

# 术中冰冻病理对肺结节胸腔镜手术 切除范围的指导意义\*

于 雷\*\* 赵庆涛 王志康 张霄鹏 王会恩 张 华

(河北省人民医院胸外二科, 石家庄 050000)

**【摘要】 目的** 探讨肺结节术中冰冻病理与术后病理判断浸润范围上的一致性, 明确术中冰冻病理是否可以协助术者确定肺结节手术切除的范围。 **方法** 2017 年 1 月~2018 年 6 月电视辅助胸腔镜手术切除肺结节 156 例, 分析术中冰冻病理与术后病理的诊断符合率。 **结果** 术中冰冻病理诊断非典型腺瘤样增生 (atypical adenomatous hyperplasia, AAH)、原位腺癌 (adenocarcinoma in situ, AIS) 及微浸润腺癌 (minimally invasive adenocarcinoma, MIA) 103 例, 浸润性腺癌 (invasive adenocarcinoma, IA) 53 例; 术后病理证实 AAH、AIS 及 MIA 106 例, IA 50 例。根据病灶侵袭性、复发及转移的风险程度将 AAH、AIS、MIA 定义为低风险病灶, IA 定义为高风险病灶。术中冰冻病理诊断高风险病灶敏感性 98.0% (49/50), 特异性 96.2% (102/106), 准确率 96.8% (151/156)。术中冰冻病理诊断低风险病灶预测值 99.0% (102/103), 高风险病灶预测值 92.5% (49/53)。 **结论** 术中冰冻病理在判断 IA 方面具有较高的诊断符合率, 在准确区别 AAH 与 AIS 和 AIS 与 MIA 存在不确定性。在肺结节手术切除范围的制定上, 术中冰冻病理可以作为重要的指导依据。

**【关键词】** 肺结节; 术中冰冻病理; 术后病理; 肺腺癌

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**The Significance of Intraoperative Frozen Pathology for Video-assisted Thoroscopic Resection Range for Lung Nodules** Yu Lei, Zhao Qingtao, Wang Zhikang, et al. Second Department of Thoracic Surgery, Hebei General Hospital, Shijiazhuang 050000, China

Corresponding author: Yu Lei, E-mail: yulei0212@sina.com

**【Abstract】 Objective** To explore the consistency of frozen pathology in pulmonary nodule operation and the extent of infiltration judged by pathology after operation, and to determine whether intraoperative frozen pathology can help surgeons to determine the extent of pulmonary nodule resection. **Methods** We chose 156 patients with lung nodules from January 2017 to June 2018 in our hospital, all of which were given video-assisted thoracoscopic surgery. And the coincidence rate between intraoperative frozen pathology and postoperative pathological diagnosis was analyzed. **Results** Intraoperative frozen pathological diagnosis showed 103 cases of atypical adenomatous hyperplasia (AAH), adenocarcinoma in situ (AIS) and minimally invasive adenocarcinoma (MIA), and 53 cases of invasive adenocarcinoma (IA). And finally 106 cases of AAH, AIS and MIA, 50 cases of IA were confirmed by postoperative pathology. According to the risk of lesion invasion, recurrence and metastasis, we defined the AAH, AIS and MIA as the low risk lesions, and IA as the high risk lesions. The sensitivity, specificity and accuracy of intraoperative frozen pathological diagnosis were 98.0% (49/50), 96.2% (102/106), and 96.8% (151/156), respectively. The predictive value of intraoperative frozen pathology was 99.0% (102/103) for low-risk lesions and 92.5% (49/53) for high risk lesions. **Conclusions** Intraoperative frozen pathology has a high diagnostic coincidence rate in the judgment of IA, while it is uncertain to distinguish the AHH with AIS, and AIS with MIA. For determination of lung nodule resection range, intraoperative frozen pathology can be used as an important basis and guidance.

**【Key Words】** Lung nodule; Intraoperative frozen pathology; Postoperative pathology; Lung adenocarcinoma

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\*\* 通讯作者, E-mail: yulei0212@sina.com

2016 年全球范围内约 200 万肺癌新发病例,较 2006 年增长了 28%,约 170 万病人死于肺癌,无论在患病率还是在死亡率上肺癌均居所有恶性肿瘤首位<sup>[1]</sup>。随着低剂量螺旋 CT(low dose CT,LDCT)及高分辨率 CT(high resolution CT,HRCT)的普及,越来越多的肺结节被发现。肺结节的定义是边界清晰、类圆形或不规则形的病灶,影像学表现为密度增高影,直径 $\leq 30$  mm,周围可被含气肺组织包绕<sup>[2,3]</sup>。根据结节中是否含有实性成分,将肺结节分为纯磨玻璃结节、混合磨玻璃结节及实性结节<sup>[4]</sup>。持续存在的磨玻璃结节,特别是含有实性成分的结节,更倾向于恶性可能,如肺腺癌<sup>[5,6]</sup>。随着越来越多非典型腺瘤样增生(atypical adenomatous hyperplasia, AAH)、原位腺癌(adenocarcinoma in situ, AIS)及微浸润腺癌(minimally invasive adenocarcinoma, MIA)被体检发现,亚肺叶切除也逐渐被接受和推崇。如何选择手术方式,癌灶浸润范围的判断显得尤为重要。本研究对我院 2017 年 1 月~2018 年 6 月 156 例术中冰冻病理及术后病理进行一致性分析,探讨术中冰冻病理是否可以作为指导肺结节手术切除范围制定的依据。

## 1 临床资料与方法

### 1.1 一般资料

本组 156 例,男 58 例,女 98 例。年龄 27~79 岁,( $58.3 \pm 10.1$ )岁。均为体检发现肺部单发结节入院。结节位于右肺 101 例(上叶 60 例,中叶 12 例,下叶 29 例),左肺 55 例(上叶 43 例,下叶 12 例)。磨玻璃结节(ground-glass nodules,GGNs)124 例,其中纯磨玻璃结节(pure ground-glass opacity, pGGO)77 例,混合磨玻璃结节(mixed ground-glass opacity, mGGO)47 例;实性结节 32 例。肿瘤直径 3~30 mm, ( $14.1 \pm 7.7$ )mm。肺楔形切除 72 例,肺段切除 30 例,肺叶切除 54 例。

病例选择标准:①肺结节直径 $\leq 30$  mm;②完成胸腔镜手术;③有术中冰冻结果;④术后病理为 AAH 或恶性。排除标准:①术前已有明确病理;②临床资料不全者。

### 1.2 方法

1.2.1 术前准备 术前均行血常规、生化全项、凝血五项、尿常规、术前免疫八项、心电图、肺功能、心脏超声、胸部 CT 等常规检查。mGGO 或实性结节者需进一步完善头颅 MRI、骨扫描、肝胆胰脾及双侧肾上腺超声等检查,以明确是否存在远处转移;

pGGO 无须进行上述检查<sup>[7,8]</sup>。

1.2.2 病理诊断 冰冻切片诊断:术中获取肺组织以后,测定结节大小,于最大径及实性成分最多位置切开,一般为 1~4 块,包埋处理后利用冷冻切片机进行冰冻组织切片处理,控制温度为  $-22 \sim -20$   $^{\circ}\text{C}$ ,切片厚度 4~7  $\mu\text{m}$ ,并进行快速 HE 染色处理,光镜观察。诊断由 2 名高年资病理医师做出,若存在分歧需共同协商确定浸润范围,浸润程度的确定根据 2011 版国际肺癌研究协会/美国胸科学会/欧洲呼吸学会国际多学科肺腺癌分类的标准确定<sup>[9]</sup>。石蜡切片诊断:肺组织标本进行冰冻切片处理后,选择剩余肺组织用 10% 甲醛溶液固定处理,常规石蜡切片处理,切片厚度为 3~5  $\mu\text{m}$ ,再进行 HE 染色处理,光镜观察。最终诊断的得出同冰冻切片诊断。

1.2.3 手术方案的制定 根据术中冰冻病理结果,若考虑 AAH、AIS、MIA 行胸腔镜下亚肺叶切除术(病灶位于周边优势位置者行楔形切除术,切缘 $>2.0$  cm;病灶位于肺叶中心者行肺段切除或联合肺段切除术);若考虑浸润性腺癌(invasive adenocarcinoma, IA)行胸腔镜下肺叶切除+淋巴结清扫术。

## 2 结果

术中冰冻病理诊断与术后病理诊断对比见表 1。根据病灶侵袭性、复发及转移的风险程度,我们对病理结果进行整合,将 AAH、AIS 及 MIA 称为低风险病灶,IA 称为高风险病灶。术中冰冻病理诊断低风险病灶 103 例,术后病理诊断低风险病灶 102 例,升级为高风险病灶 1 例;术中冰冻病理诊断高风险病灶 53 例,术后病理确诊高风险病灶 49 例,降级为低风险病灶 4 例。术中冰冻病理诊断高风险病灶敏感性 98.0% (49/50),特异性 96.2% (102/106),准确率 96.8% (151/156)。术中冰冻病理诊断低风险病灶预测值 99.0% (102/103),高风险病灶预测值 92.5% (49/53),见表 2。

表 1 术中冰冻病理与术后病理比较

术中冰冻病理	术后病理			
	AAH	AIS	MIA	IA
AAH ( $n=12$ )	10	2	0	0
AIS ( $n=39$ )	1	31	7	0
AAH 或 AIS ( $n=10$ )	4	6	0	0
MIA ( $n=38$ )	0	7	30	1
AIS 或 MIA ( $n=4$ )	0	1	3	0
IA ( $n=53$ )	0	0	4	49

AAH:非典型腺瘤样增生; AIS:原位腺癌; MIA:微浸润腺癌; IA:浸润性腺癌

表 2 术中冰冻病理与术后病理诊断高、低风险病灶		
术中冰冻病理	术后病理	
	高风险病灶	低风险病灶
高风险病灶 (n = 53)	49	4
低风险病灶 (n = 103)	1	102

根据术中冰冻病理确定手术切除范围,术中冰冻病理提示 IA 53 例,MIA 1 例,由于位置深在靠近

气管根部行肺叶切除术,最终术后病理 IA 50 例,MIA 4 例;术中冰冻病理提示 AAH、AIS、MIA 共 102 例,行楔形切除、肺段切除术,术后病理 AAH、AIS、MIA 共 101 例,IA 1 例。由于术中冰冻病理导致手术切除范围增大 4 例,导致手术切除范围减小 1 例,术中冰冻病理指导手术切除范围准确率 96.8% (151/156),见表 3。

表 3 手术切除范围与术中冰冻、术后病理的关系				
手术切除范围		术中冰冻病理		术后病理
肺叶切除 + 淋巴结清扫 (n = 54)		MIA (n = 1)	IA (n = 53)	MIA (n = 4) IA (n = 50)
楔形切除或肺段切除 + 淋巴结采样 (n = 102)		AAH、AIS、MIA (n = 102)	IA (n = 0)	AAH、AIS、MIA (n = 101) IA (n = 1)

### 3 讨论

肺癌作为世界范围内发病率及死亡率最高的癌症之一,早期诊断及治疗愈发重要。随着胸部计算机断层扫描检查的广泛开展,越来越多无症状的肺 GGNs 被发现<sup>[10]</sup>。对于长期存在或逐渐增大,在临床上考虑为恶性的结节需要手术切除。随着胸腔镜技术的不断成熟及普及,越来越多的患者倾向于尽早切除病灶。肺叶切除同时行淋巴结清扫术是早期非小细胞肺癌手术治疗的金标准<sup>[11]</sup>。1995 年肺癌研究组进行一项前瞻性随机临床试验的研究<sup>[12]</sup>,对比临床分期 T1N0M0 肺癌患者肺叶切除与亚肺叶切除的疗效,2 组 5 年生存率并无统计学差异,但亚肺叶切除术组局部复发率明显高于肺叶切除术组,该研究巩固了肺叶切除术作为肺癌外科治疗的标准术式地位<sup>[13]</sup>。随着越来越多 I A 期腺癌、原位腺癌、微浸润腺癌及附壁生长方式为主腺癌的发现,亚肺叶切除(楔形切除或肺段切除)的地位逐渐被认可<sup>[14-16]</sup>。

2011 年国际肺癌研究协会/美国胸科学会/欧洲呼吸学会联合制定国际多学科肺腺癌分类标准,提出 AAH、AIS、MIA 等概念<sup>[9]</sup>。AIS、MIA 手术预后极佳,很少存在淋巴结转移及远处转移,完整切除后 5 年生存率可达 100%<sup>[17-20]</sup>。肺结节手术方式的选择,何时行肺叶切除,何时行亚肺叶切除,浸润范围的判断显得尤为重要。通过术前 CT 检查判断结节大小、是否为 pGGN、实性成分比例、胸膜牵引、分叶征等来确定浸润范围<sup>[21-24]</sup>是目前常用的方法,但准确性有待商榷。如何以更为精准及客观的方法于术中快速评估浸润范围,对手术方案的制定意义重大。本研究分析术中冰冻病理与术后常规病理符合

情况,将 AAH、AIS 及 MIA 定义为低风险病灶,IA 为高风险病灶。本研究结果显示术中冰冻病理诊断低风险病灶预测值 99.0% (102/103),高风险病灶预测值 92.5% (49/53),诊断低、高风险病灶准确率 96.8% (151/156)。由于术中冰冻病理受取材局限、制片和阅片时间短、标本冰晶等原因,无法做到与术后常规病理完全一致。因此,术中冰冻病理在准确划分 AAH 与 AIS、AIS 与 MIA 仍存在不确定性,需要术后核实明确,与之前相关研究相符<sup>[25]</sup>。亚肺叶对于 AIS、MIA 而言,切除范围完全足够<sup>[20,25]</sup>,所以术中冰冻病理即使无法准确判定 AIS 与 MIA,但对手术方案的制定并不影响。

综上,术中冰冻病理可以作为指导手术方案制定的重要依据,但仍有一定的局限性,在准确划分 AAH 与 AIS 和 AIS 与 MIA 上存在不足,需要不断改进方法提高诊断精准度,为以后临床方案的决策提供可靠的依据。

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