破坏及消除椎体内的肿瘤细胞<sup>[20]</sup>。RFA的基本原理也是热损毁,经皮将电极针刺入预先标记好的肿瘤部位,电极针连接电源后作用于肿瘤组织,导致肿瘤组织温度升高,因过热而产生不可逆性坏死<sup>[21-22]</sup>,同时电极针产生的高温还可在射频区域周围形成反应带,隔绝

表 4 脊柱转移瘤患者术后预后的单因素分析[例(%)]

Table 4 Single factor analysis of postoperative prognosis of patients with spinal metastases [n(%)]

Factors	n=58	Survival group (n=13)	Death group (n=45)	$\chi^2$	P
Age( years )	≥ 50	31	5( 16.13 )	1.513	0.219
	<50	27	8( 29.63 )		
Gender	Male	37	9( 24.32 )	0.018	0.892
	Female	21	4( 19.05 )		
Primary tumor	Mammary cancer	23	7( 30.43 )	2.460	0.483
	Lung cancer	16	4( 25.00 )		
	Colorectal cancer	10	1( 10.00 )		
	Other	9	1( 11.11 )		
Number of vertebral bodies involved(n)	1	20	7( 35.00 )	1.786	0.181
	≥ 2	38	6( 15.79 )		
Extraspinal bone metastases	Yes	30	3( 10.00 )	5.507	0.019
	No	28	10( 35.71 )		
Combined with underlying diseases	Yes	34	8( 23.53 )	0.059	0.808
	No	24	5( 20.83 )		
Visceral metastasis	Yes	19	1( 5.26 )	4.786	0.029
	No	39	12( 30.77 )		
Postoperative complications	Yes	18	2( 11.11 )	1.917	0.166
	No	40	11( 27.50 )		
Primary tumor nature	Slow	19	10( 52.63 )	15.427	0.000
	Moderate	27	3( 11.11 )		
	Rapid	12	0( 0.00 )		
Postoperative local radiotherapy	Yes	22	10( 45.45 )	8.791	0.003
	No	36	3( 8.33 )		
Time from diagnosis to metastasis( months )	>20	21	9( 42.86 )	6.176	0.013
	≤ 20	37	4( 10.81 )		

表 5 脊柱转移瘤患者术后预后的 COX 多因素分析

Table 5 Cox multivariate analysis of postoperative prognosis in patients with spinal metastases

Factors	Assignment	Regression coefficient	Standard error	Wald $\chi^2$	P	HR	OR 95% confidence interval
Constant	-	0.045	0.023	3.806	0.051	-	-
Visceral metastasis	1=yes, 0=no	0.216	0.091	5.663	0.017	1.241	1.039~1.483
Extraspinal bone metastasis	1=yes, 0=no	0.737	0.274	7.245	0.007	2.089	1.222~3.572
Time from diagnosis to metastasis	1=≤ 20 months, 0=>20 months	0.500	0.130	14.840	0.000	1.649	1.278~2.127
Postoperative local radiotherapy	1=no, 0=yes	0.553	0.193	8.214	0.004	1.739	1.191~2.539
Progression of primary tumor	1=rapid, 0=slow moroderate	0.874	0.240	13.214	0.000	2.397	1.496~3.840

肿瘤组织血供,进一步促进肿瘤细胞坏死<sup>[23]</sup>。赵全阳等<sup>[24]</sup>报道脊柱瘤患者完成 RFA 治疗后,术中体位耐受性和舒适性均较好,可有效控制临床症状。但近来也有研究指出<sup>[25]</sup>,RFA 治疗后,肿

瘤组织坏死萎缩后产生的空隙易造成椎体二次骨折。基于 PVP、RFA 这两项技术各自的优缺点,本研究观察 PVP 联合 RFA 治疗脊柱转移瘤患者的临床疗效,为临床治疗提供一定的

参考。本次研究结果显示,联合组术后6个月VAS、ODI评分低于PVP组,KPS评分高于PVP组,且联合组骨水泥总外渗率、术后6个月肿瘤复发率均低于PVP组,可见PVP联合RFA治疗脊柱转移瘤患者,能在一定程度上控制肿瘤的进展,减少术后并发症发生率、肿瘤复发率,改善患者生活质量。PVP治疗可有效维持病变椎体功能,维持患者正常的日常活动。联合RFA治疗后,可进一步杀灭肿瘤细胞,优势互补。同时RFA的高温作业可于肿瘤血管处相对致密的反应带,降低肿瘤复发率<sup>[26-28]</sup>。

即使近年来脊柱转移瘤治疗取得一定效果,但仍有研究表明<sup>[29]</sup>,脊柱转移瘤患者手术预后仍不十分理想。COX回归模型分析,影响脊柱转移瘤患者术后预后的危险因素主要有有内脏转移、术后无局部放疗、确诊至转移时间≤20个月、脊柱外骨转移、原发肿瘤进展迅速。骨转移时间越长的患者其预后更好,考虑可能是因为转移时间长的患者其进展速度相对较慢<sup>[30]</sup>。术后局部放疗可帮助患者进一步控制肿瘤病情,降低局部复发风险。原发肿瘤进展迅速可导致病情进展迅速,患者术后生存期明显缩短。存在内脏转移、脊柱外骨转移的患者其肿瘤转移范围广泛,导致治疗获益率下降,降低术后预后。

综上所述,PVP联合RFA治疗脊柱转移瘤患者,疗效确切。术后预后受多种因素影响,为改善患者预后,需采取针对性预防措施。本研究纳入的样本量较少,COX回归模型的可信度有待增加样本量;本研究为回顾性研究,数据获得及分析均可能存在一定的偏倚;此外,由于随访时间偏短,未考虑到临床病理资料对患者生存时间的影响;以上均为本研究的不足之处,尚需进一步验证。

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(下转第319页)

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