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后腹腔镜输尿管切开取石术对上尿路结石患者炎性因子及肾功能的影响*

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摘要 目的:探讨后腹腔镜输尿管切开取石术(RLU)对上尿路结石患者炎性因子及肾功能的影响。**方法:**选取2016年1月~2018年11月期间海南省第三人民医院泌尿外科收治的上尿路结石患者89例为研究对象,根据手术方式的不同将患者分为RLU组($n=44$)和经输尿管镜取石术(URL)组($n=45$),比较两组患者手术成功率、结石取净率、炎性因子指标[白介素-6(IL-6)、肿瘤坏死因子- α (TNF- α)、内皮素-1(ET-1)、C反应蛋白(CRP)]、肾功能指标[血尿素氮(BUN)、血肌酐(Scr)、明胶酶相关脂质运载蛋白(NGAL)]及术后并发症。**结果:**RLU组患者手术成功率、结石取净率均高于URL组($P<0.05$)。两组患者术后1d IL-6、TNF- α 、ET-1以及CRP水平均较术前升高,但RLU组低于URL组($P<0.05$)。两组患者术后1d BUN、Scr水平比较差异均无统计学意义($P>0.05$),两组患者术后1d NGAL水平较术前升高,但RLU组低于URL组($P<0.05$)。RLU组术后并发症发生率低于URL组($P<0.05$)。**结论:**RLU对上尿路结石患者的炎症刺激和肾功能影响更小,且可有效提升手术成功率、结石取净率,降低并发症发生率,有利于患者术后恢复。

关键词:后腹腔镜输尿管切开取石术;上尿路结石;炎性因子;肾功能;经输尿管镜取石术

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Effect of Retroperitoneal Laparoscopic Ureterolithotomy on Inflammatory Factors and Renal Function in Patients with Upper Urinary Tract Calculi*

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ABSTRACT Objective: To investigate the effects of retroperitoneal laparoscopic ureterolithotomy (RLU) on inflammatory factors and renal function in patients with upper urinary tract calculi. **Methods:** 89 patients with upper urinary tract stones who were admitted to the urology department of Hainan Third People's Hospital from January 2016 to November 2018 were selected as the research objects. According to the different surgical methods, the patients were divided into RLU group ($n=44$) and transureteroscopic lithotripsy (URL) group ($n=45$). The success rate of operation, stone clearance rate, inflammatory factor index [interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α), endothelin-1 (ET-1), C-reactive protein (CRP)], renal function index [BUN, creatinine (Scr), neutrophil gelatinase-associated lipocalin (NGAL)] and postoperative complications were compared between the two groups. **Results:** The success rate of operation and stone clearance rate in RLU group were higher than those in URL group ($P<0.05$). The levels of IL-6, TNF- α , ET-1 and CRP in the two groups at 1 day after operation were higher than those before operation, but the levels in RLU group were lower than those in URL group ($P<0.05$). There was no significant difference in BUN and Scr between the two groups at 1 day after operation ($P>0.05$). The level of NGAL in the two groups at 1 day after operation was higher than that before operation, but that in the RLU group was lower than that in the URL group ($P<0.05$). The incidence of postoperative complications in RLU group was lower than that in URL group ($P<0.05$). **Conclusion:** RLU has less effect on inflammatory stimulation and renal function in patients with upper urinary tract stones, and can effectively improve the success rate of operation, stone clearance rate, reduce the incidence of complications, and is conducive to the recovery of patients after operation.

Key words: Retroperitoneal laparoscopic ureterolithotomy; Upper urinary tract calculi; Inflammatory factors; Renal function;

Transureteroscopic lithotripsy

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前言

上尿路结石是临床常见的结石类型,常表现为尿痛、排尿

中断等症^[1,2]。临床治疗该病主要有药物治疗、开放手术治疗以及微创手术治疗等方式,由于上尿路结石的治疗关键在于及时清除结石,而药物治疗往往效果有限,对于结石较大者

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往往需行手术治疗^[3,4]。开放手术由于其创伤较大、术后恢复慢、感染风险大等原因,现临床已较少使用,微创手术治疗上尿路结石已成为临床趋势^[5]。后腹腔镜输尿管切开取石术(Retroperitoneal laparoscopic ureterolithotomy, RLU)^[6]以及经输尿管镜取石术(Transureteroscopic lithotripsy, URL)^[7]是临床常用的微创术式,既往研究认为 URL 创伤小、钬激光碎石效果佳,但仍有结石残留率高、结石上移等问题^[8,9],而 RLU 是目前治疗上尿路结石的新方法,其有效性尚需相关研究进行验证。鉴于此,本研究通过探讨 RLU、URL 对上尿路结石患者炎症因子及肾功能的影响,以期临床术式选择提供参考。现整理结果如下。

1 资料与方法

1.1 临床资料

选取 2016 年 1 月~2018 年 11 月期间海南省第三人民医院泌尿外科收治的上尿路结石患者 89 例为研究对象,纳入标准:(1)经 CT、超声静脉肾盂造影等检查确诊;(2)临床症状表现为尿痛尿血、腰痛、尿常规可见红细胞;(3)均具备手术指征;(4)均由同一组医师完成手术操作;(5)患者及其家属知情本次研究并已签署同意书。排除标准:(1)存在泌尿系统感染或恶性肿瘤者;(2)合并糖尿病、高血压等基础疾病者;(3)妊娠及哺乳期妇女;(4)合并心脑肝肾等脏器功能障碍者。根据手术方式的不同将患者分为 RLU 组(n=44)和 URL 组(n=45),其中 RLU 组男 29 例,女 15 例,年龄 34~62 岁,平均(49.28±5.34)岁;发病部位:左侧 25 例,右侧 19 例;结石类型:肾结石 24 例,输尿管结石 20 例;结石直径 1.05~2.53 cm,平均(1.49±0.18)cm。URL 组男 30 例,女 15 例,年龄 33~64 岁,平均(49.37±5.26)岁;发病部位:左侧 23 例,右侧 22 例;结石类型:肾结石 22 例,输尿管结石 23 例;结石直径 1.12~2.48 cm,平均(1.51±0.21)cm。两组患者一般资料比较无差异($P>0.05$),具有可比性。

1.2 方法

URL 组:麻醉方式选用连续硬膜外麻醉,手术体位选取膀胱截石位,先采用液压灌注泵对输尿管进行扩张,缓慢置入斑马导丝,随后置入输尿管镜直至输尿管结石下方,缓慢置入功率为 14.4W 钬激光光纤,将结石击碎,用异物钳取出较大的碎石块,术后常规留置双 J 管,并定期进行检查,术后 1 个月取出双 J 管。

RLU 组:麻醉方式选用连续硬膜外麻醉,手术体位选取舒适健侧卧位,于腋中线腋窝处作一横向切口(约 2 cm),腹膜钝性分离后,推开向内侧,于腋前线第 12 肋缘下作一切口,缓慢置入 Trocar(0.5 cm 规格),于腋后线肋缘与第 12 肋骨处作一切口,缓慢置入 Trocar(1.0 cm 规格),建立二氧化碳气腹,气压维持 1.35~2.00 kPa,采用超声刀清除腹膜外脂肪,切开肾周筋膜,定位结石所在处,切开取石,采用 4-0 可吸收线对输尿管或肾盂切口行间断缝合,常规留置 F5 或 F6 双 J 管,双 J 管处理同 URL 组。

1.3 观察指标

比较两组手术成功率、结石取净率及手术并发症发生情况。于术前、术后 1d 采集患者清晨空腹静脉血 4 mL,2800 r/min 离心 12 min,离心半径 10 cm,分离血清,置于 -30℃ 冰箱中待测。采用酶联免疫吸附法检测白介素 -6(Interleukin-6, IL-6)、肿瘤坏死因子 - α (Tumor necrosis factor- α , TNF- α)、内皮素 -1(Endothelin-1, ET-1)、C 反应蛋白(C-reactive protein, CRP)、明胶酶相关脂质运载蛋白(Neutrophil gelatinase-associated lipocalin, NGAL),试剂盒由武汉华美生物科技有限公司提供。采用 OLYMPUS AU2700 自动生化仪检测尿素氮(Blood urea nitrogen, BUN)、血肌酐(Serum creatinine, Scr)水平。

1.4 统计学方法

通过 SPSS21.0 软件处理统计数据,计数资料用率表示,行 χ^2 检验,计量资料用($\bar{x}\pm s$)表示,行 t 检验, $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组患者手术成功率、结石取净率比较

RLU 组患者手术成功率为 100.00%(44/44),高于 URL 组的 91.11%(41/45),组间比较差异有统计学意义($\chi^2=4.102$, $P=0.043$);RLU 组患者结石取净率为 100.00%(44/44),高于 URL 组的 86.67%(39/45),组间比较差异有统计学意义($\chi^2=6.298$, $P=0.012$)。

2.2 两组患者手术前后炎症因子水平比较

两组患者术前 IL-6、TNF- α 、ET-1 以及 CRP 水平比较无差异($P>0.05$),两组患者术后 1d IL-6、TNF- α 、ET-1 以及 CRP 水平均较术前升高,但 RLU 组低于 URL 组($P<0.05$),详见表 1。

表 1 两组患者手术前后炎症因子水平比较($\bar{x}\pm s$)

Table 1 Comparison of inflammatory factors before and after operation in two groups($\bar{x}\pm s$)

Groups	IL-6(pg/ml)		TNF- α (ng/mL)		ET-1(ng/L)		CRP(mg/L)	
	Before operation	1d after operation	Before operation	1d after operation	Before operation	1d after operation	Before operation	1d after operation
URL group (n=45)	7.41±1.26	12.86±2.36*	1.36±0.35	3.25±0.89*	57.59±6.21	73.25±5.74*	15.94±3.19	22.94±2.89*
RLU group (n=44)	7.32±1.13	8.31±2.57*	1.39±0.41	2.23±0.78*	57.68±6.10	63.47±5.46*	16.03±4.01	18.41±3.73*
t	0.355	8.703	0.372	5.745	0.069	8.232	0.117	6.413
P	0.724	0.000	0.711	0.000	0.945	0.000	0.907	0.000

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

2.3 两组患者手术前后肾功能指标比较

两组患者术前 BUN、Scr、NGAL 水平比较无差异 ($P>0.05$), 两组患者术后 1d BUN、Scr 水平比较差异均无统计学意义

($P>0.05$), 两组患者术后 1d NGAL 水平较术前升高, 但 RLU 组低于 URL 组 ($P<0.05$), 详见表 2。

表 2 两组患者手术前后肾功能指标比较 ($\bar{x} \pm s$)

Table 2 Comparison of renal function before and after operation between two groups ($\bar{x} \pm s$)

Groups	BUN (mmol/L)		Scr (μ mol/L)		NGAL (μ g/L)	
	Before operation	1d after operation	Before operation	1d after operation	Before operation	1d after operation
URL group (n=45)	6.72 $\pm$ 1.44	6.74 $\pm$ 1.17	79.75 $\pm$ 5.68	79.86 $\pm$ 6.17	3.24 $\pm$ 0.90	5.24 $\pm$ 0.85*
RLU group (n=44)	6.76 $\pm$ 1.52	6.78 $\pm$ 1.08	79.71 $\pm$ 6.17	79.82 $\pm$ 7.34	3.28 $\pm$ 0.84	4.55 $\pm$ 0.71*
t	0.127	0.167	0.032	0.028	0.217	4.152
P	0.899	0.867	0.975	0.978	0.829	0.000

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

2.4 两组患者术后并发症发生情况

URL 组术后发生肾绞痛 2 例, 高热 3 例、输尿管撕脱 2 例、穿孔 2 例、漏尿 1 例, 并发症发生率为 22.22% (10/45); RLU 组术后发生肾绞痛 1 例, 高热 1 例、漏尿 1 例, 并发症发生率为 6.82% (3/44); RLU 组术后并发症发生率低于 URL 组 ($\chi^2=4.232$, $P=0.040$)。

3 讨论

上尿路结石是常见的多发性泌尿外科疾病, 其发病机制目前尚不十分明确, 多数研究认为该病的发生主要与结石上段长期积水、结石与输尿管反复摩擦、炎性因子大量分泌有关, 故而临床针对上尿路结石的治疗关键在于消除梗阻、清理结石、保护肾功能、减少机体炎性反应等^[10-12]。通常而言, 较大的结石难以自行排出进而形成输尿管梗阻, 长期的梗阻导致患者腰腹部疼痛、血尿、尿路感染等, 严重者引起肾萎缩、肾衰竭等并发症, 因此一旦确诊需尽快进行治疗^[13-15]。然而由于结石梗阻的位置、严重程度不同, 致使患者手术方式的选择亦不尽相同。随着临床微创技术的发展, URL 及 RLU 等微创术式已逐渐广泛应用于临床, URL 可利用人体自然腔道开展手术, 而 RLU 经腹膜后入路, 可有效降低其对腹腔脏器的损害, 且只需进行一次手术即可将结石完整取出^[16-18]。现临床采用微创手术治疗已成为共识, 但采用何种手术进行治疗尚存在一定争议, 本文就此展开探讨。

本次研究结果表明, RLU 组患者手术成功率、结石取净率均高于 URL 组, 可见 RLU 具有手术成功率高、结石取净率高等优势, RLU 经后腹途径取石, 不仅可减少腹腔内其他脏器的损害, 同时通过气囊分离器还可使腹膜后结构更加清晰, 给手术操作带来便利, 加之其相关的解剖步骤为泌尿外科医师所熟悉, 可取出完整结石, 提高手术成功率^[19-21]。本次研究结果还表明两组患者术后 1d IL-6、TNF- α 、ET-1 以及 CRP 水平均较术前升高, 但 RLU 组低于 URL 组, 提示 RLU 可有效减轻上尿路结石患者机体炎性反应, 既往研究表明^[22], 手术创伤引起的组织损伤, 主要表现为炎性因子如 IL-6、TNF- α 、ET-1 以及 CRP 等水平的升高, 且其升幅与患者预后呈负相关, 同时上述炎性因子水平升高可损伤血管内皮功能, 激活血小板功能, 引发机体高凝状态影响微循环^[23-24]。这可能是由于 RLU 具有诊疗结合

的优势, 从背侧进镜, 直视下进镜可避免盲目进镜引起腹腔脏器的暴露及损伤, 降低术后粘连并发症发生风险^[25-27]。同时, 两组患者术后 1d BUN、Scr 水平组间组内比较差异均无统计学意义, 而两组患者术后 1d NGAL 水平较术前升高, 但 RLU 组低于 URL 组。BUN、Scr 是临床常用于反应机体肾脏功能的生物学指标, 而 NGAL 正常生理状态下在肾脏、肝脏以及胃等组织中存在低表达, 当发生炎性或上皮细胞损伤时, 其水平逐渐上升。研究结果可见 RLU 对上尿路结石患者肾功能影响更轻, 大量炎性因子刺激中性粒细胞致其释放 NGAL, 导致其水平迅速升高, 而当早期肾灌注量减少或发生肾缺血再灌注损伤时, NGAL 表达迅速升高, 而 BUN、Scr 由于受多种因素的影响, 其变化往往滞后, 早期不明显^[28,29]。既往相关研究显示^[30], Scr 在肾功能下降 50% 以后其水平才会出现明显改变。另外, RLU 组术后并发症发生率低于 URL 组, 提示 RLU 可有效减少术后并发症发生率。这可能是上尿路结石由于长时间梗阻, 输尿管上段扩张迂曲, URL 术中易造成输尿管撕脱、穿孔等严重并发症, 加之输尿管结石部位接近肾盂, 术中冲洗碎石极易进入肾盂, 致使中途需改用其他手术进行治疗, 增加并发症发生概率。

综上所述, RLU 可有效提高上尿路结石患者的手术成功率、结石取净率, 降低并发症发生率, 并且术后炎症反应较轻, 对患者肾功能影响更小。

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