

关于早期非小细胞肺癌手术方式选择研究进展

邵盛腾^{1*}, 衣腾飞¹, 朱 晗², 秦 坤³, 刘玉洪^{1#}

¹青岛大学附属医院胸外科, 山东 青岛

²烟台毓璜顶医院耳鼻喉科, 山东 烟台

³青岛大学附属医院急诊科, 山东 青岛

Email: #qdlyuhong@sohu.com

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摘 要

肺癌是一种常见的肿瘤, 在全球范围内有较高的发病率。近年来, 随着检查技术的进步, 早期非小细胞肺癌(non-small cell lung carcinoma, NSCLC)的发病率也随之上升。目前, 手术切除仍然是早期NSCLC的首选治疗方法, 手术方式主要包括: 肺叶切除术, 肺段切除术以及楔形切除术。本文主要探讨上述手术方式在早期非小细胞肺癌患者中的选择, 来为早期NSCLC的治疗提供参考。

关键词

非小细胞肺癌, 手术方式, 肺叶切除术, 肺段切除术, 楔形切除术

Research Progress of Surgical Approach for Early Stage Non-Small Cell Lung Carcinoma

Shengteng Shao^{1*}, Tengfei Yi¹, Han Zhu², Kun Qin³, Yuhong Liu^{1#}

¹Department of Thoracic Surgery, The Affiliated Hospital of Qingdao University, Qingdao Shandong

²Department of Otolaryngology, Yantai Yuhuangding Hospital, Yantai Shandong

³Department of Emergency, The Affiliated Hospital of Qingdao University, Qingdao Shandong

Email: #qdlyuhong@sohu.com

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Abstract

Lung cancer is a common tumor with a high incidence worldwide. With the development of ex-

*第一作者。

#通讯作者。

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amination, the incidence of early-stage non-small cell lung carcinoma (NSCLC) is increasing recently. At present, surgical resection is still the preferred treatment for early stage NSCLC, the main surgical methods include lobectomy, segmentectomy and wedge resection. Therefore, this paper focuses on the choice of above approaches for patients with early-stage NSCLC so as to provide a reference for the treatment for early-stage NSCLC.

Keywords

Non-Small Cell Lung Carcinoma, Surgical Approach, Lobectomy, Segmentectomy, Wedge Resection

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1. 引言

肺癌的特点是早期转移和淋巴扩散,存活率低,是世界许多地区与恶性肿瘤相关死亡的主要原因。随着低剂量螺旋计算机断层扫描(LDCT)和高分辨率计算机断层扫描(HRCT)在肺癌筛查中的广泛使用,早期肺癌患者的数量也不断增加,这也意味着胸外科医生在临床实践中可能会遇到更多的小周围型肺癌[1],在这些病灶中大约有 10%被证实为非小细胞肺癌(non-small cell lung cancer, NSCLC) [2]。虽然 NSCLC 的预后不甚乐观,但是 IA 期 NSCLC 的患者采取适当的手术治疗后 5 年生存率可高达 70%,甚至有获得治愈机会[3]。

毫无疑问,手术切除仍然是早期 NSCLC 的首选治疗方法。曾经肺叶切除术是早期 NSCLC 的标准手术方式,据 1995 年北美肺癌研究小组研究结果显示, I 期 NSCLC 的首选治疗方法是肺切除加根治性淋巴结清扫,与采用亚肺切除术相比,选择肺叶切除术的患者的生存率更高[4]。而且肺叶切除术被证明可以减少复发风险和优化长期生存的机会[5]。但是该研究包括不同临床阶段的患者并没有将亚肺切除术中的肺段切除术和楔形切除术分开来,因此结论受到一些专家的质疑。

近年来,随着相关临床试验结果的公布和关于这一主题的大量回顾性研究以及 meta 分析的开展,使我们对早期非小细胞肺癌标准手术方式的选择产生了疑惑,主要争论点在于是否选取亚肺叶切除术,包括肺段切除术和楔形切除术,其中肺段切除术,也可以称之为解剖性切除,是指切除一个解剖单位,通常还包括更大的淋巴结清扫范围,如果肺部的小结节在肺段切除之后,肿瘤预后方面类似于肺叶切除术,那么肺段切除术可能将会是他们首选的手术方式,因为它们切除的肺组织更少,从而可以更好地保存肺功能且不影响生存率,这一优势特别是在肺功能有限的患者或老年人中尤为显著[6]。而楔形切除术是指切除肺占位性病变部分,不考虑解剖边界的切除方式。

2. 肺叶切除术与亚肺叶切除术

目前研究亚肺叶切除术与肺叶切除术的临床试验中,最早的一项是 1995 年发布的, Ginsberg 等人认为与肺叶切除术相比,亚肺叶切除术并不能改善 I 期 NSCLC 术前的并发症、术后的死亡率或肺功能。而且由于亚肺叶切除术的死亡率和局部复发率较高。肺叶切除术仍然被认为是周围型 T1N0 非小细胞肺癌患者的首选手术方式[4]。

由国家癌症研究所(National Cancer Institute, NCI)于 2008 年开展的一项前瞻性研究 CALGB140503,其主要目的是比较临床 IA 期的 NSCLC 在肺叶切除术和亚肺叶切除术术后的生存率。其结果发现在这些

癌症患者中,术后的死亡率在肺叶和亚肺叶切除术之间几乎没有差别[7]。同样,在一项回顾性研究中筛选出肿瘤 < 3 cm 的,临床分期为 IA 的 NSCLC 患者,分别对行肺叶切除术和亚肺叶切除术的患者进行比较,发现两组患者术后生存率相当[8]。但是在另一项关于早期 NSCLC 的研究中发现,对于 I 期 NSCLC 的患者,亚肺叶切除术的生存率低于肺叶切除术,而肺段切除术的结果与肺叶切除术相当;然而对于肿瘤 ≤ 2 cm 的 IA 期 NSCLC 患者,亚肺叶切除术与肺叶切除术有着相似的生存率[9]。

磨玻璃样外观可能是另一个决定治疗方式的重要因素。人们普遍认为,对于磨玻璃成分 ≥ 50% 的结节预后较好,可以选择亚肺叶切除术[10] [11]。但是对于影像学表现为实性的结节,患者的术后风险升高且亚肺叶切除术的效果可能不如肺叶切除术[12] [13],因此有观点认为肺叶切除术仍应是实体型、临床 IA 期 NSCLC 的标准手术方式[14]。对于 T1N0M0 分期 NSCLC 的肺段切除术的术后效果可能受多种因素的影响,除了影像学表现,还有组织学亚型。据报道,亚肺叶切除术在原位癌或微浸润性腺癌可以取得较好的预后[15] [16]。还有观点认为微乳头成分是重要的预后因素,在分析了 734 例来自纪念斯隆 - 凯特琳癌症中心腺癌患者的手术切下的肺组织与预后的关系后得出结论,当微乳头成分出现时,亚肺叶切除术的预后比肺叶切除术差 5% 甚至更高[17]。

近期一项研究发现虽然在 IA 期 NSCLC 患者中行肺叶切除术和亚肺叶切除术的术后 5 年生存率相似,但是亚肺叶组患者 NSCLC 的复发风险却增加了 39%,同时发现接受肺叶切除术治疗的患者的中位淋巴结计数更高,并且得出结论亚肺叶切除与癌症复发风险增加 39% 相关。大多数接受亚肺叶切除术治疗的患者淋巴结评估并不充分,当把现有临床试验结果外推用于临床使用时,必须考虑真实世界的实际情况[18]。

值得一提的是,在老年(年龄 > 65 岁)的 I 期 NSCLC 患者中,亚肺叶切除术术后的生存率可能达到与肺叶切除术相似水平,考虑到亚肺叶切除术能更好地保留肺功能,特别是对于低 FEV1 百分比、呼吸功能储备降低的 IA 期且直径 < 2 cm 的老年 NSCLC 患者来说,可以优先选择亚肺叶切除术作为其治疗方式[19]。但是要注意进行充分的淋巴结评估[20]。对于年轻(年龄 < 35 岁)的 IA 期 NSCLC 患者,亚肺叶切除术的术后效果并不差于肺叶切除术。考虑到亚肺叶切除术能更好地保留肺功能,亚肺叶切除术可能更适合治疗年轻的 IA 期 NSCLC 患者[21]。但是也有观点认为,对于体能状态良好或复发风险较高的患者,肺叶切除术依然是最安全和符合肿瘤学的选择。

3. 肺叶切除术与肺段切除术和楔形切除术

西日本肿瘤学组和日本临床肿瘤学组于 2009 年开展一项 3 期临床试验(JCOG0802)结果表明,对于直径 ≤ 2 cm, CTR > 0.5 的浸润性周围型 NSCLC 患者,肺段切除术和肺叶切除术患者的术中和术后并发症的术后评估几乎没有差异,因此他们推荐肺段切除术应作为此类患者的标准手术方式,而不是肺叶切除术[22]。

早期 NSCLC 不仅仅局限于直径 ≤ 2 cm, CTR > 0.5 的浸润性周围型 NSCLC。Keenan RJ 等一项荟萃分析通过比较近年来相关文献指出在 I 期 NSCLC 中,肺段切除术的结果与肺叶切除术相当[6]。但是 Zhang L 的研究结果仍然支持肺叶切除术作为 I 期 NSCLC 的首选治疗方式,而且这项研究还显示对于 IA 期的 NSCLC,肺段切除术后 OS 和 LCSS 相比于肺叶切除术更差,而 RFS 组间具有可比性[23]。另一项荟萃分析[24]以及一项关于 SEER 数据库的分析[25]的结果显示,对于 IA 期的 NSCLC 肺叶切除术优于肺段切除术,但在经过倾向评分匹配后,对于 IA 期 < 2 cm 的肿瘤,肺叶切除术和肺段切除术的患者术后效果并没有显著差异。但是其他数据库研究显示了不同的结果,对于 < 2 厘米的肿瘤,肺叶切除术具有优势[26]。

对于 I 期和 IA 期,肺叶切除术显示出相对较好的预后效果,而对于 < 2 cm 的肿瘤,我们的研究未发现两组之间的肿瘤学结果存在显著差异。这也表明,对于 < 2 cm 的 NSCLC,肺段切除术可能是替代肺叶

切除术的一种有价值治疗方法[27]。

最近一项基于 SEER 数据库的分析还调查了<1 cm 的 NSCLC，肺段切除术很有希望成为其首选的手术方式[28]，肺段切除术后的五年总生存率和无病生存率与肺叶切除术的生存率相当[29]。其中，一项基于 SEER 数据库的研究结果表明对于 2.1~3.0 cm 的肿瘤，肺叶切除术仍然是标准的手术方式；但是对于不适合进行肺叶切除术的患者，肺段切除术和楔形切除术的存活率相似。对于 1.1~2.0 cm 的肿瘤，肺叶切除术和肺段切除术可导致相同的存活率，但显示出比楔形切除术观察到的更高的存活率。对于 IA 期 NSCLC 肺叶切除术、肺段切除术和楔形切除术对于≤1.0 cm 的 IA 期 NSCLC 患者是可比较的肿瘤手术[30]。但是，有研究表明对于≤1 cm 和 1~2 cm 的 NSCLC 患者肺叶切除术表现出更好的生存率。但是对于不适合进行肺叶切除术的患者，应推荐 1~2 cm 的 NSCLC 进行肺段切除术，而对于≤1 cm 的 NSCLC，外科医生可以根据手术技术和患者情况决定肺段切除术和楔形切除术[31]。

4. 肺段对比楔切

肺段切除术在 OS 和 LCSS 方面与楔形切除相比可以获得更好的结果[32]，肺段切除术是一种解剖学上的亚肺叶切除术，往往能比楔形切除术能取得更好的预后[33]。而且对于肿瘤≤2 cm 或年龄>70 岁的患者，也获得了类似的结果[32]。目前普遍认为，肺段切除术的癌症控制优于楔形切除术。作为亚肺叶切除术，肺段切除术是治疗临床 IA 期非小细胞肺癌的首选肿瘤手术[34]。

对于计算机断层扫描诊断 CTR ≤ 0.25 且 ≤ 3 个可接受亚肺叶切除的周围型小结节，西日本肿瘤学组和日本临床肿瘤学组发布的 JCOG0804 认为具有足够手术切缘的亚肺叶切除术为临床可切除的 N0 肺癌提供了足够的局部控制和无复发生存期，对 GGO 占主导的周围型肺癌进行亚肺叶切除是可行和有效的，如果合适的话可以进行解剖切除[35]。但是对于纯实体肿瘤，肺段切除术中评估淋巴结转移和足够的手术切缘可能是临床 T1a-bN0M0 肺癌可行的手术方法[36]。

对于肿瘤大小≤2 cm 的 IA 期 NSCLC，肺段切除术相较于楔形切除术可以获得更好的生存率。然而，对于≤1 cm 的 NSCLC，外科医生需要根据患者的情况和肿瘤的位置选择进行肺段切除术或者楔形切除术。这些结果应得到进一步随机临床试验的证实[37]。

5. 总结与展望

对于早期 NSCLC 手术方式的选择，不仅需要考虑肿瘤的大小，淋巴结转移情况等，早期 NSCLC 的术后效果可能受多种因素的影响，比如电子计算机断层扫描中的实性成分占比，还有组织学亚型等。而且，目前的研究更关注于对<2 厘米的肿瘤的研究，较少单独提及 2~3 cm 肿瘤以及对其进行正式比较，因为它们通常在 IA 期的框架下被分析。随着研究的深入，保证切缘的楔形切除术是否能够替代部分肺段切除术也值得进一步探讨。

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