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输尿管软镜与经皮肾镜碎石术对≤ 2 cm 肾结石患者血清 IL-6、IL-10、Cor 水平的影响及安全性研究 *

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摘要 目的: 比较输尿管软镜碎石术 (FURL) 与经皮肾镜碎石术 (PCNL) 治疗≤ 2 cm 肾结石的疗效及对患者血清白介素(IL)-6、IL-10、皮质醇(Cor)水平的影响以及手术治疗的安全性。**方法:**选择 2015 年 2 月~2017 年 2 月我院泌尿外科收治的 132 例直径≤ 2 cm 的肾结石患者作为研究对象,其中行 FURL 治疗者 72 例,行 PCNL 治疗者 60 例,比较两组围手术期相关临床指标、治疗前后肾功能以及血清 IL-6、IL-10、Cor 水平的变化。**结果:**FURL 组术后住院时间较 PCNL 组显著缩短,术后输血率较 PCNL 组显著降低($P<0.01$);两组手术时间、结石总清除率比较差异无统计学意义($P>0.05$)。PCNL 组术后 24 h Hb 值较术前显著降低($P<0.01$),FURL 组无明显变化($P>0.05$);两组术后 24 h WBC 值较术前显著升高($P<0.01$),但两组组间比较无明显差异($P>0.05$)。两组术后 1h 血清 IL-6、IL-10、Cor 水平均较术前显著升高,术后 1、3、5d 逐渐降低,FURL 组术后 1 h、1、3、5 d 血清 IL-6、IL-10、Cor 水平均较 PCNL 组各时点显著降低($P<0.01$)。两组术后 6 h、1、2 d 尿 Kim-1 及血清 CysC 水平均较术前显著升高($P<0.01$),FURL 组尿 Kim-1 水平于术后 3 d 恢复至正常水平,PCNL 组为术后 5d 恢复正常,PCNL 组血 CysC 水平于术后 3 d 恢复至正常水平,FURL 组为术后 5 d 恢复正常;FURL 组术后 2、3 d 尿 Kim-1 水平显著低于 PCNL 组同时点 ($P<0.01$), 术后 1、2、3 d 血 CysC 水平显著高于 PCNL 组同时点($P<0.01$)。**结论:**FURL 与 PCNL 治疗直径≤ 2cm 的肾结石均能取得满意的取石效果,但 FURL 手术创伤更小、出血更少,术后应激反应更轻,更有利于术后机体恢复。

关键词: 输尿管软镜; 经皮肾镜; 肾结石; 应激反应; 细胞因子

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Effects and Safety of Flexible Ureteroscope Lithotripsy and Percutaneous Nephrolithotomy on the Serum IL-6, IL-10, Cor Levels of Patients with Renal Calculus ≤ 2 cm*

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ABSTRACT Objective: To compare the clinical efficacy and safety between flexible ureteroscope lithotripsy (FURL) and percutaneous nephrolithotomy (PCNL) on the serum interleukin (IL)-6, IL-10, cortisol (Cor) levels of patients with renal calculus ≤ 2cm.
Methods: 132 cases of patients with renal calculus admitted in the urinary surgery of our hospital from February 2015 to February 2017 were selected, in which 72 cases were treated by FURL and 60 cases were treated by PVNL. The clinical indexes, changes of renal function and serum IL-6, IL-10, Cor levels before and after treatment were compared between the two groups. **Results:** The postoperative hospital stay of FURL group was obviously shorter than that of PCNL group, and the postoperative blood transfusion rate of FURL group was significantly lower than that of PCNL group ($P<0.01$). No significant difference was found in terms of surgery duration and total clearance of stones between the two groups($P>0.05$). The Hb value at 24h after operation were evidently decreased as compared with that before operation ($P<0.01$), but no significant change was found in the FURL group ($P>0.05$). The WBC values of both group at 24h after operation were significantly increased as compared with those before operation ($P<0.01$), but there was no statistic difference between the two groups ($P>0.05$). The serum IL-6, IL-10, Cor levels of both groups at 1h after operation were evidently increased as compared those before operation, and declined gradually at 1d, 3d, 5d after operation. The serum IL-6, IL-10, Cor levels of FURL group at 1h, 1d, 3d, 5d after operation were much lower than those of PCNL group at the corresponding time points ($P<0.01$). The urine Kim-1 and serum CysC levels of both groups at 6h, 1d, 2d after operation were significantly increased as compared with those before operation ($P<0.01$). The urinal Kim-1 levels of FURL group returned to normal at 3d after operation, while it took 5d for PCNL group to have it return to normal. The serum CysC level of PCNL group returned to normal at 3d after operation, while it took 5d for FURL group to have it return to

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normal. The levels of urine Kim-1 at 2d, 3d after operation of FURL group were significantly lower than those in PCNL group at the same time group ($P<0.01$), the blood CysC levels at 1, 2 and 3d after operation were significantly higher than those in PCNL group at the same time group ($P<0.01$). **Conclusion:** Both FURL and PCNL were effective in the treatment of renal calculus with a diameter $\leq 2\text{cm}$, but FURL outperforms the other with minor operation wound, less blood loss, lighter postoperative stress reaction, and better recovery.

Key words: Flexible ureteroscope lithotripsy; Percutaneous nephroscope; Renal calculus; Stress reaction; Cell factor

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前言

泌尿系结石为泌尿外科常见病及多发病，其中 40%~50% 的结石为肾结石，手术是治疗肾结石最常用的手段之一。随着现代科技的不断发展，微创手术已逐渐取代传统开放性手术成为最主要的手术治疗方式^[1,2]。治疗肾结石的微创手术主要有输尿管软镜碎石术(FURL)与经皮肾镜碎石术(PCNL)，这两种手术是泌尿外科肾结石治疗的主要手段。其中，PCNL 具有创伤小、疗效佳、安全性高等优点而被临床广泛使用，对于直径在 2 cm 以上的肾结石以及复杂性结石，PCNL 具有无法比拟的优势^[3]。FURL 可利用人体天然通道实施手术，因此创伤小，对人体免疫功能影响小^[4]。针对直径在 2 cm 以上的肾结石，临床多采取 PCNL 治疗，但对直径在 2 cm 以内的肾结石，采取何种手术方式临床仍存在争议^[5]。针对此，本研究对我院近年来收治的分别行 FURL 与 PCNL 治疗的直径 $\leq 2\text{cm}$ 的肾结石患者进行了对比，以期为直径 $\leq 2\text{cm}$ 的有手术指征的肾结石患者手术方式的选择提供参考，现报道如下。

1 资料与方法

1.1 一般资料

选择 2015 年 2 月 ~2017 年 2 月我院泌尿外科收治的 132 例直径 $\leq 2\text{cm}$ 的肾结石患者作为研究对象，其中行 FURL 治疗者 72 例，行 PCNL 治疗者 60 例。FURL 组男 39 例，女 33 例，年龄(44.8 ± 8.5)岁，体重(68.2 ± 6.7)kg，结石直径(1.52 ± 0.36)cm，结石表面积 (234.6 ± 78.6)mm²，左肾 33 例，右肾 27 例。PCNL 组男 41 例，女 31 例，年龄(45.2 ± 9.4)岁，体重(67.5 ± 6.4)kg，结石直径(1.49 ± 0.42)cm，结石表面积(228.5 ± 84.5)mm²，左肾 35 例，右肾 25 例。两组一般临床资料比较差异无统计学意义($P>0.05$)，具有可比性。

1.2 纳入及排除标准

纳入标准：(1)经临床表现、泌尿系彩超、CT、尿路平片等确诊为肾结石，且肾结石直径 $\leq 2\text{cm}$ ；(2)年龄 18~70 岁；(3)术前无泌尿系感染；(4)未合并严重内科疾病；(5)未合并其他部位结石、肿瘤等；(6)体外冲击波碎石术(ESWL)碎石失败或仍有结石残留；(7)患肾解剖结构正常，肾功能正常。

排除标准：(1)年龄 <18 岁或 >70 岁；(2)合并严重高血压、免疫系统疾病；(3)严重肾功能损害；(4)合并严重心肺功能、凝血功能障碍；(5)合并急性炎症、发热；(6)反复肾结石取石史；(7)孤立肾、移植肾、脊柱侧弯；(8)近 1 个月内使用过糖皮质激素或免疫抑制剂。

1.3 治疗方法

FURL 组：术前 1~4 周行输尿管镜检查，于患侧输尿管行

输尿管 D-J 管置入术。术前 30 min，静滴广谱抗生素。全麻后取截石位，输尿管硬镜经尿道插入至膀胱内，异物钳取出术前放置的 D-J 管，观察膀胱内是否存在病变，并寻找双侧输尿管开口，于患侧输尿管开口处插入斑马导丝，沿着斑马导丝置入输尿管硬镜至患侧输尿管内，斑马导丝置入肾盂后将输尿管硬镜退出。再沿着导丝置入输尿管软镜鞘，于软镜鞘内置入输尿管软镜直至肾盂内，找到结石后将导丝退出，随后置入 200 μm 钕激光传导光纤，钬激光功率 1J，频率 20Hz。采用钬激光将结石碎至 2 mm 以内后冲出，检查有无结石残留，是否存在活动性出血。输尿管放置 D-J 管，留置导尿。

PCNL 组：全麻后取截石位，输尿管硬镜经尿道插入，找到输尿管开口，于患侧输尿管开口处置入 1 根 F5 输尿管导管至肾盂内，做注水用。再取俯卧位，软枕垫高腰部。B 超下观察患侧肾积水及结石情况，采用 20 mL 注射器向肾脏内持续注入生理盐水，制造人工肾积水。B 超定位下采取 18G 穿刺针经皮肾穿刺入目标肾盏，见有清亮尿液流出可确认穿刺成功，随后置入斑马导丝。退出穿刺针，沿导丝采用筋膜扩张器扩张通道，由 F8 依次扩张至 F18，最后留置 F18 剥皮鞘。鞘内置入输尿管硬镜，依次达到肾盂、肾盏、输尿管上段，查找到结石后，将斑马导丝退出，采取钬激光将结石碎至 2 mm 以内后冲出，取石钳取出较大结石，查看肾盏是否有明显结石残留，是否存在活动性出血。输尿管放置 D-J 管，退出剥皮鞘后放置肾造瘘管，留置导尿。

1.4 观察指标

1.4.1 结石清除率 分别于术后 2、30、90 d 进行超声检查，若无结石残留或残留结石碎片在 2 mm 内，表明结石清除成功，统计结石总清除率。同时统计两组手术时间、术后输血情况及住院时间。

1.4.2 血红蛋白(Hb)及白细胞(WBC)检测 分别于术前、术后 24h 采用全自动血细胞分析仪检测血红蛋白 (Hb) 及白细胞 (WBC) 值。

1.4.3 血清 IL-6, IL-10, Cor 水平检测 分别于术前、术后 1 h、1、3、5d 抽取 5 mL 静脉血，4000 r/min 速度离心 10 min 后，取上清液放置于 -20℃ 冰箱中保存待测。采取酶联免疫吸附试验 (ELISA) 测定血清白介素 IL-6、IL-10 水平，采取放射免疫法测定血清皮质醇(Cor)水平。

1.4.4 尿损伤分子 -1(Kim-1)、血清胱抑素 C(CysC)测定 分别于术前、术后 6h、1、2、3、5d 收集静脉血与尿液标本，离心取上清液后低温保存待测。尿损伤分子 -1(Kim-1)、血清胱抑素 C (CysC) 测定采取 ELISA 法。

1.5 统计学分析

采取 SPSS20.0 软件对数据做处理，其中计数资料采用 χ^2

检验,计量资料采用t检验。以P<0.05为差异具有统计学意义。

2 结果

2.1 两组手术时间、术后住院时间、结石总清除率的比较

表1 两组手术时间、术后住院时间、结石总清除率比较

Table 1 Comparison of the operation time, postoperative hospital stay and total clearance of stones between two groups

Groups	n	Operation time(min)	Postoperative hospital stay(d)	Postoperative blood transfusion rate[n(%)]	Total clearance of stones [n(%)]
FURL group	72	50.35± 10.92	3.63± 0.82	0(0)	70(97.22)
PCNL group	60	48.12± 9.38	5.24± 1.18	4(6.67)	57(95.00)
P		0.216	0.000	0.026	0.506

2.2 两组手术前后Hb值、WBC值比较

PCNL组术后24h Hb值较术前显著降低(P<0.01),FURL

组无明显变化(P>0.05);两组术后24h WBC值较术前显著升高(P<0.01),但两组组间比较无明显差异(P>0.05)。见表2。

表2 两组手术前后Hb值、WBC值比较($\bar{x}\pm s$)

Table 2 Comparison of the Hb value and WBC value between two groups before and after operation($\bar{x}\pm s$)

Groups	n	Hb value(g/L)		WBC value($\times 10^9/L$)	
		Before operation	24h after operation	Before operation	24h after operation
FURL group	72	110.67± 8.35	108.23± 7.12	6.40± 1.25	7.64± 1.67*
PCNL group	60	112.82± 6.78	100.18± 7.56*	6.36± 1.47	7.92± 1.54*
P		0.112	0.000	0.866	0.322

Note: compared within the group before and after operation, *P<0.01.

2.3 两组手术前后不同时点血清IL-6、IL-10、Cor水平比较

两组术后1h血清IL-6、IL-10、Cor水平均较术前显著升高,术后1、3、5d逐渐降低,FURL组术后1h、1、3、5d血清

IL-6、IL-10、Cor水平均较PCNL组各时点显著降低(P<0.01)。

见表3。

表3 两组手术前后不同时点血清IL-6、IL-10、Cor水平比较($\bar{x}\pm s$)

Table 3 Comparison of the serum IL-6, IL-10 and Cor levels between two groups at different time points before and after operation($\bar{x}\pm s$)

Indexes	Groups	n	Before operation	After operation			
				1h	1d	3d	5d
IL-6 (pg/mL)	FURL group	72	8.87± 2.12	32.23± 7.35**	29.76± 7.24**	14.82± 3.18**	12.27± 2.52**
IL-10 (pg/mL)	PCNL group	60	8.65± 2.45	47.12± 8.82*	35.56± 6.53*	21.35± 3.45*	17.05± 2.12*
Cor (g/dl)	FURL group	72	3.79± 1.27	17.47± 5.84**	13.42± 2.56**	9.87± 1.64**	7.76± 1.17**
	PCNL group	60	3.81± 1.06	22.08± 6.22*	16.87± 2.81*	13.45± 1.77*	9.67± 1.24*
	FURL group	72	12.07± 3.58	19.48± 9.12**	17.34± 6.56**	12.35± 2.97**	12.53± 3.12**
	PCNL group	60	11.82± 4.12	35.63± 8.83*	21.24± 6.12*	16.62± 3.45*	15.22± 2.87*

Note: compared within the group before and after operation, *P<0.01; compared at the same time between groups, **P<0.01.

2.4 两组手术前后不同时点尿Kim-1及血清CysC水平比较

两组术后6h、1、2d尿Kim-1及血清CysC水平均较术前显著升高(P<0.01),FURL组尿Kim-1水平于术后3d恢复至正常水平,PCNL组为术后5d恢复正常,PCNL组血CysC水平于术后3d恢复至正常水平,FURL组为术后5d恢复正常;FURL组术后2、3d尿Kim-1水平显著低于PCNL组同时点(P<0.01),术后1、2、3d血CysC水平显著高于PCNL组同时点(P<0.01)。见表4。

3 讨论

开放性手术是肾结石最早采用的外科手术治疗方式,但因其创伤大、出血量多,且易并发漏尿、感染等,不利于术后机体的恢复^[6]。随着腔镜技术的不断发展,外科手术治疗逐渐从开放性手术治疗转变为微创手术治疗^[7]。PCNL自20世纪90年代以来逐渐在我国推广,并成为肾结石最常用的手术方式之一^[8]。FURL属于一项新兴腔镜技术,其与输尿管硬镜相比能达到其

表 4 两组手术前后不同时点尿 Kim-1 及血清 CysC 水平比较($\bar{x}\pm s$)Table 4 Comparison of the urine Kim-1 and serum CysC levels between two groups at different time points before and after operation($\bar{x}\pm s$)

Indexes	Groups	n	Before operation	After operation				
				6h	1d	2d	3d	5d
Urine Kim-1 (ng/L)	FURL group	72	73.52± 13.45	81.45± 18.77*	90.86± 20.45*	76.46± 19.23#	73.67± 15.34#	72.12± 14.82
	PCNL group	60	72.97± 15.67	83.66± 21.46*	102.54± 26.12*	92.64± 23.46*	82.24± 21.92*	73.45± 18.24
Blood CysC	FURL group	72	497.35± 82.45	561.67± 90.56*	778.24± 146.89*#	651.67± 122.34**#	567.35± 117.45*#	502.45± 102.46
	PCNL group	60	508.67± 79.32	555.31± 88.35*	585.78± 152.45*	569.62± 162.42*	510.23± 97.24	511.24± 87.56

Note: compared within the group before and after operation, *P<0.01; compared at the same time between groups, #P<0.01.

不能达到的肾盏、肾盂,与 PCNL 相比则能避免皮肾通道的建立损伤肾脏以及肾脏周围的组织器官^[9]。在 FURL 治疗过程中,即便术中结石发生移位,利用输尿管软镜也能有效处理结石^[10]。此外,输尿管软镜鞘还能保护输尿管壁,防止手术操作损伤输尿管壁。目前,大量研究证实^[11-13]FURL 手术创伤小、疼痛轻、并发症少、适应症广,具有广阔的应用前景。对于直径>2 cm 的肾结石,临床主张行 PCNL 治疗,但对于直径在 2 cm 以内的肾结石临床尚无统一意见。

本研究旨在探讨这两种手术方式在直径<2 cm 肾结石中的应用价值。结果显示 FURL 与 PCNL 的结石清除率均达到了至少 95%,表明对于直径≤2 cm 的肾结石,FURL 与 PCNL 均可取得满意的结石清除效果。FURL 组术后住院时间较 PCNL 组显著缩短,术后输血率较 PCNL 组显著降低。PCNL 术后出血较为多见,术后 Hb 丢失量多,其原因主要是 PCNL 术中建立穿刺通道可损伤肾脏与肾脏周围组织,易引起肾脏出血^[14,15]。本研究中,FURL 术后 Hb 值无明显变化,但 PCNL 术后 Hb 值较术前显著降低。为减少 PCNL 术后出血量,患者需绝对卧床数日,且临床会选择对肾造瘘管留置时间进行延长,但肾造瘘管留置时间延长后必然会延长住院时间^[16]。而 FURL 则可于术后次日拔除尿管,故 PCNL 术后住院时间与 FURL 相比显著增加。该结果与多数研究一致^[17,18]。PCNL 与 FURL 均属于侵入性手术,术中结石内的细菌可对机体产生侵袭,导致术后高热、寒战,乃至引发感染性休克,危及生命。两组术后 WBC 均有明显升高,但仍处在正常范围内。

侵入性手术可对机体产生不同程度的损害,手术应激反应程度能很好地反映出手术创伤严重程度。IL-6 是早期组织损伤敏感的标志物,手术创伤越严重,IL-6 水平升高越明显^[19]。IL-10 是 Th2 细胞生成的抗炎细胞因子,能抑制 IL-6、肿瘤坏死因子(TNF)-α 等促炎因子的释放,避免引发脓毒症等严重并发症,防止损害远处脏器^[20]。IL-10 水平持续升高则会使机体免疫功能受到抑制,导致病情加重。手术创伤可引起肾素-血管紧张素系统(RAS)被激活、下丘脑-垂体-肾上腺素皮质轴(HPA)兴奋,这两大系统的激活表明机体处在应激反应状态中。Cor 是反映机体应激反应的敏感指标,手术等不良刺激可导致 Cor 分泌增多,且刺激越明显,Cor 水平升高越显著。本研究中,两组术后 1 h 血清 IL-6、IL-10、Cor 水平均较术前显著升高,但

PCNL 组升高更明显。该结果表明 FURL 相对于 PCNL 对肾结石患者造成的应激反应更轻微,创伤更小,这与钟瑞伦等^[21]的研究基本一致,表明 FURL 与 PCNL 均能引起大量炎性因子的释放,且抗炎因子的分泌也会随之增多,但 FURL 相对于 PCNL 对肾结石患者机体应激反应更小,有利于术后恢复。

有文献报道^[22,23]FURL 与 PCNL 在碎石过程中要想维持术野清晰,需要较高的冲水灌注压,但冲水灌注压若大于肾盂生理压力,易引起肾盂内液体返流,导致肾功能受损。有研究显示^[24]当灌注压在 300 mmHg 以上时,肾盂内压力可达生理压力数十倍之多,导致尿量减少,肾盂内压力逐步升高时还可引发尿液逆流,引发肾间质水肿,导致肾间质静水压力逐渐上升,当肾内小动脉压力不及肾间质静水压力时,可造成血流停滞,引起微血栓形成,肾实质可发生缺血性改变,使肾功能受到影响。由于尿素氮、肌酐等肾功能指标易受到其他因素的影响,本研究选取了尿 Kim-1、血 CysC 这两项指标。其中,Kim-1 组织特异性高,在肾脏受到损害后其表达可明显升高,其主要反映的是肾小管损害。本研究中,两组术后 6 h、1、2 d 尿 Kim-1 水平较术前均有显著升高,FURL 组术后 2、3 d 尿 Kim-1 水平显著低于 PCNL 组,表明 FURL 与 PCNL 均可造成肾小管损伤,但 FURL 组尿 Kim-1 水平降低更快、更明显,即 FURL 引起的肾小管损害更轻。陈家璧等^[25]则是采用血清中性粒细胞明胶酶相关脂蛋白(NGAL)水平反映肾小管损害程度,其研究结果表明 FURL 组血清 NGAL 水平能更快恢复至术前水平,对肾小管的损伤程度较 PCNL 组更轻,与本研究结果一致。CysC 是反映肾小球滤过率的内源性标志物,当肾小球发生轻微损伤时,血清 CysC 水平可在损伤后 3 h 开始升高,升高越明显,表明肾小球损伤越严重。本研究中,两组术后 6 h、1、2 d 血清 CysC 水平均较术前显著升高,但 FURL 组升高更明显,表明 FURL 引起的肾小球损伤更明显。但两组术后 2 d 时的尿 Kim-1、血 CysC 水平开始逐渐下降,至术后 5 d 均恢复正常。表明 FURL 与 PCNL 引起的肾损害是可逆的。

综上所述,采取 FURL 与 PCNL 治疗直径≤2 cm 的肾结石均能取得满意的结石清除效果,但 FURL 手术创伤更小、出血更少,术后应激反应更轻,更有利于术后机体恢复。FURL 与 PCNL 均能引起一定程度的肾损害,PCNL 以肾小管为主,FURL 以肾小球为主,但这两种术式引起的肾损害是可逆的,

随着术后时间的延长,可恢复至术前状态,故PCNL与FURL均具有较高的安全性。

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