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输尿管软镜对肾结石患者肾损伤因子、凝血功能及氧化应激的影响*

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摘要 目的:探讨输尿管软镜对肾结石患者肾损伤因子、凝血功能及氧化应激的影响。**方法:**回顾性分析 2018 年 9 月~2019 年 9 月期间我院收治的 200 例肾结石患者的临床资料,根据手术方式的不同将患者分为 A 组(n=100,经皮肾镜取石术)和 B 组(n=100,输尿管软镜取石术),比较两组患者围术期指标、肾损伤因子、凝血功能及氧化应激指标,并记录两组围术期并发症发生情况。**结果:**B 组手术时间、住院时间短于 A 组,术中出血量少于 A 组($P<0.05$);两组患者结石清除率比较无差异($P>0.05$)。两组术后 1 d 血清肌酐(Scr)、中性粒细胞明胶酶相关脂质运载蛋白(NGAL)及半胱氨酸蛋白酶抑制剂 C(CysC)水平均升高,但 B 组低于 A 组($P<0.05$)。两组术后 1 d 的凝血反应时间(R 值)、血凝块形成的时间(K 值)均下降,但 B 组高于 A 组($P<0.05$);两组术后 1 d 的血块生成率(α 角)及最大宽度值(MA 值)均升高,但两组比较差异无统计学意义($P>0.05$)。两组术后 1 d 丙二醛(MDA)升高,超氧化物歧化酶(SOD)降低($P<0.05$);B 组术后 1 d 的 MDA 高于 A 组,SOD 则低于 A 组($P<0.05$)。两组术后并发症发生率对比无统计学差异($P>0.05$)。**结论:**与经皮肾镜取石术相比,输尿管软镜取石术可获得相当的治疗效果,其在改善肾功能、凝血功能及氧化应激等方面效果更佳,且不增加并发症发生率,临床应用价值较高。

关键词:输尿管软镜取石术;肾结石;经皮肾镜取石术;肾损伤因子

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Effects of Flexible Ureteroscopy on Renal Injury Factors, Coagulation Function and Oxidative Stress in Patients with Renal Calculi*

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ABSTRACT Objective: To investigate the effects of flexible ureteroscopy on renal injury factors, coagulation function and oxidative stress in patients with renal calculi. **Methods:** The clinical data of 200 cases of renal calculi admitted to our hospital from September 2018 to September 2019 were retrospectively analyzed, patients were divided into group A (n=100, percutaneous nephrolithotomy) and group B (n=100, flexible ureteroscopic lithotomy) according to different surgical methods, the perioperative indicators, renal injury factors, coagulation function and oxidative stress were compared between the two groups, and perioperative complications in the two groups were recorded. **Results:** The operative time, hospital stay in group B were shorter than those in group A, and intraoperative bleeding volume was less than that in group A ($P<0.05$). There was no difference in stone clearance rate between the two groups ($P>0.05$). Serum creatinine (Scr), neutrophil gelatinase-associated lipocalin (NGAL) and cysteine protease inhibitor C (CysC) levels were increased in both groups 1d after operative, but group B lower than group A ($P<0.05$). The coagulation reaction time (R value) and the formation time of blood clot (K value) in both groups decreased 1d after operative, but group B was higher than group A ($P<0.05$). Blood clot formation rate (α angle) and maximum width (MA value) values were increased in both groups 1d after operative, but there was no statistically significant difference between the two groups ($P>0.05$). In both groups the malondialdehyde (MDA) level was increased and superoxide dismutase (SOD) level was decreased 1d after operative ($P<0.05$), MDA in group B was higher than that in group A 1d after operative, and SOD was lower than that in group A ($P<0.05$). There was no significant difference in the incidence of postoperative complications between the two groups ($P>0.05$). **Conclusion:** Compared with percutaneous nephrolithotomy, flexible ureteroscopic lithotomy can achieve a considerable therapeutic effect, and it has a better effect in improving renal function, coagulation function and oxidative stress, and does not increase the incidence of complications and has high clinical application value.

Key words: Flexible ureteroscopic lithotomy; Renal calculi; Percutaneous nephrolithotomy; Renal injury factor

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前言

肾结石是泌尿系统的常见疾病,主要是由于各种因素作用引起尿中晶体物质浓度升高、溶解度降低而呈过饱和状态,进而析出结晶,长此以往,形成结石^[1]。临床主要表现为恶心、呕吐,腰部酸胀,严重者可导致尿路梗阻、肾功能减退或不全^[2]。据统计^[3],全球约有 5%~15%的人患有泌尿系结石,给患者生活质量带来严重影响。现临床针对肾结石的治疗主要分为保守治疗和手术治疗,而当保守治疗无法缓解患者疼痛时通常需给予手术治疗^[4]。经皮肾镜取石术、输尿管软镜取石术是临床治疗肾结石的常用术式,经皮肾镜取石术是指在患者腰部皮肤处,建立由皮肤至肾激活系统的手术通道,对肾输尿管内结石进行碎石及取石的手术方法^[5];而输尿管软镜是一种纤细、可弯曲的内窥镜,通过人体自然腔道进入肾脏,配合钬激光等先进设备,将体内结石粉碎、取出^[6]。上述两种术式均可有效清除结石,缓解患者痛苦,但当前国内外学者对于上述两种术式在肾结石治疗效果的孰优孰劣尚存在一定争议^[7,8]。本研究通过对比上述两种术式治疗肾结石的疗效,以期临床肾结石术式选择提供数据支撑。

1 资料与方法

1.1 基线资料

回顾性分析我院 2018 年 9 月~2019 年 9 月收治的 200 例肾结石患者的临床资料。本次研究已经获取本院伦理学委员会批准。纳入标准:(1)均符合《中国泌尿外科疾病诊断治疗指南(2007 版)》^[9]的标准;(2)经超声、CT 等检查确诊为肾结石;(3)临床表现为腰背区疼痛不适、肉眼血尿等症状;(4)均具备手术指征者;(5)临床病例资料完整;(6)均由同一组医师完成手术操作。排除标准:(1)合并慢性肾炎、肾病综合征等疾病者;(2)合并恶性肿瘤者;(3)合并急性慢性感染、免疫缺陷者;(4)合并精神疾患无法配合本次研究者;(5)存在严重的尿路感染者。根据手术方式的不同将患者分为 A 组(n=100,经皮肾镜取石术)和 B 组(n=100,输尿管软镜取石术),其中 A 组男 81 例,女 19 例,年龄 27~64 岁,平均(44.86±4.73)岁;结石直径 12~22 mm,平均(14.12±1.83)mm;单发结石 53 例,多发结石 47 例。B 组男 72 例,女 28 例,年龄 28~63 岁,平均(44.62±4.09)岁;结石直径 11~21 mm,平均(13.95±1.75)mm;单发结石 55 例,多发结石 45 例。两组一般资料比较无统计学差异($P>0.05$)。

1.2 方法

1.2.1 A 组手术方法 A 组给予经皮肾镜取石术,具体操作如下:全麻后气管插管,患者取截石位,在膀胱镜的辅助下将 F5

输尿管导管逆行置入患侧,连接生理盐水,留置输尿管导管。取俯卧位,B 超引导下采用 18G 针尖进入目标肾盏,随后置入工作导丝,将针鞘退出。采用一次性筋膜扩张器沿工作导丝将通道扩张至 F16,随后换用套叠式金属扩张器将通道扩张至 24F,置入金属外鞘、肾镜,采用超声碎石清石机进行碎石处理,碎石结束后行人工冲洗。手术过程中需以流速 350~400 mL/min 的速率向肾内持续泵入等渗冲洗液,术后常规留置 D-J 管、F20 肾造瘘管,均给予常规抗感染治疗。

1.2.2 B 组手术方法 B 组给予输尿管软镜取石术,具体操作如下:手术前 1~4 周给予患侧输尿管 F5 双 J 管置入术,全麻后气管插管,患者取截石位,患侧输尿管内置入硬镜,行输尿管扩张。随后患侧插入输尿管导管,置入 0.0355 镍钛超滑导丝,退出输尿管硬镜,透过输尿管软镜鞘进镜。观察肾盂、肾盏,确定结石情况。钬激光光纤经输尿管软镜置入行碎石操作,激光能量调节为 1.2J/10Hz,碎石结束后行人工冲洗。术后常规留置 D-J 管,均给予常规抗感染治疗。

1.3 观察指标

(1)比较两组患者手术时间、住院时间、术中出血量以及结石清除率。(2)记录两组患者并发症发生情况。(3)抽取患者术前、术后 1 d 的清晨空腹肘静脉血 4 mL,3900 r/min 离心 12 min,离心半径 15 cm,分离血清,置于 -30℃ 冰箱中待测。其中氧化应激指标如超氧化物歧化酶(Superoxide dismutase, SOD)、丙二醛(malondialdehyde, MDA)以及肾损伤因子如肌酐(creatinine, Scr)、中性粒细胞明胶酶相关脂质运载蛋白(Neutrophil gelatinase-associated lipocalin, NGAL)及半胱氨酸蛋白酶抑制剂 C(Cysteine protease inhibitor C, CysC)均采用酶联免疫吸附试验检测,血栓弹力图试验采用血栓弹力图凝血分析仪进行,记录凝血功能指标如凝血反应时间(R 值)、血凝块形成的时间(K 值)、血块生成率(α 角)及最大宽度值(MA 值)等参数。

1.4 统计学方法

所有研究数据分析均采用 SPSS 25.0 统计学软件。计量资料以均值±标准差表示,实施 t 检验,计数资料以%表示,实施卡方检验,检验标准设置为 $\alpha=0.05$ 。

2 结果

2.1 两组患者围术期指标比较

B 组手术时间、住院时间短于 A 组,术中出血量少于 A 组($P<0.05$);两组患者结石清除率比较无差异($P>0.05$);详见表 1。

表 1 两组患者围术期指标比较

Table 1 Comparison of perioperative indicators between the two groups

Groups	Operative time(min)	Intraoperative bleeding volume(mL)	Hospital stay(d)	Stone clearance rate(%)
Group A(n=100)	63.49±6.24	48.27±5.36	8.28±1.57	91(91.00)
Group B(n=100)	52.47±7.03	26.58±4.24	6.36±0.95	92(92.00)
t/ χ^2	11.724	31.737	10.463	0.064
P	0.000	0.000	0.000	0.800

2.2 两组肾损伤因子比较

两组术前血清 Scr、NGAL、CysC 水平比较差异无统计学

意义 ($P>0.05$); 两组术后 1 d 血清 Scr、NGAL、CysC 水平均升高, 但 B 组低于 A 组 ($P<0.05$); 详见表 2。

表 2 两组肾损伤因子比较($\bar{x}\pm s$)Table 2 Comparison of renal injury factors between the two groups($\bar{x}\pm s$)

Groups	Scr($\mu\text{mol/L}$)		NGAL($\mu\text{g/L}$)		CysC($\mu\text{g/L}$)	
	Before operation	1d after operation	Before operation	1d after operation	Before operation	1d after operation
Group A(n=100)	59.41 $\pm$ 7.16	74.57 $\pm$ 6.23*	3.49 $\pm$ 0.53	5.37 $\pm$ 0.42*	505.66 $\pm$ 51.16	788.51 $\pm$ 92.15*
Group B(n=100)	59.32 $\pm$ 6.53	67.58 $\pm$ 7.65*	3.54 $\pm$ 0.42	4.71 $\pm$ 0.45*	503.47 $\pm$ 48.29	657.51 $\pm$ 83.09*
t	0.093	7.085	0.739	10.722	0.311	10.558
P	0.926	0.000	0.614	0.000	0.756	0.000

Note: Compared with before operation, * $P<0.05$.

2.3 两组凝血功能比较

两组 R 值、K 值、 α 角、MA 值比较无差异 ($P>0.05$); 两组术

后 1 d 的 α 角、MA 值均升高, 但 A 组、B 组组间比较差异无统计学意义 ($P>0.05$), 详见表 3。

后 1 d 的 R 值、K 值均下降, 但 B 组高于 A 组 ($P<0.05$); 两组术

表 3 两组凝血功能比较($\bar{x}\pm s$)Table 3 Comparison of coagulation function between the two groups($\bar{x}\pm s$)

Groups	R value(min)		K value(min)		α angle($^{\circ}$)		MA value(min)	
	Before operation	1d after operation	Before operation	1d after operation	Before operation	1d after operation	Before operation	1d after operation
Group A (n=100)	6.48 $\pm$ 0.91	4.82 $\pm$ 0.59*	2.66 $\pm$ 0.42	1.94 $\pm$ 0.37*	44.06 $\pm$ 5.13	47.41 $\pm$ 5.28*	46.50 $\pm$ 6.26	51.95 $\pm$ 5.29*
Group B (n=100)	6.51 $\pm$ 0.78	5.45 $\pm$ 0.67*	2.62 $\pm$ 0.36	2.28 $\pm$ 0.39*	43.89 $\pm$ 6.18	46.98 $\pm$ 5.26*	46.48 $\pm$ 7.24	50.83 $\pm$ 6.32*
t	0.250	7.057	0.723	6.325	0.212	0.577	0.021	1.359
P	0.803	0.000	0.420	0.000	0.833	0.565	0.983	0.176

Note: Compared with before operation, * $P<0.05$.

2.4 两组氧化应激指标比较

两组术前血清 MDA、SOD 水平比较无差异 ($P>0.05$); 两组

术后 1 d 的 MDA 升高, SOD 降低 ($P<0.05$); B 组术后 1 d 的 MDA 高于 A 组, SOD 则低于 A 组 ($P<0.05$); 详见表 4。

表 4 两组氧化应激指标比较($\bar{x}\pm s$)Table 4 Comparison of oxidative stress indicators between the two groups($\bar{x}\pm s$)

Groups	MDA(U/mL)		SOD(mmol/L)	
	Before operation	1d after operation	Before operation	1d after operation
Group A(n=100)	0.56 $\pm$ 0.12	0.72 $\pm$ 0.09*	84.24 $\pm$ 6.68	73.79 $\pm$ 6.57*
Group B(n=100)	0.58 $\pm$ 0.09	0.93 $\pm$ 0.11*	84.28 $\pm$ 7.64	58.06 $\pm$ 5.52*
t	1.333	14.776	0.039	18.331
P	0.184	0.000	0.969	0.000

Note: Compared with before operation, * $P<0.05$.

2.5 术后并发症比较

A 组术后出现 5 例短暂性低热、3 例出血、2 例短暂性高热, 术后并发症发生率为 10.00%(10/100); B 组术后出现 3 例短暂性低热、3 例出血、3 例短暂性高热, 术后并发症发生率为 9.00%(9/100); 两组术后并发症发生率对比无差异 ($\chi^2=0.058$, $P=0.809$)。

3 讨论

肾结石是指发生于肾盂、肾盏、肾盂与输尿管连接部的结石, 好发于青壮年群体^[10]。结石的形成机制及其复杂, 通常认为与以下几个方面有关: 抑制结石生成的物质减少; 肾小球上皮细胞受损是结石形成的重要病理基础; 高草酸尿症使得尿液成石物质处于高饱和状态^[11-13]。肾结石发作时患者常常剧痛难忍, 对于药物治疗无法缓解症状者应尽早接受手术治疗。随着微创技术的飞速发展, 经皮肾镜取石术、输尿管软镜取石术等微创术式逐渐获得临床医师和患者的青睐^[14, 15]。输尿管镜和经皮肾

镜是定位和治疗肾结石的可视设备,其中经皮肾镜取石术是经皮肾穿刺造口的方法治疗肾结石,但由于其有创性,术后可能出现出血、感染等并发症^[16,17]。而输尿管软镜取石术则是一种利用人体天然通道的手术,体表无伤口,具有更大的微创优势,但对于输尿管狭窄进镜困难者不适用^[18,19]。

Scr 主要通过肾小球滤过排泄;CysC 是一种非糖基化碱性低蛋白,肾脏是其唯一的代谢途径;NGAL 是一种损伤诱导的转铁蛋白,在肾脏中通过转铁蛋白转运促进肾小管上皮细胞分化;当肾小球滤过功能下降时可导致上述肾功能指标水平迅速升高^[20-22]。血栓弹力图是评价凝血状态和功能的手段,主要包括 R 值、K 值、 α 角及 MA 值等参数^[23]。此外,本研究中所涉及两种术式虽为微创术式,但仍属于有创术式,将导致机体产生不同程度的氧化应激^[24]。其中 SOD 是一种重要的抗氧化酶,机体损伤程度越大,SOD 消耗越严重;MDA 是脂质过氧化的最终产物,可反映机体脂膜过氧化的程度^[25,26]。本次研究结果中,两种手术方式均可对患者肾功能、凝血功能、氧化应激程度产生一定损伤,但输尿管软镜取石术的各方面损伤程度均更轻。分析其原因,经皮肾镜取石术为有创操作,可引起不同程度的氧化应激反应,同时在手术过程中需冲水灌注方可获得清晰视野,而当灌注压大于肾盂生理压力时可引起肾盂液体返流,导致肾间质水肿,随后可出现静水压升高现象,静水压超过肾小动脉压力时可引起机体血流停滞,造成凝血功能障碍,进一步发展引起肾实质缺血缺氧性病变,影响患者肾功能^[27,28]。而输尿管软镜取石术可避免肾穿刺这一步骤,减少手术对肾脏及其周围组织的损伤。此外,本研究结果中结石清除率、并发症发生率比较无差异,可见两种术式均可获得相当的治疗效果,且安全性较好。同时 B 组手术时间、住院时间短于 A 组,术中出血量少于 A 组,这主要是因为经皮肾镜碎取石术中需建立经皮扩张通道,加之术中肾镜方向调转时会加重肾黏膜撕裂,可对肾实质造成一定损害,延长术后恢复期^[29],而输尿管软镜取石术经人体自然腔道进入肾盂,对人体损伤程度轻,术后恢复快^[30]。

综上所述,与经皮肾镜取石术相比,输尿管软镜取石术可获得相当治疗效果,且其在改善肾功能、凝血功能及氧化应激等方面效果更佳,安全性好,患者恢复更快,临床应用价值较高。

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