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肾脏部分切除手术对 T_{1a} 期肾癌患者炎症因子与肝肾功能的影响 *

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摘要 目的:探讨肾脏部分切除手术对 T_{1a} 期肾癌患者炎症因子与肝肾功能的影响。**方法:**回顾性分析我院 2013 年 6 月至 2016 年 12 月收治的 91 例 T_{1a} 期肾癌患者的临床资料,按治疗方式不同分为对照组与试验组,对照组 48 例接受后腹腔镜根治性肾癌切除术治疗,试验组 43 例接受后腹腔镜肾脏部分切除手术治疗。比较两组的手术指标、治疗前后血清炎症因子、肝肾功能的变化及并发症发生情况。**结果:**对照组的手术时间、术中出血量均少于试验组($P<0.05$)。治疗后,试验组血清 IL-1 变化值低于对照组 $[-19.47\pm 2.57]\mu\text{g/L}$ 比 $[-41.61\pm 6.38]\mu\text{g/L}$ 、IL-6 变化值低于对照组 $[-8.71\pm 1.05]\text{ng/L}$ 比 $[-18.96\pm 3.10]\text{ng/L}$ 、CRP 变化值低于对照组 $[-12.72\pm 1.54]\text{mg/L}$ 比 $[-17.46\pm 2.64]\text{mg/L}$ 、TNF- α 变化值低于对照组 $[-5.66\pm 0.15]\text{ng/L}$ 比 $[-14.33\pm 2.04]\text{ng/L}$ 、BUN 变化值低于对照组 $[-1.53\pm 0.19]\text{mmol/L}$ 比 $[-3.01\pm 0.79]\text{mmol/L}$ 、AST 变化值低于对照组 $[-15.29\pm 2.46]\text{U/L}$ 比 $[-33.70\pm 3.78]\text{U/L}$ 、ALT 变化值低于对照组 $[-19.46\pm 2.27]\text{U/L}$ 比 $[-34.02\pm 5.51]\text{U/L}$, 试验组 Ccr 变化值低于对照组 $[(19.78\pm 2.94)\text{mL/min}$ 比 $(28.26\pm 3.52)\text{mL/min}$]、GFR 变化值低于对照组 $[(14.45\pm 1.48)\text{mL/min}$ 比 $(29.36\pm 1.91)\text{mL/min}$]、除 CRP 和 GFR 外,其余指标差异均有统计学意义($P<0.05$)。对照组和试验组并发症发生率分别为 16.67%(8/48)和 9.30%(4/43),两组比较差异无统计学意义($P>0.05$)。**结论:**后腹腔镜肾脏部分切除手术治疗 T_{1a} 期肾癌患者的临床效果优于后腹腔镜根治性肾癌切除术治疗,其对患者炎症因子及肝肾功能的影响较小,安全性更高。

关键词:肾癌;肾脏部分切除术;炎症因子;肝功能;肾功能

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Effects of Partial Nephrectomy on the Serum Inflammatory Factors Levels, Liver and Kidney Function of T_{1a} Patients with Kidney Cancer*

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ABSTRACT Objective: To investigate the effects of the partial nephrectomy on inflammatory factors, liver and kidney function in patients with kidney cancer at T_{1a} stage. **Methods:** Retrospective analysis of 91 cases of patients with kidney cancer at T_{1a} stage from June 2013 to December 2016. According to the different treatments, patients were divided into control group and experimental group. 48 cases of patients selected as control group, were treated with posterior laparoscopic radical nephrectomy therapy; 43 cases of patients set as treatment group, which were treated with posterior laparoscopic partial nephrectomy. The changes of serum inflammatory factors before and after treatment, liver and kidney function and complications in the both group were compared. **Results:** The operation time and intra-operative blood of control group were lower than the experimental group, the difference was statistically significant ($P<0.05$). The levels of serum IL-1 $[-19.47\pm 2.57]\mu\text{g/L}$ vs $[-41.61\pm 6.38]\mu\text{g/L}$, IL-6 $[-8.71\pm 1.05]\text{ng/L}$ vs $[-18.96\pm 3.10]\text{ng/L}$, CRP $[-12.72\pm 1.54]\text{mg/L}$ vs $[-17.46\pm 2.64]\text{mg/L}$, TNF- α $[-5.66\pm 0.15]\text{ng/L}$ vs $[-14.33\pm 2.04]\text{ng/L}$, BUN $[-1.53\pm 0.19]\text{mmol/L}$ vs $[-3.01\pm 0.79]\text{mmol/L}$, AST $[-15.29\pm 2.46]\text{U/L}$ vs $[-33.70\pm 3.78]\text{U/L}$, ALT $[-19.46\pm 2.27]\text{U/L}$ vs $[-34.02\pm 5.51]\text{U/L}$, Ccr $[(19.78\pm 2.94)\text{mL/min}$ vs $(28.26\pm 3.52)\text{mL/min}$, and GFR $[(14.45\pm 1.48)\text{mL/min}$ vs $(29.36\pm 1.91)\text{mL/min}$, were all lower in treatment group than in control group. Except for CRP and GFR, the differences of all the items between the two groups were statistically significant ($P<0.05$). Complication rate of the control group and the experimental group was 16.67%(8/48) and 9.30% (4/43), there was no significantly differences in both group ($P>0.05$). **Conclusions:** The clinical effect of partial nephrectomy with retroperitoneoscope in treating T_{1a} stage renal cancer is better than that of radical nephrectomy with retroperitoneoscope, it has little effect on the inflammatory factors and liver and kidney function, more secure.

Key words: Kidney cancer; Partial nephrectomy; Inflammatory factors; Liver function; Kidney function

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前言

肾癌为肾脏常见恶性肿瘤,起源于泌尿小管上皮,多发于中老年男性人群,遗传、饮食、酗酒、吸烟等是其常见诱因,多数患者早期临床表现不明显,待出现肿块、疼痛、血尿肾癌三联症时多已进展至晚期,导致临床预后不佳^[1,2]。根治性肾切除术是既往治疗肾癌的最有效的方式,但相关研究^[3,4]显示其可导致明显的全身和局部损害效应,诱导过度的炎症反应,影响肝肾功能,引起内环境紊乱。

近年来,随着 CT、MRI、超声等影像学技术的不断进步,临床对于肾癌的治疗方式已发生改变^[5,6]。最初肾脏部分切除术仅开展于双肾肾癌、孤立肾肾癌等疾病,但国内外泌尿外科最新指南显示 T_{1a} 期肾癌患者行肾部分切除术治疗几乎可达到与传统根治性切除术的效果,且可彻底清除癌症病灶,对患者存活及远期复发无影响,可尽可能的保留功能性肾单位,减少或者避免血液透析^[7,8]。但肾脏部分切除手术是否具有减轻创伤、安全等优势目前并不明确。因此,本研究主要探讨了肾脏部分切除手术对 T_{1a} 期肾癌患者炎症因子与肝肾功能的影响。

1 资料与方法

1.1 一般资料

选择我院 2013 年 6 月至 2016 年 12 月收治的 91 例 T_{1a} 期肾癌患者,入选标准:符合肾癌 T_{1a} 期相关诊断标准^[9](临床经超声、CT、病理检查等确诊为肾癌,仅局限于肾包膜内,未见远处转移);手术指征明确;心、肝肺等重要器官无病变;均为右侧发病。排除凝血功能异常;肾畸形、孤立肾;腹腔手术史者。对照组中,26 例男,22 例女;年龄 45~69 岁,平均(62.88±6.86)岁;肿瘤直径 2~4 cm,平均(3.20±0.41)cm。试验组中,20 例男,23 例女;年龄 46~68 岁,平均(60.12±7.93)岁;肿瘤直径 2~4 cm,平均(3.15±0.46)cm。两组的临床基线资料比较差异无统计学意义(P>0.05),具有可比性。

1.2 治疗方法

对照组接受后腹腔镜根治性肾癌切除术治疗,常规实施气管插管麻醉,指导患者为健侧卧位,于 12 肋下腋后线 2~3 cm 处选择纵形状切口为第 1 个操作孔。将腰背筋膜进行钝性分离,并向自制球囊扩张器注入 500~800 mL 生理盐水,扩张后腹膜腔隙,排水后将气囊取出,经穿刺孔置入 10 mm Trocar 将腹

腔镜置入,并创建气腹。在腋中线髂棘上缘、腋前线肋缘下缘 1.0 cm、1.5 cm 取皮肤切口,分别置入 10 mm、5 mm Trocar。先分离肾周筋膜背侧,下至髂血管水平,上至膈肌,钝性游离肾脏后方至肾门,游离肾动脉后夹闭,用 Hem-O-lock 分别夹闭肾动、静脉并离断,处理肾上、下极,将输尿管分离至低位并夹闭离断,将肾脏连同肾周脂肪、肾筋膜等切除,放置引流管,逐层缝合切口。

试验组接受后腹腔镜肾脏部分切除手术治疗,麻醉及位置同对照组,于 12 肋下腋后线 2~3 cm 处选择纵形状切口,将腰背筋膜及肌层进行钝性分离。并向自制球囊扩张器注入 500~800 mL 生理盐水,扩张后腹膜腔隙,排水后将气囊取出。在腋中线髂棘上缘、腋前线肋缘下缘 1.0 cm、0.5 cm 取皮肤切口,并置入 10 mm、5 mm Trocar,于 12 肋下腋后线取切口,并放置 10 mm Trocar。于后腹腔间隙注入 CO₂,保持压力为 13~15 mmHg,套管内放置腹腔镜,并于操作孔内放置器械。将肾周脂肪游离,使术野完全显露,于腰大肌表层将肾动脉游离,阻断肾动脉。将瘤体边缘外 1.0 cm 左右取超声刀分离,切割并止血。肿瘤完全切除,伴集合系统受损者取可吸收线进行修补缝合,肾脏创面取止血纱布进行填压,并用倒齿线间断缝合。松开血管夹,使肾血供恢复,未见活动性出血后,取出标本,于肾周置入引流管,将切口关闭。

1.3 观察指标

于术前及术后 24 h 抽取患者 2 mL 空腹静脉血,将其进行常规处理,并于低温环境中保存待检。选用酶联免疫法进行白细胞介素 -1、6(IL-1、IL-6)、C 反应蛋白(CRP)、肿瘤坏死因子 -α(TNF-α)、谷草转氨酶(AST)和谷丙转氨酶(ALT)、血尿素氮(BUN)测定。计算内生肌酐清除率(Ccr)、肾小球滤过率(GFR)。

1.4 统计学方法

选用 SPSS 18.0 进行本研究的数据处理,计量资料以($\bar{x} \pm s$)表示,组间比较选用 t 检验进行,用[(例)%]表示计数资料,组间比较用 χ^2 检验,以 P<0.05 为差异有统计学意义。

2 结果

2.1 两组手术指标的比较

对照组的手术时间、术中出血量均少于试验组,两组比较差异有统计学意义(P<0.05),见表 1。

表 1 两组手术指标的比较($\bar{x} \pm s$)

Table 1 Comparison the surgical index between two groups($\bar{x} \pm s$)

Groups	Operation time/min	Intraoperative blood loss/mL
Control group(n=48)	135.71± 15.23	113.21± 13.40
Test group(n=43)	159.60± 19.01	131.79± 16.79
P	0.000	0.000

2.2 两组治疗前后血清炎症因子水平的比较

治疗前,两组血清 IL-1、IL-6、TNF-α 和 CRP 水平比较差异无统计学意义(P>0.05);治疗后,两组血清 IL-1、IL-6、TNF-α 水平均较治疗前明显上升(P<0.05),且试验组以上指标水平均明显低于对照组,差异有统计学意义(P<0.05),两组治疗后血清

CRP 水平比较差异无统计学意义(P>0.05),见表 2。

2.3 两组治疗前后肝功能的比较

治疗前,两组肝功能指标比较差异无统计学意义(P>0.05);治疗后,两组 AST、ALT 均较治疗前明显上升(P<0.05),而试验组治疗前后 AST、ALT 水平的变化显著低于对照组,差异有统

计学意义($P<0.05$),见表 3。

表 2 两组治疗前后血清炎性因子水平的比较($\bar{x} \pm s$)

Table 2 Comparison of the serum inflammatory factors before treatment and after treatment between two groups($\bar{x} \pm s$)

Groups	IL-1/($\mu\text{g/L}$)			IL-6/(ng/L)		
	Before treatment	After treatment	Before and after treatment Average	Before treatment	After treatment	Before and after treatment Average
Control group(n=48)	27.80 $\pm$ 4.12	69.41 $\pm$ 10.50	48.61 $\pm$ 23.88	1.75 $\pm$ 0.25	20.71 $\pm$ 3.35	11.23 $\pm$ 10.60
Test group(n=43)	29.15 $\pm$ 3.51	48.62 $\pm$ 6.08	38.89 $\pm$ 11.55	1.83 $\pm$ 0.22	10.54 $\pm$ 1.27	6.19 $\pm$ 4.84
P	0.098	0.000	0.017	0.111	0.000	0.005

Continue table

Groups	CRP/(mg/L)			TNF- α /(ng/L)		
	Before treatment	After treatment	Before and after treatment Average	Before treatment	After treatment	Before and after treatment Average
Control group(n=48)	2.70 $\pm$ 0.27	20.16 $\pm$ 2.91	11.43 $\pm$ 9.75	21.39 $\pm$ 2.16	35.72 $\pm$ 4.20	28.56 $\pm$ 8.40
Test group(n=43)	2.59 $\pm$ 0.33	15.31 $\pm$ 1.87	8.95 $\pm$ 7.07	20.88 $\pm$ 3.12	26.54 $\pm$ 3.27	23.71 $\pm$ 4.24
P	0.084	0.000	0.173	0.363	0.000	0.0010

表3 两组治疗前后肝功能的比较($\bar{x} \pm s$, U/L)

Table 3 Comparison of the liver function before treatment and after treatment between two groups ($\bar{x} \pm s$, U/L)

Groups	AST			ALT		
	Before treatment	After treatment	Before and after treatment Average	Before treatment	After treatment	Before and after treatment Average
Control group(n=48)	21.70 $\pm$ 2.92	55.40 $\pm$ 6.70	38.55 $\pm$ 19.028	20.19 $\pm$ 2.11	54.21 $\pm$ 7.62	37.20 $\pm$ 19.29
Test group(n=43)	22.13 $\pm$ 2.19	37.42 $\pm$ 4.65	29.78 $\pm$ 8.98	19.75 $\pm$ 2.60	39.21 $\pm$ 4.87	29.48 $\pm$ 11.22
P	0.433	0.000	0.0070	0.376	0.000	0.024

2.4 两组治疗前后肾功能的比较

治疗前,两组肾功能比较差异无统计学意义($P>0.05$);治疗后,两组 Ccr、GFR 均较治疗前显著降低,两组 BUN 均较治疗

前显著下降($P<0.05$),试验组治疗后差值低于对照组,差异有统计学意义($P<0.05$),见表 4。

表 4 两组治疗前后肾功能的比较($\bar{x} \pm s$)

Table 4 Comparison of the renal function before treatment and after treatment between two groups ($\bar{x} \pm s$, U/L)

Groups	Ccr/(mL/min)			BUN/(mmol/L)			GFR/(mL/min)		
	Before treatment	After treatment	Before and after treatment Average	Before treatment	After treatment	Before and after treatment Average	Before treatment	After treatment	Before and after treatment Average
Control group (n=48)	74.20 $\pm$ 8.12	45.94 $\pm$ 4.60	45.94 $\pm$ 4.60	60.07 $\pm$ 16.56	9.87 $\pm$ 1.52	34.97 $\pm$ 27.82	80.52 $\pm$ 8.31	51.16 $\pm$ 6.40	65.84 $\pm$ 17.40
Test group (n=43)	72.86 $\pm$ 9.56	53.08 $\pm$ 6.62	62.97 $\pm$ 13.09	6.79 $\pm$ 0.81	8.32 $\pm$ 1.02	7.55 $\pm$ 1.18	78.65 $\pm$ 9.54	64.20 $\pm$ 8.06	71.43 $\pm$ 11.18
P	0.472	0.000	0.000	0.666	0.000	0.000	0.320	0.000	0.0753

2.5 两组术后并发症发生情况的比较

两组术后均有出血、感染、气胸发生,对照组和试验组并发症发生率分别为 16.67%(8/48)和 9.30%(4/43),组间比较差异无统计学意义($P>0.05$)。

随着健康体检的普及及影像学技术的不断进步, T_{1a} 期小肾癌的检出率呈上升趋势,其多局限于肾脏内部,且肿瘤最大径在 4 cm 以下,属恶性肿瘤,未经及时治疗者可明显危及患者生命安全^[10,11]。手术是 T_{1a} 期肾癌的首选治疗手段,其中根治性肾切除术能够将肿瘤病灶彻底清除,并尽可能的避免远处转移

3 讨论

和局部复发,但其创伤相对较大^[12,13]。随着对肾癌生长特点及特征研究的不断深入,保留肾单位手术现已开展于临床,其操作简单,可不破坏肾血流,并尽可能的保护肾组织,但因肿瘤可能导致肿瘤残留,因此需慎重选择^[14]。肾脏部分切除手术是常用的保留肾单位术式,能够利于患侧肾功能的保存,降低肾衰发生率。有研究饱满采用肾脏部分切除术治疗 T_{1a} 期肾癌未增加患者的复发率,远期预后和根治性肾切除术相当^[15,16]。

既往肾癌手术多选用开放性方式,但其切口较大,易引起多种并发症,影响患者术后恢复。近年来,腹腔镜手术已广泛应用于临床,根据入路方式可分为经腹腔及后腹腔镜,目前国内医院多选择后者^[17,18]。经腹膜腔入路术中腹腔的操作空间相对较大,有着较强的立体感,易于解剖标识的识别,且利于肾蒂阻断期间的低温保存及肾脏前外侧及腹侧肿瘤的处理,但手术期间容易对腹腔脏器形成干扰,影响相关脏器的功能,且不适用于伴腹部外伤及手术史者^[19,20]。腹膜后入路的空间较为狭窄,无明显的解剖标识,且对技术的可控性高,但其对腹腔镜内相关脏器的干扰较少,易于组织显露,且可于短时间内控制出血,避免尿液或者血液对腹腔形成污染,降低肿瘤播散、腹腔粘连及胃肠反应的可能性^[21,22]。临床研究报道^[23]后腹腔镜肾脏部分切除手术可能会增加手术时间,本研究结果也显示肾脏部分切除术手术时间及出血量均多于根治性肾切除术组。

手术创伤、疼痛等因素可刺激机体的中枢神经系统,从而释放系列炎性因子,激活机体的防御反应。IL-1 主要由巨噬细胞与单核细胞分泌,能够调节机体的细胞免疫,参与炎症、内分泌系统、造血系统等反应,并可促进其他炎症因子的释放^[24,25]。IL-6 可刺激 B 细胞生成抗体,引起 T 细胞出现活化、增殖,从而调节机体的免疫应答,且可刺激炎性因子的释放,导致全身炎症反应,是机体组织损伤及炎症反应程度的特异性指标^[26]。CRP 能够起到调节炎症反应、免疫反应等系列生物学作用,其作为一种急性时相蛋白,机体正常状态下含量极低,创伤、炎症等可诱导其浓度增加^[27]。TNF- α 作为一种单核因子,主要经巨噬细胞与单核细胞合成并分泌,是造成创伤炎症反应与免疫受损的关键因子^[28]。本研究结果显示两组术后血清 IL-1、IL-6、CRP 及 TNF- α 水平均较术前上升,证实手术能够引起炎症因子的表达上调,但肾脏部分切除手术组上升幅度较小,说明其对组织的创伤程度较轻,能够避免机体应激反应的加剧,可能与其能够保留肾单位,因此对机体形成的创伤较小有关。

肾癌手术时,电刀热辐射能够破坏肝细胞^[29],麻醉药物、手术操作可影响肝脏血流,导致肝脏发生急性损伤,引起 AST 及 ALT 浓度增加。本研究显示两组术后 AST 及 ALT 水平均有上升,但肾脏部分切除手术组上升幅度更小,说明其能减轻肝功能受损,考虑与其术后炎性因子的变化较小,从而减轻对肝脏的刺激有关。同时,两组术后 Ccr、GFR 均降低,BUN 明显上升,但肾脏部分切除手术组变化幅度更小,提示其对肾功能的影响较为轻微,能够利于肾功能的保护^[17,18]。

综上所述,后腹腔镜肾脏部分切除手术治疗 T_{1a} 期肾癌患者的临床效果优于后腹腔镜根治性肾癌切除术治疗,其对患者炎性因子及肝肾功能的影响较小,安全性更高。

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