

实性肺结节的良恶性分析

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摘 要

肺癌是目前发病率和死亡率居首位的恶性肿瘤, 对肺癌进行早期诊断是降低死亡率的关键。早期肺癌主要表现为肺结节, 目前肺结节的检出率越来越高, 而其中实性肺结节是检出最多的结节类型, 对实性肺结节进行良恶性鉴别是重点。本文综述了实性肺结节的影像学及临床危险因素。影像学表现如结节大小、形态、边缘特征及生长速度, 结合患者的年龄、吸烟史、家族史等临床信息, 有助于评估实性肺结节的良恶性。

关键词

肺癌, 肺结节, 实性肺结节, 良恶性, 鉴别诊断

Benign and Malignant Analysis of Solid Pulmonary Nodules

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Abstract

Lung cancer is the malignant tumor with the highest morbidity and mortality rate, and early diagnosis of lung cancer is the key to reducing the mortality rate. Early lung cancer is mainly manifested as lung nodules, and the detection rate of lung nodules is getting higher and higher, among which solid lung nodules are the most frequently detected nodule type, and it is important to differentiate the benign and malignant nature of solid lung nodules. This article reviews the imaging and clinical risk factors of solid lung nodules. Imaging manifestations such as nodule size, morphology, margin characteristics,

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and growth rate, combined with clinical information such as the patient's age, smoking history, and family history, are helpful in assessing the benign or malignant nature of solid lung nodules.

Keywords

Lung Cancer, Lung Nodules, Solid Lung Nodules, Benign and Malignant, Differential Diagnosis

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1. 总述

肺癌是目前发病率和死亡率最高的恶性肿瘤[1]。2022年,全球新发肺癌病例近250万,导致180万人死亡[1]。肺癌5年生存率低于20% [1],早期诊断和治疗是降低肺癌死亡率的关键。

早期肺癌多表现为肺结节。计算机断层扫描的广泛应用显著提高了肺结节的检出率,在健康人群中,胸部CT检测到肺结节的概率高达25%~30% [2]。大多数检出的肺结节是良性的,只有少数为恶性。美国的一项研究纳入了377名直径为8~20 mm的肺结节患者,其中恶性肿瘤的患病率为25% [3]。

肺结节分为实性结节、纯磨玻璃结节和混合磨玻璃结节,其中实性肺结节是最常见类型,在被检出的肺结节中占比接近80% [4]。实性肺结节密度高,并覆盖血管及支气管影像[5]。与纯磨玻璃结节和混合磨玻璃结节相比,实性肺结节的恶性概率低,但其恶性程度高、侵袭性强和预后更差[6]-[8]。在中国的一项研究中,8392名职工参与了LDCT筛查,肺癌检出率为2.1%,其中仅4%为实性肺结节[9]。有文献报道,IA期肺腺癌患者中,实性结节组的5年总生存率为68.9%,低于亚实性结节组的91.2% [6]。

大多数小实性肺结节是良性的,其病理结果多种多样,80%为肉芽肿和肺内淋巴结,10%为错构瘤,10%为其他良性病变[5]。实性肺结节的误诊率高,主要通过影像学表现结合临床特征进行分析,良恶性鉴别诊断是难点。

2. 影像学特征

2.1. 结节大小

结节越大,恶性肿瘤的风险越大[10]。小于6 mm的结节,恶性概率小于1%;6 mm至8 mm的结节,恶性概率为1%至2%,较大的实性肺结节(8~30 mm)恶变概率从极低(<1%)到高(>70%)不等[11]。目前尚无明确的大小临界值来判断结节的良恶性[3]。

2.2. 结节生长及生长速度

结节生长及生长速度是鉴别肺实性结节良恶性的主要指标[12]。结节生长定义为结节直径增加1.5 mm,或结节体积增加25%。如果结节有生长,则使用体积倍增时间(VDT)进一步评估肺结节生长速度[13]。VDT > 400天表明结节生长较慢[14],VDT介于25~400天高度提示恶性肿瘤[15]。然而对于体积 < 300 mm³的孤立性肺结节,VDT ≤ 400天并不能很好地鉴别良恶性,VDT ≤ 600天在这种情况下更具有鉴别能力[12]。对于2年或更长时间内无生长的实性结节,通常认为是良性结节[4] [16] [17]。

肺结节通常使用最大直径、平均直径和体积来测量[5]。体积测量在评估结节大小和生长速度方面较直径表现更好,指南建议将体积评估纳入到肺结节的风险评估中[5]。评估时应该注意心血管运动对肺结

节体积的影响, 尤其对小肺结节影响更大[17]。

2.3. 结节形态

内部有钙化现象和脂肪密度的实性肺结节更可能是良性肺结节[4] [12] [16]。良性结节的钙化主要表现为弥漫性、中央性、爆米花样和层流状[5] [12]。肺癌病灶中很少观察到钙化, 即使有钙化, 也常表现为无定形或点状钙化现象。只有少数恶性肺结节会有密集钙化的表现, 如原发性骨恶性肿瘤的肺转移灶[5]。结节内部含有脂肪密度成分提示错构瘤可能[15]。具有卫星病变的实性肺结节应注意肺结核和肺隐球菌病可能[18]。

结节边缘规则、清晰和光滑常提示良性结节[5] [12], 如炎性假瘤、错构瘤和肺内淋巴结[19]。也有研究发现, 在 $<8\text{ mm}$ 的恶性实性肺结节中, 有21%的结节具有清晰且规则的边缘[5]。转移性肺癌也可能表现为边缘光滑的近似球形的结节[12]。结节的边缘不清、不规则或有毛刺征、分叶常提示恶性肿瘤可能。毛刺征多与肿瘤细胞阻塞淋巴管或血管有关[20]。分叶多与肿瘤组织在不同方向的生长速度不一致有关。然而, 毛刺征和分叶的特异性较低, 在良性和恶性结节之间的重叠较大[8], 所以通过仅仅毛刺征及分叶征难以对实性肺结节进行鉴别诊断, 需要结合其他影像学表现及临床表现进行良恶性鉴别诊断。

实性结节的性质最多见于炎性结节和肺癌, 两者在增强CT中都可呈现强化, 但炎性结节的表现可能随疾病进展而发生显著变化, 而肺癌表现则相对稳定。在PET/CT中, 恶性肿瘤FDG高摄取与肿瘤发展有关, 并且摄取稳步增加; 相反, 炎性结节具有葡萄糖代谢亢进, 摄取随着组织愈合而逐渐减少[21]。

2.4. 结节位置及数量

结节所在位置不同, 恶性风险也不同。右肺上叶是肺癌的独立危险因素[22], 这可能由于呼吸气流对右肺上叶支气管的影响最大, 导致烟草烟雾颗粒在该位置的沉积最多。然而, 不吸烟的人群中, 恶性肺结节也同样频繁地出现在右肺上叶[22]。但该特点在结核病高发国家并不完全适用[14] [23], 因为肺结核病灶通常也位于上叶。良性实性肺结节多位于胸膜周围[4] [24], 位于肺叶之间的裂隙和胸膜表面的肺结节通常是肺内淋巴结[14] [15]。

结节的数量也与肺癌风险相关。NELSON研究发现, 当总结节数从1个增加到4个时, 患者的肺癌风险增加, 而有5个或更多结节的患者肺癌风险降低[14] [22]。不吸烟的患者常常只有1个肺结节, 而当前正在吸烟的患者肺结节常常 ≥ 5 个, 这可能与长期吸烟导致炎症反应或肉芽肿形成有关[22]。

2.5. 是否为新发结节

随访中新发现的实性结节比基线筛查时检测到的结节具有更高的恶性风险, 即使这些新的实性结节很小[25]-[27]。肺癌风险与新发结节的大小显著相关, $<4\text{ mm}$ 的结节恶性概率为1.1%, 而 $\geq 20\text{ mm}$ 的结节的恶性概率为24.0% [27]。对于新发的实性结节, 应该制定更积极的随访策略[26]。

VDT和体积评估能较好地鉴别新发实性肺结节。有学者提出, 新发实性结节需要随访的体积大小阈值应降低至 30 mm^3 , 立即行下一步检查的阈值也应从 300 mm^3 降低至 200 mm^3 [25] [28]。新发实性结节的 $\text{VDT} \leq 600$ 天或体积 $\geq 200\text{ mm}^3$ 提示具有很高的恶性风险概率[25]。但目前针对新发结节高危阈值的界定仍需要更多临床研究数据支撑[28]。

3. 临床特征

3.1. 年龄与性别

年龄与肺癌之间的相关性已得到充分证实。肺癌的发病率随着年龄的增长而增加[9]。肺癌很少发生在35岁以下的人群中[14], 年龄 > 60 岁患肺癌的风险显著增加[29]。

目前的研究表明, 女性患肺癌的风险较男性显著增加[9] [14] [29]。有研究表明在女性无吸烟史中肺癌的检出率显著高于男性无吸烟史者[29]。女性的肺癌患病率升高可能与肺癌的遗传易感性有关, 另外也与女性更易受到除吸烟以外的其他致癌物的影响有关[9] [30]。

3.2. 吸烟

吸烟是肺癌最重要的独立危险因素[9] [14] [30]。吸烟者的肺癌风险比不吸烟者高 10~35 倍[14]。在当前正在吸烟和既往有吸烟史的人群中, 每年吸烟包数越多, 肺癌风险越高[14] [16] [31]。然而, 在良性结节患者中也有相当比例是吸烟者[16] [31]。

随着肺癌筛查计划在越来越多的国家和地区实施, 越来越多不吸烟者被检测出患有肺癌[9], 占比大约 15%~25% [30]。无吸烟史者与当前吸烟者检测到结节的“高风险”概率相似[22]。无吸烟史人群肺癌检出率的增加可能由于内源性遗传易感性和外源性环境致癌物的共同作用[29]。目前已确定无吸烟史者罹患肺癌的几个危险因素, 包括一级亲属中有肺癌家族史、暴露于有烟草烟雾的环境、长期暴露于烹饪环境和在烹饪时不使用通风设备等[29]。

3.3. 肺气肿和肺纤维化

肺气肿和肺纤维化是肺癌的独立危险因素[32]。Cottin 等将肺纤维化合并肺气肿(CPFE)定义为上肺肺气肿和下肺纤维化共存于同一个体的一种临床综合征[33]。CPFE 患者患肺癌的风险比单纯肺气肿患者高, 与特发性肺纤维化患者相似[26]。然而, 与肺气肿相关的恶性和良性结节在 CT 中的特征重叠程度明显高于非肺气肿相关的结节[5]。

3.4. 家族史

一级亲属患有肺癌的肺结节患者, 其恶性风险概率是无肺癌家族史人群的 1.51 倍, 且早发肺癌的风险更高[29]。对于女性来说, 一级亲属的肺癌家族史是最重要的危险因素之一[30]。有研究表明, 在无吸烟史者中, 母亲患肺癌比父亲患肺癌对子女的影响更大[29]。母源传播的高风险可能与性染色体、性别特异性激素因子、线粒体 DNA 及基因组印记有关[29]。家族风险不仅反映了遗传倾向, 还反映了共同的暴露环境[30]。

3.5. 其他

吸入致癌物如石棉、铀和氡是公认的肺癌危险因素[14]。此外, 体力活动水平较低、慢性呼吸系统疾病、消化系统疾病、肝胆疾病、高血压或糖尿病病史也可能增加肺癌患病风险[34]。有研究报告, 较低水平的高密度脂蛋白胆固醇与肺癌风险增加有关[16], 低密度脂蛋白胆固醇水平升高与良性肺结节的存在呈正相关[16]。

与美国相比, 南亚和东亚无吸烟史女性的肺癌患病率较高[29]。非洲裔黑人和夏威夷原住民的肺癌发病率较高[14]。

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