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胸膜腔黏连对非小细胞肺癌患者行胸腔镜下肺叶切除术的影响分析

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摘要 目的:分析胸膜腔黏连对非小细胞肺癌患者行胸腔镜下肺叶切除术的影响,探讨患者行胸腔镜下肺叶切除术后发生并发症的影响因素。**方法:**收集 2014 年 1 月到 2017 年 12 月份在我科行胸腔镜下肺叶切除的非小细胞肺癌患者,通过检索电子病历和电话随访的方式收集患者的基本资料,包括性别、年龄、BMI 指数、是否吸烟、一秒用力呼气容积百分比(Percentage predicted forced expiratory volume in 1 s, FEV1 %)、美国麻醉医师协会评分(American Society of Anesthesiologists, ASA)、术后病理结果和术前并发症等资料。收集患者手术相关情况,包括胸膜是否黏连、手术时间、术中出血、术中中转开胸、术后引流、住院时间、并发症和术后 30 天死亡,根据患者是否有胸膜黏连将其分为两组,对比分析两组基本情况和术后情况,观察胸膜黏连对术中及术后的影响。根据术后是否发生并发症将患者分为两组,对比分析两组的指标,并对有差异的指标进行 Logistic 回归分析,探讨胸膜黏连是否为术后并发症的独立危险因素和其他危险因素。**结果:**根据纳入排除标准,共有 447 例患者纳入研究,其中有 142 例患者术中发现胸膜黏连,胸膜黏连的患者手术时间、术中出血、中转开胸、术后前两天引流量、引流时间、术后住院时间和术后并发症发生率均高于胸膜没有黏连的患者($P < 0.05$)。术后发生并发症的患者年龄、女性比例、吸烟人数、术前呼吸并发症、胸膜黏连、ASA 评分和手术时间均高于术后未发生并发症的患者($P < 0.05$)。胸膜黏连($OR = 4.185, P = 0.020$)、ASA 评分($OR = 1.143, P = 0.001$)、吸烟($OR = 3.329, P = 0.005$)、手术时间延长($OR = 1.623, P = 0.038$)和术前呼吸合并症($OR = 2.713, P = 0.027$)均是术后发生并发症的独立危险因素。**结论:**胸膜黏连增加了非小细胞肺癌患者行胸腔镜下肺叶切除术的手术难度、术中中转开胸和术后并发症发生的风险。

关键词:胸膜黏连;非小细胞肺癌;胸腔镜;肺叶切除;并发症

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Effect of Pleural Adhesion on the Thoracoscopic Lobectomy in Patients with Non-small Cell Lung Cancer

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ABSTRACT Objective: To analyze the effect of pleural adhesion on the thoracoscopic lobectomy in patients with non-small cell lung cancer, and explore the influencing factors of postoperative complications after thoracoscopic lobectomy. **Methods:** Patients with non-small cell lung cancer who underwent thoracoscopic lobectomy in our department from January 2014 to December 2017 were collected. The basic data of patients were collected by searching electronic medical records and telephone follow-up, including gender, age, BMI index, Percentage predicted forced expiratory volume in 1 s (FEV1%), American Society of Anesthesiologists (ASA), postoperative pathological findings, and preoperative complications. The patient's surgery-related conditions were collected, including pleural adhesion, operative time, intraoperative bleeding, intraoperative conversion, postoperative drainage, length of hospital stay, complications, and 30-day postoperative death. Patients were divided into two groups according to whether they had pleural adhesion or not. The basic information and postoperative conditions of the two groups were compared and analyzed. The effects of pleural adhesion on intraoperative and postoperative results were observed. In addition, the patients were divided into two groups according to whether they had postoperative complications or not. The indexes of two groups were comparatively analyzed. Logistic regression analysis was performed to investigate the risk factors for postoperative complications. **Results:** According to the inclusion and exclusion criteria, a total of 447 patients were included in the study and 142 patients had pleural adhesion. The operative time, intraoperative bleeding, conversion to thoracotomy, drainage at two days after surgery, drainage time, postoperative hospital stay, and postoperative complications of patients with pleural adhesion were higher than those of patients without pleural adhesion ($P < 0.05$). The age, female proportion, smoking number, preoperative

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respiratory complications, pleural adhesion, ASA score, and operation time of patients with postoperative complications were higher than those without postoperative complications ($P < 0.05$). Pleural adhesion ($OR = 4.185$, $P = 0.020$), ASA scores ($OR = 1.143$, $P = 0.001$), smoking ($OR = 3.329$, $P = 0.005$), extended operative time ($OR = 1.623$, $P = 0.038$) and preoperative respiratory complications ($OR = 2.713$, $P = 0.027$) were independent risk factors for the postoperative complications. **Conclusions:** Pleural adhesion increases the difficulty of thoracoscopic lobectomy in patients with non-small cell lung cancer, intraoperative conversion, and risk of postoperative complications.

Key words: Pleural adhesion; Non-small cell lung cancer; Thoracoscopic; Lobectomy; Complications

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前言

肺癌是一种预后相对较差的常见癌症,手术治疗已成为早期非小细胞肺癌(non-small cell lung cancer, NSCLC)的一种常规治疗方法^[1]。近年来,越来越多的人采用电视辅助胸腔镜(video-assisted thoracoscopic surgery, VATS)对可手术的NSCLC患者进行治疗。研究表明相对于开胸手术,VATS创伤较小、术后疼痛轻、术后恢复较快^[2-4]。虽然手术设备和手术技术逐年改善,但VATS术后并发症仍高达30%左右^[5-6],尤其是如果术中遇到较致密的胸膜腔黏连,术后并发症的发生率可能更高。

正常状态下,胸膜腔间皮有调节胸膜腔液体平衡的能力^[7,8],发生炎症反应时,这种调节能力的减弱会导致胸膜腔积液^[9,10]。长期的炎症反应会导致胸膜腔黏连的形成^[11],胸膜腔黏连形成后会进一步破坏胸膜腔液体循环的能力^[12]。术中胸膜腔黏不仅增加了手术难度,还可能和术中中转开胸率升高相关^[13-15],此外,还有研究表明胸膜腔黏连可能和术中出血增多、术后延长漏气相关^[14,16-18]。因此,本研究主要探讨了胸膜黏连对行VATS肺叶切除的NSCLC患者术中及术后的影响,以期为临床上VATS肺叶切除提供参考。

1 材料与方法

1.1 一般资料

收集2014年1月至2017年12月于我科行VATS下单肺叶切除的NSCLC患者。纳入排除标准:①肿瘤大小 $< 7\text{ cm}$;②术前薄层CT扫描提示肺癌且淋巴结 $< 1.5\text{ cm}$;③未侵犯叶支气管;④没有肺部手术史;⑤术前检查未见明显手术禁忌症;⑥术后病理确诊为原发性NSCLC。关于患者能否行手术切除参照胸外科肺癌手术指南^[19]。手术均是同一医疗组进行的标准三孔VATS,术后患者均转至ICU过渡,术后第一天由ICU医生决定是否转至我科普通病房,返回病房后均实施标准的术后护理。患者拔出引流管后可以下地活动,呼吸正常未见明显气短、气促,且严重并发症和症状得到良好控制时出院。

1.2 评估指标

收集患者的基本临床资料,包括性别、年龄、BMI指数、是否吸烟、FEV1%、术前ASA评分、术后病理结果和术前并发症等资料,将术前肺部感染、肺不张、慢性阻塞性肺疾病(Chronic obstructive pulmonary disease, COPD)、胸腔积液等定义为肺部合并症,将高血压、冠心病、心梗、心律失常定义为心脏合并症,其他合并症包括糖尿病、肾功能不全。

记录患者手术相关情况,包括胸膜是否黏连、手术时间、术中出血、术中中转开胸、术后引流、术后住院时间、并发症和术

后30天死亡,参照法国胸腔和血管外科数据库分类标准^[20]将术后肺炎、肺不张、胸腔积液、肺血栓、急性呼吸窘迫综合征、术后新出现心律失常、心梗定义为心肺并发症,将气胸、血胸、皮下气肿、延长漏气、支气管哮喘、乳糜胸定义为手术并发症。

1.3 统计学分析

所有数据采用SPSS 20.0进行统计学分析,连续型变量以"均值 $\pm$ 标准差"表示,组间比较采用t检验,计数资料以百分率表示,组间差异采用卡方检验或者Fisher精确检验分析,影响因素分析采用Logistic回归分析进行分析,设定 $P < 0.05$ 为差异有统计学意义。

2 结果

根据纳入排除标准,共有447例患者纳入研究,平均年龄为 68.9 ± 11.5 岁,女性213例(47.7%),术中有16例(3.6%)患者中转开胸,术后30天内有6例患者死亡(1.3%),术后有124例(27.7%)患者发生并发症,447例患者中有142例患者术中发现胸膜黏连。

2.1 患者术前基本资料

根据患者是否有胸膜腔黏连将患者分为两组,两组患者在年龄、性别、BMI指数、吸烟状况、ASA评分、肿瘤分期、肿瘤位置、肿瘤病理类型和术前合并症均没有统计学差异($P > 0.05$),见表1。

2.2 胸膜黏连对手术及术后并发症的影响

胸膜黏连的患者手术时间、术中出血量、术中中转开胸率、术后前两天引流量和引流管放置时间均显著高于没有黏连的患者($P < 0.001$),术后住院时间、总体并发症和手术相关并发症发生率亦均高于没有黏连的患者($P < 0.05$),两组患者术后30天内死亡率比较没有统计学差异($P = 0.084$),见表2。

2.3 是否发生术后并发症的患者的资料对比

术后共有124例患者发生并发症,根据患者是否发生并发症,将患者分为两组。术后发生并发症患者的年龄、女性比例、吸烟比例、术前呼吸合并症、胸膜黏连比例、ASA评分和手术时间均显著高于术后没有发生并发症的患者($P < 0.05$),两组患者的BMI指数、FEV1%和肿瘤分期比较差异无统计学意义($P > 0.05$),见表3。

2.4 发生术后并发症的危险因素

为探讨术后发生并发症的危险因素,我们以表3中有差异的变量作为自变量,包括年龄、性别比例、是否吸烟、术前是否有呼吸合并症、是否有胸膜黏连、ASA评分和手术时间,将是否发生并发症作为因变量进行Logistic回归分析,最后胸膜黏连($OR = 4.185$, $P = 0.020$)、ASA评分($OR = 1.143$, $P = 0.001$)、吸烟

(OR=3.329, P=0.005)、手术时间延长(OR=1.623, P=0.038)和呼吸合并症(OR=2.713, P=0.027)进入方程,是术后发生并发症的独立危险因素,见表 4。

表 1 患者术前基本资料

Table 1 Preoperative basic data of patients

Parameters	Pleural adhesion		t/x ²	P value
	No(n=305)	Yes(n=142)		
Age (Year)	68.7± 9.1	69.2± 10.2	0.520	0.603
Gender: Male (n, %)	140, 45.9	73, 51.4	1.178	0.278
BMI	24.4± 11.7	24.7± 12.1	0.250	0.803
Smoking (n, %)	133, 43.6	73, 51.4	1.966	0.161
ASA ≥ 3 points (n, %)	156, 51.1	77, 54.2	0.368	0.544
NSCLC staging (n, %)				
I	164, 53.8	79, 55.6		
II	131, 43.0	52, 36.6	5.127	0.077
> II	10, 3.3	11, 7.7		
Pathology (n, %)				
Adenocarcinoma	234, 76.7	106, 74.6		
Squamous cell carcinoma	71, 23.3	36, 25.4	0.229	0.632
FEV1%	86.7± 27.2	83.7± 33.5	1.006	0.315
Tumor location (n, %)				
Right upper lobe	106, 34.6	51, 35.9		
Right middle lobe	26, 8.5	11, 7.7		
Right lower lobe	63, 20.7	27, 19.0	0.593	0.964
Left upper lobe	57, 18.7	25, 17.6		
Left lower lobe	53, 17.4	28, 19.7		
Comorbidity (n, %)				
Respiratory comorbidity	131, 43.0	65, 45.8		
Heart comorbidity	46, 15.1	26, 18.3	0.224	0.894
Others	60, 19.7	32, 22.5		

表 2 患者术后基本情况

Table 2 Basic situation of patients after operation

Parameters	Pleural adhesion		t/x ²	P value
	No(n=305)	Yes(n=142)		
Surgery time (minutes)	126.2± 57.3	153.4± 61.5	4.564	< 0.001
Intraoperative bleeding (mL)	65.3± 73.4	97.6± 121.4	3.479	< 0.001
Conversions (n, %)	4, 1.2	12, 8.5	14.309	< 0.001
Drainage on first day after surgery (ml)	313.4± 210.5	457.3± 221.6	6.616	< 0.001
Drainage on 2nd day after surgery (ml)	224.6± 153.7	347.5± 206.4	7.027	< 0.001
Drainage time (days)	2.5± 0.8	3.4± 1.1	9.779	< 0.001
Postoperative hospital stay (days)	5.2± 1.3	7.4± 1.6	15.450	< 0.001
Complication (n, %)				
Total complications	75, 24.6	49, 34.5	4.475	0.029
Cardiopulmonary complications	51, 16.7	27, 19.0	3.178	0.075
Surgical complications	36, 11.8	37, 26.1	14.405	< 0.001
Death within 30 days (n, %)	2, 0.7	4, 2.8	-	0.084

表 3 术后是否发生并发症的患者的基本资料

Table 3 Basic information of patients with and without complications after operation

Parameters	Complications occurrence		t/x ²	P value
	Yes(n=124)	No(n=323)		
Age (Year)	70.8± 11.1	68.1± 10.7	2.364	0.019
Gender: Male (n, %)	69, 55.6	144, 44.6	4.396	0.036
BMI	24.5± 12.5	24.3± 11.9	0.157	0.875
Smoking (n, %)	74, 59.7	131, 40.6	13.193	<0.001
FEV1%	82.4± 26.5	87.0± 27.9	1.582	0.114
Respiratory comorbidity (n, %)	67, 54.0	129, 39.9	7.229	0.007
Pleural adhesion (n, %)	49, 39.5	75, 23.2	4.475	0.029
ASA ≥ 3 points (n, %)	76, 61.3	157, 48.6	5.776	0.016
Surgery time (minutes)	149.6± 58.3	129.2± 56.9	3.371	<0.001
Stage I (n, %)	64, 51.6	169, 52.3	0.018	0.893

表 4 Logistic 回归分析

Table 4 Logistic Regression Analysis

Parameters	B value	SE	Wals	P value	Exp(B)
Pleural adhesion	1.432	0.614	5.431	0.020	4.185
ASA ≥ 3 points	0.133	0.041	10.399	0.001	1.143
Smoking	1.203	0.427	7.932	0.005	3.329
Surgery time	0.484	0.233	4.312	0.038	1.623
Respiratory comorbidity	0.998	0.452	4.865	0.027	2.713

3 讨论

胸膜黏连多是继发于炎症、肿瘤、结核和创伤,胸腔积液内的纤维蛋白沉积于胸膜表面,导致壁层胸膜和脏层胸膜黏连或者肉芽组织增生,黏连的部分是薄结缔组织构成的纤维钙化桥,包含小血管和神经,肺癌的局部侵犯、局部组织增生和新生血管形成往往会形成胸膜腔黏连,是肺癌患者的常见表现,曾被视为 VATS 肺叶切除的手术禁忌症^[21,22]。随着医疗技术的进步和设备的改进,越来越多的胸外科医生可以通过 VATS 行肺叶切除,尤其是对于膜状和条索状黏连,需要术者找准间隙,术中仔细分离,但较为致密的黏连显著影响术中视野显露同时也增加了术中分离肺内组织的难度,增加了术中出血风险和术中中转开胸率^[23]。我们的研究显示行 VATS 肺叶切除的患者中,有 27.7% 患者有胸膜黏连,胸膜黏连的患者术中中转开胸率高于没有胸膜黏连的患者,而且术后手术并发症也多,可能与术后引流时间延长相关。胸膜腔黏连增加了术中中转开胸率和术后并发症的发生可能是以下几个原因:首先,胸膜黏连由于增加了手术的难度,尤其是处理包含有血管和神经的黏连时,会显著增加术中出血,在分离肺表面和壁层胸膜时很容易引起漏气,漏气往往在术后几天内可以消失,但术后仍有一部分患者会出现漏气延长^[24],严重漏气会引起气胸影响术后肺复张,加重肺水肿和肺不张,导致术后肺炎的发生,因此胸膜黏连会增加术后并发症的发生。其次,胸膜黏连的形成往往提示慢性炎

症,影响肺泡换气功能,引起术后肺炎和其他并发症的发生。最后,当胸外科医生面对胸膜黏连时为避免出血往往操作要小心,手术时间延长,更换操作设备时增加操作孔伤口周围组织撕裂,增加皮下气肿出现的可能性,麻醉时间延长后也增加了患者术后肺不张和肺炎的发生^[25]。我们的研究也证实了手术时间的延长是术后并发症发生的独立危险因素。对于胸膜腔黏连的患者,术前应高度警惕,影像学检查可反映部分胸膜增厚和膈肌位置,选择合适的手术间隙,手术开始打开壁层胸膜后用手指探查评估黏连程度,如果是部分黏连可综合利用钝性和锐性分离方法,如果黏连是广泛和较为致密且手指探查困难时可以考虑开胸手术。

有研究表明胸膜间皮细胞通过各种细胞信号转导有调节胸腔内液体循环的能力,胸膜黏连可损害胸膜间皮细胞调节液体循环的能力^[2]。本研究结果显示胸膜黏连患者术后引流较多且引流时间长,可能是由于胸膜间皮细胞调节液体平衡能力受损所致,尤其是当胸膜黏连累积到下部分胸腔时^[26]。此外,我们还发现吸烟和有术前呼吸系统合并症是术后发生并发症的独立危险因素,吸烟和合并有呼吸系统疾病的人往往存在慢性炎症,引起肺泡毛细血管间隔厚度变化和换气功能受损,导致术后并发症发生。

本研究有以下不足,作为回顾性研究有自身的弊端,比如选择偏倚、数据的完整性和同质性无法得到完全保证等。在判断患者是否存在胸膜腔黏连时主要依据患者的手术记录和影

像学检查,通过手术记录我们只能得到患者是否有胸膜腔黏连,但对于胸膜腔黏连的致密程度和范围无法进行准确评估,为解决以上问题,仍需要大样本多中心的前瞻性研究。

我们的研究表明,胸膜黏连增加了手术难度和中转开胸率、延长了手术时间、减缓了患者术后康复速度并增加了术后并发症发生的风险。在术前应仔细评估胸膜黏连程度,尤其是合并有呼吸系统疾病、术前 ASA 评分较高的吸烟患者,应认真评估患者手术风险,在术前充分和患者进行沟通,在术后积极预防相关并发症的发生。

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