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后腹腔镜根治术对肾癌患者免疫功能的影响 *

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摘要 目的：探讨后腹腔镜肾癌根治术对患者免疫功能的影响。**方法：**选择 2013 年 5 月 -2015 年 5 月在我院接受手术治疗的肾癌患者 67 例，根据手术方法不同分为研究组（37 例）及对照组（30 例）。研究组患者采用后腹腔镜肾癌根治术治疗，对照组患者采用传统开放手术治疗。观察并比较两组患者的手术时间、术中出血量、住院时间以及手术前后患者外周血 T 淋巴细胞亚群的变化情况。**结果：**研究组患者的手术时间、术中出血量及住院时间均少于对照组，差异具有统计学意义（P＜0.05）。两组患者术前外周血 T 淋巴细胞 $CD3^+$、$CD4^+$、$CD8^+$ 及 $CD4^+/CD8^+$ 比较，差异无统计学意义（P>0.05）；两组患者术后外周血 T 淋巴细胞 $CD3^+$、$CD4^+$ 及 $CD4^+/CD8^+$ 明显降低，但研究组高于对照组，差异具有统计学意义（P<0.05）；两组患者术后 $CD8^+$ 比较，差异无统计学意义（P>0.05）。**结论：**与传统开放手术相比较，后腹腔镜肾癌根治术对患者免疫功能的影响较小，手术时间短，术中出血量少，临床疗效显著，值得推广及应用。

关键词：肾癌；后腹腔镜根治术；传统开放手术；免疫功能

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Effect of Retroperitoneal Laparoscopic Radical Nephrectomy on Immune Functions of Patients with Renal Cell Carcinoma*

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ABSTRACT Objective: To investigate the effect of retroperitoneal laparoscopic radical nephrectomy on the immune function of patients with renal cell carcinoma. **Methods:** 67 cases with renal carcinoma who were treated in our hospital from May 2013 to May 2015 were selected and according to the different operation methods, the patients were divided into the study group (37 cases) and the control group (30 cases). The patients in the study group were treated with retroperitoneal laparoscopic radical nephrectomy, and the patients in the control group were treated with conventional open surgery. Then the duration of the operation, the amount of blood loss, the hospitalization and the changes of T lymphocyte subsets in the peripheral blood of patients were observed and compared between the two groups before and after operation. **Results:** The duration of the operation, the amount of blood loss and hospitalization of patients in the study group were less than those of the control group, and the differences were statistically significant (P<0.05); There was no statistically significant difference about the levels of $CD3^+$, $CD4^+$, $CD8^+$ and $CD4^+/CD8^+$ in the peripheral blood of patients between the two groups before surgery (P>0.05); The levels of $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ in the peripheral blood of patients in the two groups decreased after the operation, while the study group was higher than that of the control group, and the differences were statistically significant (P<0.05); There was no statistically significant difference about $CD8^+$ in the peripheral blood of patients between the two groups after the operation (P>0.05). **Conclusion:** Compared with the conventional open surgery, the retroperitoneal laparoscopic radical nephrectomy has less influence on the immune functions of patients with renal cell carcinoma, with shorter operation time, less blood loss, and better clinical curative effect, which is worthy of clinical application.

Key words: Renal cell carcinoma; Retroperitoneal laparoscopic radical nephrectomy; Conventional open surgery; Immune function

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前言

肾癌（Kidney cancer）是一种源于肾近曲小管、对放疗和化疗均不敏感的恶性肿瘤，其发生及发展与吸烟、遗传、高血压、肥胖等因素有关[1,2]。近年来我国肾癌发病率逐渐升高，严重影响患者的身心健康[3]。传统开放手术因创伤性较大且术后恢复时间长具有一定的局限性，不利于患者预后[4]。近年来研究表明，后腹腔镜技术是从传统开放手术发展而来，更为安全有效[5]。

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相关研究证实,恶性肿瘤患者多存在机体免疫功能的改变[6]。因此，本研究通过观察患者外周血 T 淋巴细胞亚群的变化情况，探讨后腹腔镜肾癌根治术对患者机体免疫功能的影响,现将结果报告如下。

1 资料与方法

1.1 临床资料

选择 2013 年 5 月 -2015 年 5 月在我院接受手术治疗的肾癌患者 67 例，所有患者临床分期为 $T_1N_0M_0$～$T_2N_0M_0$，经腹部 CT 和术后病理检查确诊。根据手术方法不同将所选研究对象分为研究组(37 例)和对照组(30 例)。两组患者资料比较,差异无统计学意义(P＞0.05),具有可比性。其中,研究组包括男 23 例、女 14 例;年龄 31～71 岁,平均年龄(49.51± 2.42)岁;肿瘤直径 4.5~9.5 cm;病灶位置:左肾 16 例、右肾 21 例;肿瘤分期:$T_1N_0M_0$ 22 例、$T_2N_0M_0$ 15 例。对照组包括男 18 例、女 12 例;年龄 34～70 岁,平均年龄(51.53± 3.05)岁;肿瘤直径 4.2~9.1 cm;病灶位置:左肾 19 例、右肾 11 例;肿瘤分期:$T_1N_0M_0$ 18 例、$T_2N_0M_0$ 12 例。见表 1。

表 1 两组患者的临床资料比较

Table 1 Comparison of clinical data of patients between the two groups

Groups	Gender		Mean age (years)	Tumor size (cm)	Lesions site		Tumor stages	
	Male	Female			Left	Right	$T_1N_0M_0$	$T_2N_0M_0$
Study group (n=37)	23	14	49.51± 2.42	4.5~9.5	16	21	22	15
Control group (n=30)	18	12	51.53± 3.05	4.2~9.1	19	11	18	12

Note: compared between two groups, P>0.05.

1.2 手术方法

患者均采用全身麻醉,体位采用健侧卧位。对照组取腰部第 11 肋间切口,术中沿腰大肌前缘分离至肾动脉后方,游离肾动脉后结扎,然后分离肾脏周围组织并切断输尿管,结扎肾静脉后再分别切断肾动静脉。研究组患者先在腋后线肋缘下切开,止血钳撑开后置入自制气囊,注入 600-800 mL 气体,建立后腹腔,开孔位置设置在腋中线髂嵴上及腋前线肋缘。清除腹膜外脂肪组织后游离并切断输尿管,Hem-o-lok 夹处理肾动脉、肾静脉后完整游离肾脏，肾脏标本放入标本袋，另取下腹部 5～7 cm 斜切口取出。观察两组患者的手术时间、术中出血量及住院时间。

1.3 T 淋巴细胞亚群检测

所有患者于清晨空腹采集外周抗凝血 2 mL，采用 Anti-$CD3^+$-FITC 检测 $CD3^+$、$CD4^+$ 和 $CD8^+$ 水平，$CD4^+$-PE 和 $CD8^+$-APC 试剂盒购自北京生物科技公司，实验操作方法严格按照试剂盒说明书进行。

1.4 统计学方法

采用 SPSS19.0 统计软件进行数据分析,计量资料用($\bar{x}$± s)表示,组间比较采用 t 检验,P＜0.05 为差异有统计学意义。

2 结果

2.1 两组患者的手术情况比较

研究组患者的手术时间为(93.42± 20.24)min、术中出血量为(64.93± 15.36)mL、住院时间为(6.18± 1.06)d;对照组患者的手术时间为(107.66± 28.02)min、术中出血量为(105.54± 24.81)mL、住院时间为(8.09± 1.37)d;研究组患者的手术时间、术中出血量及住院时间均少于对照组，差异具有统计学意义(P＜0.05)。见表 2。

表 2 两组患者的手术情况比较($\bar{x}$± s)

Table 2 Comparison of operation situations of patients in the two groups

Groups	n	Operation time (min)	Blood loss (mL)	Hospitalization (d)
Control group	30	107.66± 28.02	105.54± 24.81	8.09± 1.37
Study group	37	93.42± 20.24*	64.93± 15.36*	6.18± 1.06*

Note: compared with control group, *P<0.05.

2.2 两组患者手术前后外周血 T 淋巴细胞亚群指标的变化情况

两组患者术前外周血 T 淋巴细胞 $CD3^+$、$CD4^+$、$CD8^+$ 及 $CD4^+/CD8^+$ 比较,差异无统计学意义(P>0.05);两组患者术后外周血 T 淋巴细胞 $CD3^+$、$CD4^+$ 及 $CD4^+/CD8^+$ 明显降低，但研究组高于对照组,差异具有统计学意义(P<0.05);两组患者术后 $CD8^+$ 比较,差异无统计学意义(P>0.05)。见表 3。

表 3 两组患者手术前后外周血 T 淋巴细胞亚群比较($\bar{x}$± s)

Table 3 Comparison of T lymphocytes subset in peripheral blood of patients between two groups before and after the operation

Groups	Time	$CD3^+$(%)	$CD4^+$(%)	$CD8^+$(%)	$CD4^+/CD8^+$
Control group (n=30)	Before operation	1130.72± 256.18	812.06± 108.01	408.33± 59.58	1.55± 0.34
	After operation	805.12± 104.16*	599.38± 65.34*	521.64± 62.31	1.39± 0.15*
Study group (n=37)	Before operation	1124.64± 232.13	820.17± 107.32	498.87± 56.94	1.53± 0.37
	After operation	872.37± 115.02*#	631.82± 88.31*#	491.68± 54.26	1.31± 0.32*#

Note: compared with before operation, *P<0.05; compared with control group after operation, #P<0.05.

3 讨论

目前临床普遍采用手术切除的方法治疗肾脏肿瘤,术中将整个肾脏连同包覆其外的筋、输尿管上段、淋巴腺等广泛性的切除[7,8]。传统开放手术过程中为减少对腹腔内器官的影响,一般从患者腰部切口进入,并于腹膜外间隙将肾脏分离切除,但手术时间长、且术中出血量多,对患者机体造成的损伤较大,不利于患者预后[9,10]。近年来研究表明,后腹腔镜肾癌根治术能够在保持传统腰部手术途径优点的基础上,更加直接准确的分离肾脏,因此对患者机体的影响较小[11,12]。相关研究显示,后腹腔镜肾癌根治术能够减少手术时间和术中出血量,有利于患者术后恢复,因此住院时间较短[13]。本研究结果显示,研究组患者的手术时间、术中出血量及住院时间均少于对照组,差异具有统计学意义($P<0.05$)。这与相关研究结果相似[14],说明与传统开放手术相比较,后腹腔镜肾癌根治术对患者机体造成的损伤较小,有利于患者尽快恢复。

T 细胞是由一群功能不同的异质性淋巴细胞组成的,相关研究证实,T 淋巴细胞亚群是观察机体细胞免疫功能的重要指标,机体通过功能各异的 T 淋巴细胞亚群来发挥免疫调控作用[15]。CD3 在成熟的 T 淋巴细胞表面均能表达;$CD4^+$ 是机体发挥免疫功能的重要因子,其能够通过细胞因子介导对肿瘤细胞进行杀伤,因此对机体细胞免疫功能具有正向调节作用[16];而 $CD8^+$ 虽然对靶细胞具有一定的杀伤作用,但却能够抑制机体免疫应答,因此对机体免疫功能具有负向调节作用[17]。有研究显示,当机体免疫功能出现变化时,$CD3^+$、$CD4^+$、$CD8^+$ 等 T 淋巴细胞亚群水平会降低[18]。还有研究表明,肿瘤、创伤、手术均会降低患者的细胞免疫功能,造成 T 淋巴细胞亚群的变化[19]。本研究结果显示,两组患者术前外周血 T 淋巴细胞 CD3+、$CD4^+$、$CD8^+$ 及 $CD4^+/CD8^+$ 比较,差异无统计学意义($P>0.05$);两组患者术后外周血 T 淋巴细胞 $CD3^+$、$CD4^+$ 及 $CD4^+/CD8^+$ 明显降低,但研究组高于对照组,差异具有统计学意义($P<0.05$);两组患者术后 $CD8^+$ 比较,差异无统计学意义($P>0.05$)。这与相关研究结果一致[20],说明与传统开放手术相比,后腹腔镜肾癌根治术对患者机体的免疫功能影响较小,有利于患者术后自身免疫功能调节,从而提高手术根治肿瘤的临床效果。

综上所述,与传统开放手术相比较,后腹腔镜肾癌根治术对患者免疫功能的影响较小,手术时间短,术中出血量少,临床疗效显著,值得推广及应用。

参 考 文 献(References)

[1] Laheurte C, Galaine J, Beziaud L, et al. Immunoprevalence and magnitude of HLA-DP4 versus HLA-DR-restricted spontaneous CD4 (+) Th1 responses against telomerase in cancer patients [J]. Oncoimmunology, 2016, 5(5): e1137416

[2] Huang H, Luo Y, Liang Y, et al. CD4 (+)CD25 (+) T Cells in primary malignant hypertension related kidney injury [J]. Sci Rep, 2016, 9(6): 27659

[3] Zhang CH, Huang Y. Effect of Peripheral Blood $CD4^+$ $CD25^+$ Regulatory T Cell on Postoperative Immunotherapy for Patients with Renal Carcinoma[J]. Asian Pac J Cancer Prev, 2016, 17(4): 2027-2030

[4] Lyons JD, Mittal R, Fay KT, et al. Murine Lung Cancer Increases $CD4^+$T Cell Apoptosis and Decreases Gut Proliferative Capacity in Sepsis[J]. PLoS One, 2016, 11(3): e0149069

[5] Guinan EC, Cole GA, Wylie WH, et al. Ex Vivo Costimulatory Blockade to Generate Regulatory T Cells From Patients Awaiting Kidney Transplantation[J]. Am J Transplant, 2016, 16(7): 2187-2195

[6] Luque Y, Jamme M, Rabant M, et al. Long-term CD4 lymphopenia is associated with accelerated decline of kidney allograft function [J]. Nephrol Dial Transplant, 2016, 31(3): 487-495

[7] Kim H, Lee H, Lee G, et al. Phospholipase A2 inhibits cisplatin-induced acute kidney injury by modulating regulatory T cells by the CD206 mannose receptor[J]. Kidney Int, 2015, 88(3): 550-559

[8] Devaud C, Westwood JA, Teng MW, et al. Differential potency of regulatory T cell-mediated immunosuppression in kidney tumors compared to subcutaneous tumors [J]. Oncoimmunology. 2014, 3 (11): e963395

[9] Zhang Q, Jia Q, Deng T, et al. Heterogeneous expansion of CD4+ tumor-infiltrating T-lymphocytes in clear cell renal cell carcinomas[J]. Biochem Biophys Res Commun, 2015, 458(1): 70-76

[10] Asma G, Amal G, Raja M, et al. Comparison of circulating and intratumoral regulatory T cells in patients with renal cell carcinoma [J]. Tumour Biol, 2015, 36(5): 3727-3734

[11] Conlon KC, Lugli E, Welles HC, et al. Redistribution, hyperproliferation, activation of natural killer cells and CD8 T cells, and cytokine production during first-in-human clinical trial of recombinant human interleukin-15 in patients with cancer [J]. J Clin Oncol, 2015, 33(1): 74-82

[12] Wesa AK, Mandic M, Taylor JL, et al. Circulating Type-1 Anti-Tumor CD4 (+) T Cells are Preferentially Pro-Apoptotic in Cancer Patients[J]. Front Oncol, 2014, 29(4): 266

[13] 崔海军, 阎成全, 张慧民, 等. 后腹腔镜肾脏手术对机体应激的影响[J]. 现代生物医学进展, 2016, 16(18): 3547-3550, 3455
Cui Hai-jun, Yan Cheng-quan, Zhang Hui-min, et al. Influence of Retroperitoneal Laparoscopic Operation on Traumatic Stress Response [J]. Progress in Modern Biomedicine, 2016, 16 (18): 3547-3550, 3455

[14] Wallin JJ, Bendell JC, Funke R, et al. Atezolizumab in combination with bevacizumab enhances antigen-specific T-cell migration in metastatic renal cell carcinoma[J]. Nat Commun, 2016, 30(7): 12624

[15] Gigante M, Pontrelli P, Herr W, et al. miR-29b and miR-198 overexpression in CD8+ T cells of renal cell carcinoma patients down-modulates JAK3 and MCL-1 leading to immune dysfunction [J]. J Transl Med, 2016, 11(14): 84

[16] Ravichandran K, Wang Q, Ozkok A, et al. CD4 T cell knockout does not protect against kidney injury and worsens cancer [J]. J Mol Med (Berl), 2016, 94(4): 443-455

[17] Zhao H, Li T, Novak J, et al. Comprehensive analyses of tumor immunity: implications for cancer immunotherapy [J]. Genome Biol, 2016, 17(1): 174

[18] Monette A, Ceccaldi C, Assaad E, et al. Chitosan thermogels for local expansion and delivery of tumor-specific T lymphocytes towards enhanced cancer immunotherapies[J]. Biomaterials, 2016, 75: 237-249

[19] Ge L, Shan Z, Han Q, et al. Effectiveness of allogeneic CD3AK cells on transplanted human renal cell cancer in mice with severe combined immune deficiency[J]. J BUON, 2016, 21(2): 399-406

[20] Shanker A, Pellom ST Jr, Dudimah DF, et al. Bortezomib Improves Adoptive T-cell Therapy by Sensitizing Cancer Cells to FasL Cytotoxicity[J]. Cancer Res, 2015, 75(24): 5260-5272