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单孔与三孔胸腔镜肺叶切除术对周围型肺癌患者炎症因子、T 淋巴细胞亚群和生活质量的影响 *

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摘要 目的:探讨单孔与三孔胸腔镜肺叶切除术对周围型肺癌患者炎症因子、生活质量、T 淋巴细胞亚群的影响。**方法:**回顾性分析我院于 2016 年 12 月~2019 年 10 月间收治的 80 例周围型肺癌患者的临床资料。根据手术方式的不同将其分为 A 组(n=39, 行三孔胸腔镜肺叶切除术)、B 组(n=41, 单孔胸腔镜肺叶切除术), 比较两组患者围术期指标、血清炎症因子、外周血 T 淋巴细胞亚群、生活质量及并发症情况。**结果:**两组术中淋巴清扫个数、术中出血量对比无差异($P>0.05$), B 组术后引流管拔除时间、切口长度短于 A 组, 手术时间长于 A 组, 视觉模拟评分法(VAS)评分低于 A 组($P<0.05$)。两组术后并发症发生率比较无差异($P>0.05$)。两组术后 3 d、术后 7 d 降钙素原(PCT)、肿瘤坏死因子- α (TNF- α)、C 反应蛋白(CRP)及 CD8⁺ 水平均较术前升高, 术后 7 d 上述指标较术后 3 d 降低, 且 B 组术后 3 d、术后 7 d 上述指标水平低于 A 组($P<0.05$)。两组术后 3 d、术后 7 d 的 CD4⁺、CD4⁺/CD8⁺ 均较术前降低, 术后 7 d 上述指标较术后 3 d 升高, 且 B 组术后 3 d、术后 7 d 上述指标水平高于 A 组($P<0.05$)。两组术后 3 个月情感状况、功能状况、社会/家庭状况、附加状况、身体状况评分均升高, 且 B 组高于 A 组($P<0.05$)。**结论:**与三孔胸腔镜肺叶切除术相比, 采用单孔胸腔镜肺叶切除术治疗周围型肺癌, 可获得与其相当的治疗效果, 同时还可减少术中损伤, 降低炎症因子水平, 减轻免疫抑制和炎症应激, 提高患者生活质量, 且不增加并发症发生率。

关键词:单孔胸腔镜肺叶切除术; 三孔胸腔镜肺叶切除术; 周围型肺癌; 炎症因子; T 淋巴细胞亚群; 生活质量

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Effects of Single Hole and Three Hole Thoracoscopic Lobectomy on Serum Inflammatory Factors and Peripheral Blood T Lymphocyte Subsets and Quality of Life in Patients with Peripheral Lung Cancer*

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ABSTRACT Objective: To investigate the effect of single hole and three hole thoracoscopic lobectomy on inflammatory factors, quality of life and T lymphocyte subsets in patients with peripheral lung cancer. **Methods:** The clinical data of 80 patients with peripheral lung cancer who were admitted to our hospital from December 2016 to October 2019 were analyzed retrospectively. According to the different operation methods, they were divided into group A(n=39, three hole thoracoscopic lobectomy) and group B(n=41, single hole thoracoscopic lobectomy). The perioperative indexes, serum inflammatory factors, peripheral blood T lymphocyte subsets, quality of life and complications of the two groups were compared. **Results:** There was no significant difference between the two groups in the number of lymph node dissection and the amount of intraoperative hemorrhage($P>0.05$). The time of drainage tube removal after operation and incision length were shorter than those of group A, the operation time of group B was longer than that of group A, and visual analogue scale (VAS) score was lower than that of group A($P<0.05$). There was no significant difference in the incidence of postoperative complications between the two groups ($P>0.05$). The levels of procalcitonin (PCT), tumor necrosis factor- α (TNF- α), C-reactive protein (CRP) and CD8⁺ of the two groups at 3d after operation and 7 d after operation were higher than those before operation, the above indexes at 3 d after operation were lower than those after operation 7 d, and the levels of above indexes of group B at 3 d after operation and 7 d after operation were lower than those of the group A ($P<0.05$). The CD4⁺ and CD4⁺/CD8⁺ of the two groups at 3 d after operation and 7 d after operation were lower than those before operation, the above indexes at 3 d after operation were higher than those after operation 7 d, and the levels of above indexes of group B at 3 d after operation and 7 d after operation were higher than those of the group A ($P<0.05$). The scores of emotional status, functional status, social/family status, additional status and physical status of the two groups increased at 3 months after operation, and the scores in group B were higher than those in group A ($P<0.05$). **Conclusion:** Compared with the three hole

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thoroscopic lobectomy, the single hole can achieve the same therapeutic effect in peripheral lung cancer, at the same time, it can reduce the intraoperative injury, reduce the immunosuppression and inflammatory stress, improve the quality of life of patients, and do not increase the incidence rate of complications.

Key words: Single hole thoroscopic lobectomy; Three hole thoroscopic lobectomy; Peripheral lung cancer; Inflammatory factors; T lymphocyte subsets; Quality of life

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前言

周围型肺癌是指起自三级支气管以下,呼吸性细支气管以上的肺癌,以腺癌较为多见。肺叶切除术是常用的治疗方法之一,与传统的开胸手术相比,胸腔镜下的手术操作具有疼痛较轻、安全指数高、术后恢复快等优势,受到了较多医师及患者的喜爱^[1-3]。通常情况下,胸腔镜肺叶切除术多选取三孔,但不论手术大小,均为有创操作,患者可产生一定程度的炎性应激,引起免疫抑制,在增加并发症发生几率的同时,还容易引起肿瘤复发与转移,降低患者生活质量,威胁患者生命安全^[4-6]。近年来临床医师逐渐将两孔甚至单孔胸腔镜肺叶切除术应用于临床,该术式的重点在于放弃辅助操作孔,只用一个主操作孔完成所有手术操作,以减少术中损伤^[7]。本研究通过对比胸腔镜肺叶切除术采用单孔与三孔对周围型肺癌患者外周血 T 淋巴细胞亚群及血清炎症因子的影响,以期为临床治疗提供参考。

1 资料与方法

1.1 基线资料

回顾性分析 2016 年 12 月~2019 年 10 月我院接收的 80 例周围型肺癌临床资料。纳入标准:(1)经病理检查后确诊为周围型肺癌;(2)手术操作均由同一组医师完成;(3)均符合手术指征者,临床资料完整;(4)术前临床分期为 I、II 期;(5)术前胸部 CT 提示肿瘤局限于 1 个肺叶内,未侵及胸壁大血管,肿瘤直径 ≤ 5 cm,未发现远处转移者。排除标准:(1)合并其它重要实质脏器障碍者;(2)既往有相关部位手术史者;(3)伴有其他呼吸系统慢性疾病,如肺结核、慢性阻塞性肺疾病等;(4)存在明显的胸膜增厚和粘连等情况;(5)无法正常沟通交流者;(6)伴主支气管、中央型肺癌侵犯肺门者。根据手术方式的不同将其分为 A 组($n=39$,三孔胸腔镜肺叶切除术)、B 组($n=41$,单孔胸腔镜肺叶切除术),其中 A 组男 23 例,女 16 例,平均年龄(49.62 ± 5.71)岁;平均体质量指数(23.97 ± 0.95) kg/m^2 ;平均肿瘤直径(3.42 ± 0.35)cm;临床分期:I 期 21 例,II 期 18 例;病灶位置:上叶 15 例,中叶 14 例,下叶 10 例。B 组男 24 例,女 17 例,平均年龄(49.25 ± 5.53)岁;平均体质量指数(23.91 ± 0.98) kg/m^2 ;平均肿瘤直径(3.38 ± 0.32)cm;临床分期:I 期 22 例,II 期 19 例;病灶位置:上叶 16 例,中叶 14 例,下叶 11 例。两组一般资料对比无差异($P>0.05$),具有可比性。

1.2 方法

两组体位取健侧卧位,单肺通气,腋下垫棉垫,采用复合静脉麻醉,双腔气管插管,B 组患者予以单孔胸腔镜肺叶切除术,于腋前线第 5 肋间作一长约 5 cm 的切口,切口放置保护套,置入 30° 胸腔镜(规格:10 mm),探查清楚胸腔肺组织和周围组

织粘连情况后,行肺叶切除及淋巴结清扫术,术后于切口后角留置胸腔闭式引流管。A 组患者予以三孔胸腔镜肺叶切除术,分别于腋中线第 7 肋间作一长约 2 cm 的切口,置入胸腔镜探查病灶位置和邻近组织的解剖情况,于腋后线第 5 或 6 肋间作一长约 2 cm 的切口作为副操作孔,于腋前线第 3 或 4 肋间作一长约 5 cm 的切口作主操作孔,切口放置保护套。其余手术器械、术中清扫淋巴结、术后操作均与 B 组一致。

1.3 观察指标

(1)记录两组术中出血量、手术时间、术后引流管拔除时间、切口长度、术中淋巴结清扫个数及术后视觉模拟评分法(VAS)^[8]评分。其中 VAS 评分 0~10 分,0 分表示无痛,10 分表示难以忍受的疼痛。(2)记录两组漏气、切口感染、吸入型肺炎、心房颤动及胸腔积液等并发症情况。(3)抽取两组患者术前、术后 3 d、术后 7 d 的肘静脉血 3 mL,常规离心待测。参考试剂盒(上海生工生物工程技术有限公司)说明书步骤,采用酶联免疫吸附法检测降钙素原(PCT)、肿瘤坏死因子- α (TNF- α)及 C 反应蛋白(CRP)水平。另取相同时间点肘静脉血 3 mL,采用美国库尔特公司(COULTER)生产的 EPICSXL 流式细胞仪检测外周血 T 淋巴细胞亚群水平:CD4⁺、CD8⁺,并计算 CD4⁺/CD8⁺。(4)随访 3 个月,随访方式门诊复查,采用肺癌患者癌症治疗功能量表(FACT-L)^[9]评价患者生活质量,其中 FACT-L 包括 5 个项目 36 个条目,包括情感状况(6 条目)、功能状况(7 条目)、社会/家庭状况(7 条目)、附加状况(9 条目)、身体状况(7 条目)。各条目均采用 0~4 分 5 级规范用语评分法,正向条目正向计分,逆向条目反向计分。总体得分越高,表明生活质量越好。

1.4 统计学方法

采用 SPSS20.0 进行数据分析。计数资料以率的形式表示,行卡方检验。计量资料以($\bar{x} \pm s$)的形式表示,行 t 检验。检验标准设置为 $\alpha=0.05$ 。

2 结果

2.1 围术期指标比较

B 组手术时间长于 A 组,术后引流管拔除时间、切口长度短于 A 组,VAS 评分低于 A 组($P<0.05$),两组术中淋巴结清扫个数、术中出血量对比无差异($P>0.05$),详见表 1。

2.2 炎症因子水平比较

两组术前 CRP、PCT、TNF- α 比较无差异($P>0.05$),两组术后 3 d、术后 7 d 血清 CRP、PCT、TNF- α 水平较术前升高,两组术后 7 d 上述指标较术后 3 d 降低,但术后 3 d、术后 7 d B 组上述指标水平低于 A 组($P<0.05$),详见表 2。

表 1 两组围术期指标比较($\bar{x} \pm s$)Table 1 Comparison of perioperative indexes between the two groups($\bar{x} \pm s$)

Groups	Amount of intraoperative hemorrhage(mL)	Operation time (min)	Time of drainage tube removal after operation(d)	Incision length (cm)	Number of lymph node dissection(n)	VAS score(score)
Group A(n=39)	83.79± 8.56	159.73± 14.69	5.36± 0.38	8.89± 1.37	12.71± 1.52	4.72± 0.69
Group B(n=41)	84.41± 9.37	183.75± 13.39	4.14± 0.49	5.32± 0.31	12.88± 1.42	3.39± 0.53
t	0.309	7.650	12.400	16.259	0.517	9.697
P	0.759	0.000	0.000	0.000	0.606	0.000

表 2 两组炎症因子水平比较($\bar{x} \pm s$)Table 2 Comparison of inflammatory factors between the two groups($\bar{x} \pm s$)

Groups	CRP(mg/L)			PCT(ng/mL)			TNF-α(ng/L)		
	Before operation	3 d after operation	7 d after operation	Before operation	3 d after operation	7 d after operation	Before operation	3 d after operation	7 d after operation
Group A (n=39)	4.75± 0.83	13.03± 3.24 ^a	7.83± 1.40 ^{ab}	0.09± 0.02	0.23± 0.06 ^a	0.15± 0.04 ^{ab}	23.09± 2.53	35.61± 3.57 ^a	29.68± 3.73 ^{ab}
Group B (n=41)	4.72± 0.77	8.96± 1.33 ^a	5.89± 0.92 ^{ab}	0.09± 0.01	0.18± 0.03 ^a	0.10± 0.03 ^{ab}	23.15± 2.41	29.46± 3.62 ^a	24.71± 1.92 ^{ab}
t	0.168	7.415	7.359	0.000	4.749	6.345	0.109	7.647	7.547
P	0.867	0.000	0.000	1.000	0.000	0.000	0.914	0.000	0.000

Note: compared with before operation, ^a $P<0.05$; compared with 3 d after operation, ^b $P<0.05$.

2.3 两组 T 淋巴细胞亚群比较

两组术前 CD4⁺、CD4⁺/CD8⁺、CD8⁺ 比较差异无统计学意义 ($P>0.05$), 两组术后 3 d、术后 7 d CD4⁺、CD4⁺/CD8⁺ 均较术前降低, 术后 7 d 上述指标较术后 3 d 升高, 且 B 组术后 3 d、术后

7 d 以上指标水平高于 A 组 ($P<0.05$), 两组术后 3 d、术后 7 d 的 CD8⁺ 较术前升高, 术后 7 d CD8⁺ 较术后 3 d 降低, 且 B 组术后 3 d、术后 7 d CD8⁺ 低于 A 组 ($P<0.05$), 详见表 3。

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

Groups	CD4 ⁺ (%)			CD8 ⁺ (%)			CD4 ⁺ /CD8 ⁺		
	Before operation	3 d after operation	7 d after operation	Before operation	3 d after operation	7 d after operation	Before operation	3 d after operation	7 d after operation
Group A (n=39)	45.36± 5.26	35.52± 5.41 ^a	40.16± 6.15 ^{ab}	27.53± 3.54	35.90± 5.02 ^a	31.62± 3.90 ^{ab}	1.65± 0.23	0.99± 0.21 ^a	1.27± 0.22 ^{ab}
Group B (n=41)	45.64± 6.87	40.83± 4.31 ^a	42.93± 5.06 ^{ab}	27.36± 4.27	32.16± 4.30 ^a	29.66± 4.54 ^{ab}	1.67± 0.27	1.26± 0.22 ^a	1.45± 0.29 ^{ab}
t	0.204	4.868	2.205	0.193	3.585	2.067	0.356	5.610	3.116
P	0.839	0.000	0.030	0.847	0.001	0.042	0.723	0.000	0.003

Note: compared with before operation, ^a $P<0.05$; compared with 3 d after operation, ^b $P<0.05$.

2.4 两组并发症发生情况比较

两组术后并发症发生率比较无差异 ($P>0.05$), 详见表 4。

表 4 两组并发症发生情况比较 [例(%)]

Table 4 Comparison of complications between the two groups [n(%)]

Groups	Leak	Incision infection	Aspiration pneumonia	Atrial fibrillation	Pleural effusion	Total incidence rate
Group A(n=39)	1(2.56)	2(5.13)	1(2.56)	1(2.56)	1(2.56)	6(15.38)
Group B(n=41)	1(2.44)	1(2.44)	0(0.00)	1(2.44)	1(2.44)	4(9.76)
χ^2						0.579
P						0.447

2.5 两组生活质量对比

两组术前情感状况、功能状况、社会 / 家庭状况、附加状况、身体状况评分对比差异无统计学意义 ($P>0.05$), 两组术后 3

个月情感状况、功能状况、社会 / 家庭状况、附加状况、身体状况评分均升高, 且 B 组高于 A 组 ($P<0.05$), 详见表 5。

表 5 两组生活质量对比 ($\bar{x} \pm s$)
Table 5 Comparison of quality of life between the two groups ($\bar{x} \pm s$)

Groups	Emotional status		Functional status		Social / family status		Additional status		Physical status	
	Before operation	3 months after operation	Before operation	3 months after operation	Before operation	3 months after operation	Before operation	3 months after operation	Before operation	3 months after operation
Group A (n=39)	13.89±3.65	18.67±3.95*	14.23±4.25	18.39±0.87*	14.09±3.94	17.31±4.69*	18.04±4.35	23.60±4.21*	13.32±4.31	17.56±4.53*
Group B (n=41)	13.56±3.02	20.14±2.79*	14.91±4.36	21.97±1.95*	14.98±3.87	20.86±4.71*	18.09±5.36	25.80±2.14*	13.34±4.29	19.11±4.57*
t	0.441	4.556	0.332	7.275	0.126	5.279	0.046	2.983	0.187	4.470
P	0.660	0.000	0.741	0.000	0.900	0.000	0.964	0.004	0.852	0.000

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

3 讨论

随着低剂量螺旋 CT 扫描的普及以及患者保健意识的增强, 肺癌的早期确诊率不断升高, 针对处于这一时期的肺癌患者, 手术治疗是其最佳治疗方案^[10-12]。肺叶切除术作为周围型肺癌的常用治疗方案, 经历了以传统的开胸手术逐渐过渡至微创胸腔镜手术的过程, 随着胸腔镜手术中手术方法持续改进、手术器械持续创新以及术者手术熟练度持续提高, 胸腔镜肺叶切除术已成为临床治疗周围型肺癌的最常见的办法^[13-15]。胸腔镜肺叶切除术常用三孔操作, 虽也属于微创, 但手术本身为创伤性操作, 围术期间患者应激反应较大, 进而抑制患者免疫功能^[16,17]。故在手术中如何尽可能的减少创伤, 减轻应激反应及免疫抑制已成为临床医师的关注重点。单孔胸腔镜技术于 1998 年首次提出, 早期常应用于简单胸部疾病的治疗中^[18]。而至 2011 年, 单孔胸腔镜技术发展至了新高度。有等学者报道单孔胸腔镜技术治疗肺癌患者, 包括完整的淋巴结清扫及肺叶切除^[19]。目前, 越来越多的学者尝试将其应用于周围型肺癌的治疗, 证实其优势及术后效果显著。

本次研究结果显示, B 组引流管拔除时间、切口长度、VAS 评分均优于 A 组, 且淋巴结清扫个数、术中出血量无差异。可见单孔可获得与三孔技术相当的治疗效果, 同时单孔技术可减少术中损伤, 降低患者术后疼痛, 有利于患者术后恢复。而本研究中显示单孔技术所用手术时间略长于三孔技术, 可能是因为单孔技术中所有手术操作器械、胸腔镜镜杆均由此孔进入胸腔, 术中暴露受限, 操作器械可能相互碰撞, 较三孔手术难度更大, 故而耗时更长^[20-22]。肺叶切除术可引起机体肾上腺皮质分泌增加、炎症应激反应、交感神经兴奋, 并出现各种伤害性反应, 造成机体免疫功能降低, 严重者甚至发展为急性呼吸窘迫综合征^[23,24]。CRP 是机体受到炎症性刺激时水平会急剧上升的急性时相蛋白^[25,26]。PCT 由细菌脂多糖细菌产生, 其水平增高可提示机体发生感染^[27]。TNF- α 作为前炎症细胞因子, 主要由活化的单核巨噬细胞产生, 是启动炎症反应的关键细胞因子^[28]。从机体免疫功能指标来看, CD8⁺/CD4⁺ 具有相互调节作用,

CD4⁺/CD8⁺ 水平较低时, 提示机体免疫应答能力较低。本研究中两组患者均有不同程度的炎症应激、免疫抑制情况, 但单孔胸腔镜肺叶切除术可有效减轻免疫抑制及炎症反应。可能是因为单孔胸腔镜肺叶切除术术中损伤小, 可大大降低对患者神经、肌肉、血管的损伤, 有效减轻炎症刺激, 同时术后疼痛感减轻, 可加快机体恢复, 为患者及时恢复免疫功能做准备^[29,30]。此外, 两种手术方案均安全可靠, 并可有效提高患者生活质量, 可能是因为单孔胸腔镜肺叶切除术创伤较小, 患者术后恢复快, 可早日回归正常的工作中, 提高其生活幸福感, 生活质量明显改善。值得注意的是, 由于单孔胸腔镜手术切口较为固定, 对操作视野有一定的影响, 其针对肺叶切除术的治疗仍处于阶段性成功的情况, 需施术者对此类手术的熟练度较高才能更好的完成手术。

综上所述, 与三孔胸腔镜肺叶切除术相比, 周围型肺癌采用单孔胸腔镜肺叶切除术可获得相当的治疗效果, 同时还可减少术中损伤, 减轻免疫抑制和炎症应激, 有效提高生活质量, 且不增加并发症发生率。

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