

·临床研究·

同期双侧单孔胸腔镜手术在双肺多发结节治疗中的应用

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摘要:【目的】探讨同期双侧单孔胸腔镜手术在双肺多发结节治疗中的应用价值。【方法】回顾性收集2020年8月至2021年8月期间在中国科学技术大学附属第一医院胸外科行同期双侧单孔胸腔镜手术的40例患者的临床病理资料和围手术期资料。男性12例,女性28例;平均年龄(52±8.8)岁,中位数为[52.5(47.25~58)]岁。【结果】40例患者共切除107个肺结节,85个为恶性。病理诊断有30例多原发肺癌,6例单原发肺癌。手术出血量(48.87±19.29)mL,中位数为[40(30~67.5)]mL,手术时间(147.70±54.24)min,中位数为[145(113.5~170)]min,淋巴结清扫数6.20±9.13,中位数为[3(0~12)]个,术后首日NRS评分5.08±2.23。胸腔引流总量为(375.95±243.69)mL,中位数为[292.5(215~517.5)]mL。平均胸引管留置时间为(3.38±1.49)min,中位数为[3(3~4)]d,术后平均住院时间为(4.08±1.81)d,中位数为[4(3~5)]d。围手术期无死亡病例,并发症包括2例切口感染,3例一过性房颤,1例肺持续漏气,1例咯血,所有患者均顺利出院。【结论】同期双侧单孔胸腔镜手术治疗双肺多发结节是安全可行的,对于心肺功能良好,无严重基础疾病的有手术指征的双肺结节患者可作为首选治疗方案。

关键词:单孔胸腔镜手术;同期手术;双肺多发结节;多原发肺癌

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Simultaneous Bilateral Pulmonary Resections by Uniportal Video-assisted Thoracic Surgery for Bilateral Multiple Pulmonary Nodules

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Abstract:【Objective】To explore the application of simultaneous bilateral uniportal video-assisted thoracic surgery in the treatment of bilateral multiple pulmonary nodules.【Methods】The clinical and pathological characteristics, and perioperative data were analyzed in thoracic surgery from August 2021 to August 2021 at Department of Thoracic Surgery, the First Affiliated Hospital of University of Science and Technology of China. During the study period, 40 patients were included in the study, of which 12 were male, 28 were female, the average age was (52±8.8) [52.5(47.25~58)] years.【Results】A total of 107 nodules were resected, with 85 malignancy nodules, including 30 patients with bilateral primary lung cancer, 6 patients with primary lung cancer on one side. All patients underwent bilateral uniportal video-assisted thoracoscopic surgery (Uni-portal VATS), the average intraoperative blood loss was (48.87±19.29) [40(30~67.5)] mL, the average operation time was (147.70±54.24) [145(113.5~170)] min, the average number of resected lymph nodes was (6.20±9.13) [3(0~12)], the average NRS score in the 1st postoperative day was (5.08±2.23), the average pleural drainage was (375.95±243.69) [292.5(215.0~517.5)] mL. the average thoracic drainage time was (3.38±1.49) [3(3~

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4)] days, and the average postoperative hospital stay was (4.08 ± 1.81) [4(3~5)] days. Postoperative complications including: 2 cases of infection, 3 cases of atrial fibrillation, 1 case of hemoptysis for more than 1 week and 1 case of persistent air leakage for more than 3 days. All of them improved after treatment, and there were no serious complications and deaths in perioperative period.【Conclusion】 Simultaneous bilateral pulmonary resections via uniportal VATS is a safe and feasible minimally invasive procedure for patients with bilateral multiple pulmonary nodules.

Key words: uniportal video-assisted thoracoscopic surgery; simultaneous; bilateral multiple pulmonary nodules; multiple primary lung cancers

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最新全球癌症统计显示,2018年新发肺癌病例210余万例,因肺癌相关的死亡例数占所有与恶性肿瘤死亡相关人数的18.4%^[1]。国家癌症中心发布的恶性肿瘤流行情况显示,2015年肺癌的发病率和死亡率均居首位,5年总生存率约19.7%^[2]。筛查仍是早期发现肺癌的唯一途径,随着大众健康意识的增强和体检普及率的增高,越来越多的早期肺癌被发现。双侧多发性肺结节(bilateral multiple pulmonary nodules, BMPN)的检出率越来越高,其中多原发肺癌(multiple primary lung cancers, MPLC)占很大比例^[3-4]。胸腔镜手术凭借其创伤小、恢复快等优势成为肺癌外科治疗的一线方案^[5]。对于需要切除的单发肺结节,通过1次胸腔镜手术即可完成外科治疗。对于需要切除的BMPN,目前没有标准的治疗方案,大多数医疗中心通常分2次甚至多次手术切除。若能同期完成双侧手术,不仅减少2次麻醉及手术的风险,还能减轻患者的经济负担和心理压力,对于心肺功能良好的患者可以选择。我们回顾性收集了2020年8月~2021年8月期间在我科接受同期双侧单孔胸腔镜肺手术的患者,总结分析患者的临床病理资料、围手术期资料以探讨同期双侧单孔胸腔镜手术在肺外科治疗中的价值,现将结果报告如下。

1 材料与方 法

1.1 病例资料

回顾性收集2020年8月~2021年8月期间在中国科学技术大学附属第一医院胸外科收治的双肺结节患者的资料。纳入标准:需切除的肺结节有手术指征:经消炎随访复查后存在着早期肺癌的影像学征象如血管束征、胸膜凹陷征、空泡征等,或随访过程中结节变大、实行成分增加经综合评估后

为高危结节。且双侧至少各有一个需手术切除;肺功能正常,无远处转移等手术禁忌;接受同期双侧单孔胸腔镜肺手术。排除标准:要求分期手术;心肺功能异常,年龄高于70岁,合并严重的心脑血管疾病等基础疾病不能耐受同期双侧手术。研究院伦理委员会批准(编号:2022-RE-065),所有患者知情同意。

所有患者手术前行胸部薄层CT扫描加病灶三维重建,心电图,肺功能,腹腔彩超等检查,60岁以上的患者加做超声心动图检查;2 cm以上的实性结节的患者加做头颅磁共振、全身骨显像等检查,中央型病变另行支气管镜检查;术前常规行血检查。

经病理诊断明确的浸润性腺癌采用AJCC第8版TNM分期系统进行分期^[6]。多原发肺癌按Martini-Melamed标准诊断^[7],每个病灶独立分期。

1.2 手术方法

根据双侧肺结节的位置、大小、肺功能和术中冰冻等情况制定手术方案,部分结节术前行CT引导下一次性肺结节定位针定位。预期肺切除范围较小侧先行手术(楔形侧优于肺段侧,肺段侧优于肺叶侧);如双侧切除范围相当,则先行右侧手术。

患者静脉吸入复合麻醉,双腔气管插管或单腔管联合封堵管进行单肺通气,侧卧位,取腋前线与腋中线间第4或第5肋间长约3~4 cm小切口,切口放置切口保护套。胸腔镜探查胸腔有无积液、粘连和播散结节,根据术中结节情况选择切除范围如楔形切除、肺段切除或肺叶切除,若术中冰冻结果提示为浸润性肺癌继续行纵隔淋巴结清扫术。操作孔处留置26#引流管接水封瓶或硅橡胶引流管接球。一侧术毕后,重新翻身至对侧卧位,同法行对侧手术。

采用数字评定量表(numeric rating scale, NRS)评估患者术后疼痛强度。分为无痛(NRS=0)、轻度

(NRS=1~3)、中度(NRS=4~6)和重度(NRS=7~10)疼痛4个等级。

术后常规行胸部X线(Chest X Radiograph, CXR)检查,双肺复张良好,胸腔无积气积液,每日胸引量200 mL以下且无漏气时拔除胸管。出院后定期随访。

1.3 观察指标

收集患者的临床资料、围手术期资料和病理资料。临床资料包括年龄,性别,吸烟史,肺癌家族史,结节位置、数目和大小,术前合并症和影像学表现等;围手术期资料包括手术方式,手术时间,术中出血量,胸腔引流液总量,胸引管留置时间,术后住院时间,术后首日NRS评分以和并发症(咯血、切口感染、肺漏气、心律失常等);病理资料包括TNM分期,病理类型和病理诊断。

1.4 统计学方法

SPSS 19.0统计学软件对数据进行分析。定量资料用均数±标准差($\bar{x} \pm s$)和中位数(下四分位数~上四分位数)[$M(P_{25} \sim P_{75})$]表示,分类资料用频数(n)和百分比(%)表示。

2 结果

共40例患者纳入该研究。其中男性12例,女性28例;平均年龄(52 ± 8.8)岁,中位数为[52.5(47.3~58.0)]岁;年龄范围:(27~69)岁。其中8例男性有吸烟史;6例有肺癌家族史;其中2例合并有高血压病,2例合并有糖尿病,2例合并有脑血管疾病,2例合并有窦性心律失常,1例同时合并有糖尿病和窦性心律失常(表1)。

术前胸部CT共发现133个肺结节,其中手术切除107个肺结节,剩余未切除的26个肺结节是经术前评估无手术指征且不能简单楔形切除者。其中26例切除2个肺结节,14例切除2个以上结节。结节大小在1 cm以下有31个,1~2 cm有59个,2~3 cm有17个。分别位于右上肺29(27.10%),右中肺6(5.61%),右下肺17(15.89%),左上肺40(37.38%),左下肺15(14.02%)。影像学征象表现为纯磨玻璃(pure ground-glass nodule, pGGN)有37(34.58%),混合磨玻璃(mixed Ground-Glass Nodule, mGGN)有54(50.47%),实性结节有16(14.95%;表1,图1)。

表1 病例资料

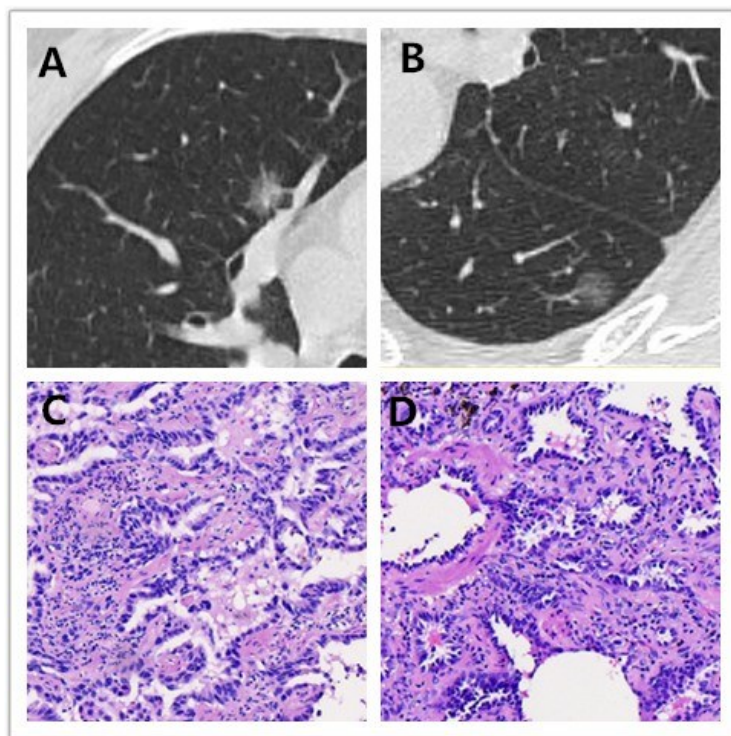
Table 1 Clinical characteristics of 40 patients

[n (%), ($\bar{x} \pm s$), $M(P_{25} \sim P_{75})$]

Characteristics	Patients
Age/years	52±8.8 [52.5(47.3~58.0)]
Sex	
Male	12(30%)
Female	28(70%)
Smoking history	
Yes	8(20%)
No	32(80%)
Preoperative complications	
Hypertension	2
Diabetes	3
Arrhythmia	3
Cerebrovascular disease	2
Number of nodules	
2	26(65%)
>2	14(35%)
Classification	
pGGN	37(34.58%)
mGGN	54(50.47%)
Solid nodule	16(14.95%)
Lesion location	
Right upper lobe	29(27.10%)
Right middle lobe	6(5.61%)
Right lower lobe	17(15.89%)
Left upper lobe	40(37.38%)
Left lower lobe	15(14.02%)
Family history of cancer	
Yes	6(15%)
No	34(85%)
Lesion size/cm	
≤1	31(28.97%)
(1,2]	59(55.14%)
(2,3]	17(15.89%)

GGN: ground glass nodule.

40例患者均接受同期双侧胸腔镜肺手术且R0切除,其中接受肺叶—亚肺叶切除者10例(肺叶—楔形8例,肺叶—肺段2例);亚肺叶—亚肺叶切除



One case of patient with BMPN. Preoperative CT image of mGGN in the right upper lobe, pGGN in the left lower lobe of a 52-year-old male. The size of mGGN(A) is 10 mm and pathology is adenocarcinoma(C, HE, $\times 200$), with the spiculated sign. The size of the pGGN(B) is 9.5 mm and pathology is MIA(D, HE, $\times 200$), with the vascular convergence sign. BMPN: bilateral multiple pulmonary nodules, CT: computed tomography, GGN: ground glass nodule, MIA: minimally invasive adenocarcinoma.

图1 1例双肺多发结节CT和病理资料

Fig. 1 CT and Pathologic characteristics of 1 patient with BMPN

者30例(肺段—肺段3例,肺段—楔形11例,楔形—楔形16例)。40例患者的手术出血量 48.87 ± 19.29 mL,中位数为[40(30~68)] mL,手术时间(147.70 ± 54.24) min,中位数为[145(114~170)] min,淋巴结清扫数 6.20 ± 9.13 ,中位数为[3(0~12)]个,术后首日NRS评分 5.08 ± 2.23 。胸腔引流总量为 375.95 ± 243.69 ,中位数为[292.5(215.0~517.5)] mL。平均胸引管留置时间为 3.38 ± 1.49 ,中位数为[3(3~4)] d,术后平均住院时间为(4.08 ± 1.81) d,中位数为[4(3~5)] d。围手术期无死亡和严重并发症病例,轻微并发症共7例,其中2例切口感染,3例一过性房颤,1例肺漏气超过1周,1例咯血超过1周,以上患者均治愈出院(表2)。

病理诊断为原发肺癌的有36例,其中多原发肺癌有30例,单原发肺癌有6例。切除的107个结节中有85个为恶性,其中腺癌19个,微浸润腺癌42个,原位癌24个,其余22个非癌结节中18个为非典型腺瘤样增生。每个结节根据TNM独立分

期,其中0期有19个,IA1期有7个,IA2期有3个,IA3期有5个,IB期及以上者有2个(表3)。

3 讨论

随着高分辨率计算机断层扫描(high-resolution computed tomography, HRCT)逐渐成为肺癌早期筛查和诊断的重要手段^[8],影像学上出现了磨玻璃阴影(ground-glass opacity, GGO)与磨玻璃结节(ground-glass nodule, GGN),GGN的临床特征包括恶性肿瘤和良性疾病,例如局灶性间质纤维化、炎症、出血和腺癌等^[9]。然而,早期肺癌影像学表现多为肺磨玻璃样结节^[10]。PETCT对于肺结节的诊断敏感性和特异性约80%左右,假阳性及假阴性率均高,尤其直径1 cm以下者敏感性更差^[11]。CT引导下经皮肺穿刺是取得病理诊断的方法之一,但因取得组织少,假阴性率高^[12]。肺结节良恶性鉴别诊

表2 手术资料

Table 2 Surgical characteristics

[*n* (%), ($\bar{x} \pm s$), *M* ($P_{25} \sim P_{75}$)]

Variables	Patients
Surgical procedures/s	
L-W	8
L-S	2
S-S	3
S-W	11
W-W	16
Operative time/min	147.70±54.24 [145 (114 ~ 170)] min:44, max:275
Surgical blood loss/mL	48.87±19.29 [40 (30 ~ 68)] min:45, max:140
Number of lymph nodes/ <i>n</i>	6.20±9.13 [3 (0 ~ 12)] min:0, max:18
Pleural drainage/mL	375.95±243.69 [292.5 (215.0 ~ 517.5)] min:35, max:1 125
Chest tube duration/d	3.38±1.49 [3 (3 ~ 4)] min:2, max:11
Postoperative admission duration/d	4.08±1.81 [4 (3 ~ 5)] min:2, max:11
Postoperative complications	
Pulmonary air leakage	1
Hemoptysis	1
Infection of incisional wound	2
Arrhythmia	3
NRS score in the 1 st postoperative day/d	5.08±2.23 [5 (4 ~ 6)] min:3, max:8

L: lobectomy; S: segmentectomy; W: wedge resection; NRS: numeric rating scale.

断的金标准是手术切除后的病理诊断。本研究中,经病理证实为肺癌的有36例,诊断率90%,其中多原发肺癌75%,单原发肺癌15%。纳入研究的40例患者共有133个肺结节,根据判读有107个结节切除,其中85个为恶性,恶性率为79.44%。肺癌患者多结节的发生率约为0.2%~20%^[13],与本研究结果相符。多原发肺癌、肺内转移癌均表现为多发肺结节,多原发肺癌与肺内转移癌的治疗方案和远期

表3 病理资料

Table 3 Pathologic characteristics

[*n* (%), *n*]

Variables	Patients
Pathological diagnosis	
SMPLC	30 (75%)
Single primary lung cancer	6 (15%)
Bilateral benign nodules	4 (10%)
TNM stage	
0	19
IA1	7
IA2	3
IA3	5
IB	2
Pathological type	
Adenocarcinoma	19 (17.76%)
MIA	42 (39.25%)
AIS	24 (22.43%)
AAH	18 (16.82%)
Others	4 (3.73%)

AIS: adenocarcinoma in situ; AAH: atypical adenomatous hyperplasia; MIA: minimally invasive adenocarcinoma; SMPLC: synchronous multiple primary lung cancers.

预后差异明显,临床医生需准确判断肺内多结节的性质以免误诊。我们的经验是根据ACCP指南、亚洲共识指南、Fleischner协会指南、肺结节诊治中国专家共识和NCCN非小细胞肺癌临床实践指南所推荐的肺结节影像学处理策略进行分析及比较^[14],对于影像学表现为周围型分布、形态孤立的、密度混杂的类圆形结节影尤其伴有伴毛刺分叶,支气管空泡征,胸膜牵拉或血管束集等特点者,需密切随访,把握手术时机。

胸腔镜的出现标志着胸外科微创时代的开端,经过多年的发展,我科单孔胸腔镜可以完成各类肺切除手术,在生活质量、术后急慢性疼痛、术后并发症等方面均优于三孔胸腔镜手术,单孔胸腔镜让肺手术更微创^[15-17]。伴随着技术的发展,近年来早期肺癌越来越多的术式由肺叶切除术向解剖性肺段切除术过度,肺段切除术在完整切除病变的同时,保留了更多的肺组织^[18]。若同期完成双侧肺手术,单孔胸腔镜手术也间接的进一步微创。本研究中,肺

叶—亚肺叶切除者10例;亚肺叶—亚肺叶切除者30例。手术出血量(48.87 ± 19.29) [$40(30\sim 68)$] mL,手术时间(147.70 ± 54.24) [$145(114\sim 170)$] min,淋巴结清扫数(6.20 ± 9.13) [$3(0\sim 12)$]个。我们对于双侧多发肺结节拟行同期手术的原则包括:①术前充分评估每个独立结节的手术指征和需要切除的范围。②切除范围同期不超过十个肺段。若双侧均需行肺叶切除术,除右中肺外,建议分期手术;一侧肺需行联合肺叶切除或袖式切除甚至全肺切除术,则不建议行同期双侧手术。微浸润和原位腺癌行亚肺叶切除(楔形或肺段切除术)。癌前病变定期随访或者在总切除范围不大基础上同侧可楔形切除情况下予以顺带切除。③侧切除范围相当,则先行右侧手术;若定位后有少量气胸,则气胸侧先行手术,防止术中气胸进一步加重。④术中根据冰冻结果结合患者病变大小、实体成分比例和影像学表现综合诊断,必要时调整手术方式。

双肺结节行分期手术是相对安全的,但分期手术存在两次手术间隙肿瘤进展,经济和心理负担等问题,同期双侧手术存在创伤相对较大,术后疼痛明显,恢复困难等问题。研究表明,综合评估术前的影像学表现、心肺功能储备等,选择合适的病人制定合理的手术方式进行双侧同期胸腔镜手术是安全的^[19-21]。本研究中,术后首日NRS评分 5.08 ± 2.23 。胸腔引流总量为(375.95 ± 243.69) [$292.5(215.0\sim 517.5)$] mL。平均胸引管留置时间为(3.38 ± 1.49) [$3(3\sim 4)$] d,术后平均住院时间为(4.08 ± 1.81) [$4(3\sim 5)$] d。围手术期无严重并发症,2例患者出院后切口感染,经门诊积极换药治疗后治愈;3例患者一过性房颤,经对症治疗后好转,随访中没有再发作;1例患者持续重度漏气,证实是肺大疱破裂所致,经手术切除肺大疱后顺利出院;1例肺叶-肺段切除的患者出现咯血,经消炎止血等治疗后于术后11天顺利出院。本研究证实同期双侧手术是安全可行的,我们的经验是:①适应症的严格把握:心肺功能评估良好,避免高龄或者有心肺基础疾病者。②术前充分评估:术前常规行薄层胸部CT加病灶三维重建,对于非外周肺结节不能楔形切除者行3D重建模型精准定位,非胸膜下结节使用一次性肺结节穿刺针进行术前定位。

③制定合理的手术方式:主要结节侧避免行全肺切除、联合肺叶切除和袖式切除,若评估后确需进行上述手术方式则建议分期手术。除右中肺外,不建议同期行肺叶-肺叶切除手术。④术中精细操作:利用荧光腔镜技术完成精准肺段、亚段切除,能快速地显示段间交界,可以明显缩短手术时间。复杂肺段等手术残面有漏气者可使用断装线加缝残端,蛋白粘合剂喷洒创面等方法减少肺漏气的发生。对于楔形切除且无漏气者可留置细软管负压球,可有效减轻术后疼痛^[22]。⑤围手术期快速康复:术前术后加强肺功能锻炼,术后加强呼吸道管理,指导饮食加强营养,早期下床活动,加强疼痛管理,积极预防并发症,促进康复。

1898年,Billroth首次报道了一例多原发癌患者^[23],1924年,Beyreuther首次描述了多原发癌的概念,1975年,Martini和Melamed^[7]描述了第一个MPLC的诊断标准^[24]。MPLC是指同一患者同时或先后发现肺部有两个或以上的原发性肺癌。目前MPLC发生的机制尚不清楚,有学者认为是多部位基因突变所致^[25]。本研究中75%(30/40)的患者证实为多原发肺癌,分期大多在IA期甚至更早,大多为非吸烟的年轻女性。目前MPLC没有权威的治疗指南,我们的建议是:①多学科团队(multidisciplinary team,MDT)会诊^[26],综合各学科意见的为病人制定出最合理的治疗方案;②对于早期的MPLC,优先考虑手术治疗,适合的患者选择行同期双侧单孔胸腔镜手术;③不能行同期双侧手术者先行处理主病灶,间隔4~6周后分期手术;④不需要切除的病灶在随访过程中有恶变的倾向,评估后若不能再次手术者可考虑行射频消融治疗或者立体定向放疗^[27-28]。

综上所述,同期双侧单孔胸腔镜肺手术治疗双肺多发结节是安全可行的。对于心肺功能良好,无严重基础疾病的双肺结节患者。严格掌握手术适应症,合理的术前规划,精准地术中操作,围手术期的规范管理可有效减少并发症,可使其最大化受益。本研究为回顾性研究,存在样本量相对较少、随访时间相对较短等不足,需要更大样本量和更长时间随访的研究进一步验证。

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