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单孔与三孔胸腔镜肺癌根治术对患者 T 淋巴细胞亚群、应激反应及生活质量的影响*

蔡 南 张志锋[△] 洪祎纯 黄加铭 黄豪达

(中山大学附属揭阳医院胸心外科 广东 揭阳 522000)

摘要 目的: 探讨单孔与三孔胸腔镜肺癌根治术对患者 T 淋巴细胞亚群、应激反应及生活质量的影响。**方法:** 选择 2016 年 2 月~2018 年 9 月期间我院收治的肺癌根治术患者 127 例为研究对象,依据随机数字表法将其分成单孔组($n=63$,采用单孔胸腔镜肺癌根治术治疗)和三孔组($n=64$,采用三孔胸腔镜肺癌根治术治疗),比较两组患者手术及临床指标、T 淋巴细胞亚群、应激反应指标及生活质量评分,并观察两组患者术后并发症发生情况。**结果:** 单孔组术中出血量少于三孔组,住院时间短于三孔组,而手术时间长于三孔组($P<0.05$),而两组淋巴结清扫个数、术后引流时间、术后引流量比较差异无统计学意义($P>0.05$)。术后 1d、术后 7d 单孔组皮质醇、生长激素、 PGE_2 均低于三孔组($P<0.05$)。术后 3d 单孔组 $CD3^+$ 、 $CD4^+$ 以及 $CD4^+/CD8^+$ 高于三孔组($P<0.05$)。术后 3 个月单孔组躯体疼痛、社会功能、情感职能、平均分数高于三孔组($P<0.05$)。两组患者术后并发症总发生率比较无差异($P>0.05$)。**结论:** 与三孔胸腔镜肺癌根治术相比,单孔胸腔镜肺癌根治术可减少患者术中出血量,缩短住院时间,减轻机体应激反应,对免疫功能损害较轻,且可有效改善患者生活质量。

关键词: 单孔胸腔镜;三孔胸腔镜;肺癌根治术;T 淋巴细胞亚群;应激反应;生活质量

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Effects of Single-port and Three-port Thoracoscopic Radical Resection of Lung Cancer on T Lymphocyte Subsets, Stress Response and Quality of Life in Patients*

CAI Nan, ZHANG Zhi-feng[△], HONG Yi-chun, HUANG Jia-ming, HUANG Hao-da

(Department of Cardiothoracic Surgery, The Affiliated Jieyang Hospital of Sun Yat-sen University, Jieyang, Guangdong, 522000, China)

ABSTRACT Objective: To investigate the effects of single-port and three-port thoracoscopic radical resection of lung cancer on T lymphocyte subsets, stress response and quality of life. **Methods:** 127 cases of radical resection of lung cancer who were received in our hospital from February 2016 to September 2018 were selected as subjects of study. They were divided into single-port group ($n=63$, treated by single-port thoracoscopic radical lung cancer) and three-port group ($n=64$, treated by three-port thoracoscopic radical lung cancer) according to the random number table method. The operative and clinical indexes, T lymphocyte subsets, stress response indexes and quality of life scores were compared between the two groups, and the occurrence of complications after operation was observed. **Results:** The amount of bleeding during operation in single-port group was less than that in three-port group, the hospitalization time was shorter than that in three-port group, and the operation time was longer than that in three-port group ($P<0.05$). There was no significant difference in the number of lymph node dissection, postoperative drainage time and postoperative drainage volume between the two groups ($P>0.05$). The levels of cortisol, growth hormone and PGE_2 in the single-port group were lower than those in the three-port group at 1d and 7d after operation ($P<0.05$). The $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ in the single-port group were higher than those in the three-port group at 3d after operation ($P<0.05$). The body pain, social function, emotional function and average score of the single-port group were higher than those of the three-port group at 3 months after operation ($P<0.05$). There was no significant difference in the total incidence rate of postoperative complications between the two groups ($P>0.05$). **Conclusion:** Compared with three-port thoracoscopic radical resection of lung cancer, single-port thoracoscopic radical resection of lung cancer can reduce amount of bleeding, shorten hospitalization time, alleviate body stress response, lessen the damage to immune function, and effectively improve the quality of life of patients.

Key words: Single-port thoracoscopy; Three-port thoracoscopy; Radical resection of lung cancer; T lymphocyte subsets; Stress response; Quality of life

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作者简介:蔡南(1985-),男,本科,主治医师,研究方向:胸心外科,E-mail: cai85117@sina.com

[△] 通讯作者:张志锋(1976-),男,本科,副主任医师,研究方向:胸心外科,E-mail: feng8699@126.com

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前言

肺癌是临床常见的恶性肿瘤,其已成为危害我国人民生命安全的恶性肿瘤之首,且伴随着人们健康意识的提高以及我国医学诊断技术的进步,越来越多的早期肺癌患者不断被确诊^[1,2]。早期肺癌的治疗主要以手术治疗为主,而以往传统的开胸手术创伤较大,风险较高,加之术后患者疼痛剧烈,并发症较多,因此寻找一种更有效的手术方法显得尤为重要^[3]。既往多中心、大宗的临床资料显示^[4,5],胸腔镜肺癌根治术可获得与传统的开胸手术类似的治疗效果,且胸腔镜肺癌根治术因其手术创伤小、视野效果佳、术后患者恢复快等优点而广受医生以及患者青睐^[6,7]。通常胸腔镜肺癌根治术为三孔操作,但其不可避免的给患者带来应激反应和免疫抑制^[8]。随着微创理念的深入,单孔胸腔镜开始应用于临床,该项术式操作要点在于只保留一个操作孔,放弃辅助操作孔以避免给患者造成胸痹神经及组织损伤^[9,10]。本研究通过探讨单孔与三孔胸腔镜肺癌根治术对患者T淋巴细胞亚群、应激反应及生活质量的影响,以期为临床术式选择提供参考。

1 资料和方法

1.1 临床资料

选取我院于2016年2月~2018年9月收治的127例肺癌根治术患者。纳入标准:(1)所有患者均符合国际肺癌研究协会制定的第八版关于肺癌的诊断标准^[11];(2)经胸部CT、肺穿刺组织病理活检证实为非小细胞肺癌;(3)能耐受全身麻醉手术;(4)患者及其家属知情本次研究且已签署了同意书。排除标准:(1)合并心肺肾等脏器功能不全者;(2)既往胸部已有手术史者;(3)合并中央型肺癌侵犯肺门、主支气管者;(4)合并血液疾病者;(5)肿块过大或已累及血管,已发生肿瘤转移者。将所有患者依据随机数字表法分成单孔组($n=63$)和三孔组($n=64$),其中单孔组男42例,女21例;年龄45~76岁,平均(53.29 ± 3.88)岁;肺部病灶区域:右上叶14例,右中叶11例,右下叶12例,左上叶13例,左下叶13例;癌症TNM分期:I期29例,II期34例;癌症类型:鳞癌31例,腺癌32例;合并症:合并吸烟史者38例,合并糖尿病患者21例。三孔组男42例,女22例;年龄44~75岁,平均(52.38 ± 4.06)岁;肺部病灶区域:右上叶15例,右中叶12例,右下叶10例,左上叶15例,左下叶12例;癌症TNM分期:I期30例,II期34例;癌症类型:鳞癌35例,腺癌29例;合并症:合并吸烟史者36例,合并糖尿病患者23例。两组患者一般资料比较差异无统计学意义($P>0.05$)。此次研究已获我院伦理委员会评审批准通过。

1.2 研究方法

两组体位均取侧卧位,采用双腔气管插管性全麻。三孔组患者采取三孔胸腔镜肺癌根治术治疗,具体如下:分别取腋前线第4肋间、腋中线第7肋间以及腋后线第9肋间作长约3cm(操作孔)、1cm(观察孔)、1.5cm(操作孔)大小的切口,于操作孔处行肺叶切除术以及淋巴结清扫,术后切口处常规放置引流管。单孔组患者采取单孔胸腔镜肺癌根治术治疗,具体如下:肺下叶手术切除者于术侧第5肋间作一长约3cm切口,肺中叶、肺上叶手术切除者于术侧第4肋间腋前线和腋中线作一长约3cm切口,皮肤逐层切开后,将肋间肌中部切断,进入胸腔,切口处放置软质切口保护套,胸腔镜下辅助完成肺叶切除术,同时行淋巴结清扫,术后切口处常规放置引流管。所有患者术后给予静脉镇痛、抗生素预防感染、吸氧、止血、雾化等常规对症支持治疗。

1.3 观察指标

(1)比较两组手术及临床指标,包括淋巴结清扫个数、术中出血量、手术时间、术后引流时间、术后引流量、住院时间。(2)分别于术前、术后1d、术后7d采集患者的空腹静脉血2mL,以2800 r/min速率离心12 min,离心半径为8 cm,分离血清,置于-30℃冰箱中待测。采用放射免疫分析法检测皮质醇、生长激素、前列腺素 E_2 (Prostaglandin E_2 , PGE_2)水平,试剂盒来源于罗氏诊断产品(上海)有限公司,严格遵守试剂盒操作说明进行。(3)分别于术前、术后3d采集患者的空腹静脉血2mL,通过Becton, Dickinson and Company公司BD FACSCalibur型流式细胞仪测定 $CD3^+$ 、 $CD4^+$ 、 $CD8^+$,并计算 $CD4^+/CD8^+$ 值。(4)分别于术前、术后3个月采用健康调查简表(Health Survey Form-36, SF-36)^[12]对患者生活质量进行评估, SF-36量表分8个维度,包括生理职能、躯体疼痛、生理机能、精神健康、活力、健康状况、社会功能、情感职能。每个维度总分为100分,分数越高生活质量越高。(5)记录两组并发症发生情况。

1.4 统计学方法

选用SPSS21.0统计软件进行统计分析,计数资料用率(%)表示,采用 χ^2 检验。计量资料用($\bar{x} \pm s$)表示,采用t检验,检验标准设置为 $\alpha=0.05$ 。

2 结果

2.1 两组患者手术及临床指标比较

单孔组患者术中出血量少于三孔组,住院时间短于三孔组,而手术时间长于三孔组($P<0.05$),两组患者淋巴结清扫个数、术后引流时间、术后引流量比较差异无统计学意义($P>0.05$)。详见表1。

表1 两组患者手术及临床指标比较($\bar{x} \pm s$)

Table 1 Comparison of operative and clinical indexes between two groups($\bar{x} \pm s$)

Groups	Amount of bleeding during operation(mL)	Operation time (min)	Number of lymph node dissection(n)	Postoperative drainage time(d)	Postoperative drainage volume(mL)	Hospitalization time(d)
Three-port group($n=64$)	156.89 $\pm$ 9.30	146.27 $\pm$ 11.24	14.27 $\pm$ 2.24	5.37 $\pm$ 1.83	721.27 $\pm$ 27.26	9.73 $\pm$ 1.46
Single-port group($n=63$)	127.14 $\pm$ 10.13	162.18 $\pm$ 9.73	13.92 $\pm$ 3.62	5.28 $\pm$ 1.34	718.37 $\pm$ 31.25	8.14 $\pm$ 1.35
t	17.245	8.523	0.656	0.316	0.558	6.374
P	0.000	0.000	0.513	0.753	0.578	0.000

2.2 两组患者应激反应指标比较

两组患者术前皮质醇、生长激素、PGE₂ 比较差异无统计学意义 ($P>0.05$), 两组患者术后 1d、术后 7d 皮质醇、生长激素、

PGE₂ 均高于术前, 且先升高后降低 ($P<0.05$), 术后 1d、术后 7d 单孔组患者皮质醇、生长激素、PGE₂ 均低于三孔组 ($P<0.05$)。详见表 2。

表 2 两组患者应激反应指标比较 ($\bar{x}\pm s$)Table 2 Comparison of stress response indexes between two groups ($\bar{x}\pm s$)

Groups	Cortisol (ng/mL)			Growth hormone (ng/mL)			PGE ₂ (pg/mL)		
	Before operation	1d after operation	7d after operation	Before operation	1d after operation	7d after operation	Before operation	1d after operation	7d after operation
Three-port group (n=64)	68.58±11.32	114.28±12.86*	89.06±10.14* [#]	1.24±0.27	2.76±0.44*	1.98±0.31* [#]	104.97±12.84	194.78±12.31*	154.88±12.26* [#]
Single-port group (n=63)	68.65±10.48	92.37±11.61*	78.05±9.19* [#]	1.22±0.33	2.19±0.53*	1.52±0.57* [#]	104.84±13.36	176.47±10.87*	129.19±10.46* [#]
t	0.036	10.073	6.408	0.374	6.599	5.662	0.056	8.880	12.694
P	0.971	0.000	0.000	0.709	0.000	0.000	0.956	0.000	0.000

Note: compared with before operation, * $P<0.05$; compared with 1d after operation, [#] $P<0.05$.

2.3 两组患者 T 淋巴细胞亚群比较

两组患者术前 CD3⁺、CD4⁺ 以及 CD4⁺/CD8⁺ 比较差异无统计学意义 ($P>0.05$), 两组患者术后 3d CD3⁺、CD4⁺ 以及

CD4⁺/CD8⁺ 均较术前降低, 但单孔组 CD3⁺、CD4⁺ 以及 CD4⁺/CD8⁺ 高于三孔组 ($P<0.05$)。详见表 3。

表 3 两组患者 T 淋巴细胞亚群比较 ($\bar{x}\pm s$)Table 3 Comparison of T lymphocyte subsets between two groups ($\bar{x}\pm s$)

Groups	CD3 ⁺ (%)		CD4 ⁺ (%)		CD4 ⁺ /CD8 ⁺	
	Before operation	3d after operation	Before operation	3d after operation	Before operation	3d after operation
Three-port group (n=64)	69.19±8.26	57.75±8.63*	37.48±9.18	28.26±7.11*	1.74±0.82	1.12±0.61*
Single-port group (n=63)	69.26±10.41	63.46±9.34*	37.53±8.68	33.95±8.92*	1.76±0.73	1.44±0.66*
t	0.042	3.579	0.032	3.978	0.145	2.838
P	0.967	0.000	0.975	0.000	0.885	0.005

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

2.4 两组患者生活质量比较

两组患者术前 SF-36 量表各维度评分以及平均评分比较差异无统计学意义 ($P>0.05$), 两组患者术后 3 个月生理机能、躯体疼痛、社会功能、活力、平均评分均较术前升高 ($P<0.05$), 单孔组生理机能、情感职能亦较术前升高 ($P<0.05$), 而单孔组患者健康状况、精神健康与术前相比差异无统计学意义 ($P>0.05$), 三孔组患者生理机能、健康状况、情感职能、精神健康与术

前相比差异无统计学意义 ($P>0.05$), 术后 3 个月单孔组患者躯体疼痛、社会功能、情感职能、平均评分高于三孔组 ($P<0.05$)。详见表 4。

2.5 两组患者术后并发症比较

两组患者术后并发症总发生率比较无差异 ($P>0.05$)。详见表 5。

表 4 两组患者生活质量比较 ($\bar{x}\pm s$, 分)Table 4 Comparison of quality of life between two groups ($\bar{x}\pm s$, scores)

Groups	Time	Physical limitations	Physiological function	Body pain	Health condition	Social function	Vitality	Emotional function	Mental health	Average score
Three-port group (n=64)	Before operation	48.79±11.64	44.36±9.08	42.35±8.36	62.73±10.14	61.29±10.24	62.71±8.94	45.38±8.46	66.26±10.28	54.23±10.26
	3 months after operation	51.62±9.15	63.46±9.28*	53.07±10.28*	63.68±12.46	66.83±8.64*	73.92±7.28*	48.23±9.37	67.28±9.83	62.31±6.08*
Single-port group (n=63)	Before operation	48.83±9.73	44.62±8.52	42.37±9.05	62.85±9.38	61.33±9.58	62.86±9.72	45.41±9.72	66.31±9.28	54.32±11.43
	3 months after operation	52.69±11.61*	63.52±10.49*	61.29±11.71* [#]	63.71±10.36	77.84±7.19* [#]	74.06±10.25*	55.61±10.35* [#]	67.34±10.29	64.51±6.12* [#]

Note: compared with before operation, * $P<0.05$; compared with three-port group, [#] $P<0.05$.

表 5 两组患者术后并发症比较【例(%)】

Table 5 Comparisons of postoperative complications between two groups [n(%)]

Groups	Pleural effusion	Pulmonary infection	Atelectasis	Pulmonary embolism	Arrhythmia	Total incidence rate
Three-port group(n=64)	4(6.25)	2(3.13)	1(1.56)	1(1.56)	5(7.81)	13(20.31)
Single-port group(n=63)	3(4.76)	2(3.17)	0(0.00)	0(0.00)	4(6.35)	9(14.29)
χ^2						0.805
<i>P</i>						0.370

3 讨论

肺癌是发病率和死亡率增长最快的恶性肿瘤之一^[13]。胸腔镜术式是治疗肺癌的一种重要手段,但胸腔镜手术属于创伤性操作,患者术中易引发较大的应激反应,同时还会造成机体不同程度的免疫抑制,而对于绝大多数肺癌患者而言,术中应激反应、免疫抑制程度与预后具有密切关系^[14,15]。三孔胸腔镜手术是临床应用较多的治疗术式,但既往研究表明,实施三孔胸腔镜手术可能对机体免疫功能产生一定影响,同时还可增加癌症复发及转移的可能性,影响患者预后^[16]。近年来,随着外科技术的发展,三孔胸腔镜手术逐渐发展成为两孔、单孔,其中单孔胸腔镜手术最先于胸膜活检手术中所应用,随后渐渐在交感神经链切断术以及外伤等较为简单的胸部手术中广泛使用^[17-19]。

本研究中,单孔组和三孔组淋巴结清扫个数、术后引流时间、术后引流量比较差异无统计学意义,但单孔组术中出血量少于三孔组,住院时间短于三孔组,术后3个月生活质量优于三孔组,提示单孔胸腔镜术式可获得与三孔胸腔镜术式类似的治疗效果,但单孔胸腔镜术式治疗肺癌患者术中出血量较少,住院时间较短,患者术后生活质量明显提升。分析原因主要是因为单孔胸腔镜术式仅保留了一个主操作孔,无需其他的辅助性操作孔,减少了术中损伤,因而出血量明显减少,可促进患者尽早恢复,提高患者生活质量^[20,21]。但本研究中单孔术式手术时间长于三孔术式,这可能是由于单孔术式手术操作均在一个孔内完成,存在术野小的局限,增加了手术操作难度^[22,23]。本研究结果显示,两组患者术后1d、术后7d皮质醇、生长激素、PGE₂均高于术前,且先升高后降低,术后1d、术后7d单孔组皮质醇、生长激素、PGE₂低于三孔组,可见与三孔肺癌根治术相比,单孔胸腔镜肺癌根治术治疗可以减轻患者的应激反应。皮质醇是创伤应激性反应的反馈因子,机体在应激状态下可导致皮质醇水平显著升高^[24]。PGE₂是重要的致痛炎性物质,是应激反应的敏感指标^[25]。生长激素具有促进蛋白质合成、加快组织修复、减少机体应激反应等效果^[26]。单孔胸腔镜术式患者应激反应更轻的原因因为单孔胸腔镜术式具有更佳的微创特性,可较好的控制手术伤口,减少术中创伤,因而可有效改善应激反应指标水平,降低机体应激性反应程度^[27]。CD3⁺、CD4⁺以及CD4⁺/CD8⁺均属于T淋巴细胞亚群,可较好的反映出患者的免疫功能。本研究结果显示,单孔组和三孔组患者术后3d CD3⁺、CD4⁺以及CD4⁺/CD8⁺均较术前降低,但单孔组高于三孔组,可见单孔组免疫抑制程度较三孔组低。这可能是由于单孔胸腔镜术式明显减少了切口,一般情况下选择患者前胸壁胸大肌下缘或是旁缘肌肉较少区域的肋间制作切口,可避免破坏切口区域的神经以

及肌肉组织,同时还可避免对患者胸背部神经以及肌肉的破坏,对患者免疫功能造成的影响也相对较小^[28-30]。另外,本研究结果显示,两组患者术后并发症总发生率比较无统计学差异,可见单孔胸腔镜术式不会增加并发症发生率,安全性较好。

综上所述,与三孔肺癌根治术相比,单孔胸腔镜肺癌根治术治疗肺癌可减少患者术中出血量,缩短住院时间,且对机体的应激反应和免疫功能造成的影响也较小,可提高患者术后生活质量,安全可靠。

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