

• 临床研究 •

妊娠对肺部磨玻璃结节生长的影响

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[摘要] 目的: 通过单中心回顾性队列评估妊娠与磨玻璃结节生长之间的关系。方法: 回顾性分析44例因肺部磨玻璃结节行孕前和分娩后胸部CT扫描的妊娠孕妇的临床和影像学资料。根据影像学特征, 将磨玻璃结节分为纯磨玻璃结节、异质性磨玻璃结节和部分实性结节。磨玻璃结节的大小定义为胸部CT扫描轴位图像中的最大直径, 而观察间隔定义为孕前和分娩后胸部CT检查之间的时间间隔。当磨玻璃结节最大直径增加2 mm、固体成分增加2 mm或出现新的固体成分时, 则被认为磨玻璃结节出现了生长。结果: 在44例中, 共检出70个磨玻璃结节, 其中包括66个纯磨玻璃结节和4个异质性磨玻璃结节。其中43个磨玻璃结节直径<6 mm, 22个直径6.0~7.9 mm, 4个直径8.0~9.9 mm, 1个直径≥10 mm。在779 d的中位观察间隔(范围为337~2 795 d)内, 未观察到磨玻璃结节出现生长。结论: 妊娠不太可能导致肺部直径较小的纯磨玻璃结节生长。因此, 育龄期女性患者如有怀孕计划, 无需过度担心此类纯磨玻璃结节的生长问题。

[关键词] 磨玻璃结节; 生长; 妊娠**[中图分类号]** R814.42**[文献标志码]** A**[文章编号]** 1007-4368(2024)10-1396-05**doi:** 10.7655/NYDXBNSN240812

Influence of pregnancy on the growth of pulmonary ground glass nodules

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[Abstract] **Objective:** To evaluate the relationship between pregnancy and the growth of ground glass nodules (GGNs) through a single-center retrospective cohort analysis. **Methods:** Clinical and radiologic data of 44 pregnant women who underwent pre- and post-pregnancy chest CT scans due to pulmonary GGNs were retrospectively reviewed. Based on imaging characteristics, the GGNs were divided into the pure GGNs (PGGNs), heterogeneous GGNs (HGGNs), and part solid nodules (PSN). The size of a GGN was determined as the maximum diameter in axial chest CT images, and the observation interval was the time between pre- and post-pregnancy chest CT scans. Growth of a GGN was defined as an increase of 2 mm in the maximum diameter, an increase of 2 mm in the solid component, or the appearance of new solid component. **Results:** Among the 44 pregnant women, 70 GGNs were detected, including 66 PGGNs and 4 HGGNs. Of these, 43 GGNs had a diameter of < 6 mm, 22 were between 6.0 and 7.9 mm, 4 were between 8.0 and 9.9 mm, and 1 GGN was ≥10 mm. No growth of pulmonary GGNs was observed at a median observing interval of 779 days (ranging from 337 to 2 795 days). **Conclusion:** Pregnancy is unlikely to cause the growth of pulmonary PGGNs with a small diameter. Therefore, women of child-bearing age who plan to become pregnant need not be overly concerned about the growth of such GGNs.

[Key words] ground glass nodule; growth; pregnancy

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近年来, 随着肺癌低剂量CT筛查的推广, 肺部磨玻璃结节(ground glass nodules, GGN)的检出率显

著增加。GGN被定义为CT肺窗图像中可观察到的圆形或类圆形高密度病变, 不掩盖其内走行的血管和支气管影, 呈现出磨玻璃样的特征^[1]。尽管随访时持续存在的GGN具有较高的肿瘤风险, 但它也可能是由肉芽肿、肺泡出血或间质纤维化等疾病引起

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的^[2-4]。指南通常建议对风险较低的GGN进行随访,而对于风险较高或有生长趋势的GGN则建议进行手术切除^[5-6]。

据报道,妊娠是影响哮喘、结节病和淋巴管平滑肌瘤病等肺部疾病自然病程的明确因素^[7-8]。然而,妊娠是否会导致肺部GGN的生长仍然未知,因此许多育龄期女性患者对GGN的生长问题感到恐慌。此前,Bai等^[9]曾报道妊娠对肺部GGN没有显著影响,这是首次对妊娠与肺部GGN相关性进行的研究,但他们研究的样本量(仅有4例)较为有限。因此,本研究旨在利用单中心的样本扩充此类病例的研究。

1 对象和方法

1.1 对象

回顾性分析2015年1月—2023年6月于南京医科大学第一附属医院接受分娩同时患有肺部GGN的患者44例,共70个GGN病灶。入组标准:患者于本院分娩时的临床资料及孕前、分娩后的影像学资料完整。排除标准:①既往有恶性肿瘤病史;②妊娠期患有严重肺炎;③GGN直径<3 mm。收集患者的临床信息,包括孕前最后1次CT检查时的年龄、分娩时的年龄、怀孕次数、分娩次数及妊娠期并发症、吸烟史以及家族肿瘤病史。本研究得到了南京医科大学第一附属医院伦理委员会的批准(2023-SR-038)。

1.2 方法

1.2.1 影像学检查

胸部CT扫描采用Siemens Definition AS+128排多层螺旋CT,患者取仰卧位,双臂上举,于吸气末进行全肺扫描,范围包括胸廓入口至肾上腺。扫描参数:管电压120 kV;管电流100 mAs;矩阵512×512;层厚5 mm;螺距0.9,重建厚度1.5 mm。(肺窗窗宽:1 500 HU,窗位:-400 HU;纵隔窗窗宽:350 HU,窗位:40 HU;重建后观察图像。

1.2.2 CT图像分析

根据先前的研究,GGN的生长被定义为:①与初始CT扫描相比,后1次CT图像中的GGN最大尺寸至少增加了2 mm;②GGN固体成分的尺寸增加了至少2 mm;③GGN出现了任何尺寸的新固体部分^[10]。由2名分别具有3年和8年工作经验的胸部放射诊断医师独立分析比较患者怀孕前的最后1次CT扫描图像和分娩后的第1次CT扫描图像,意见不同时协商取得一致。定义这2次CT扫描之间的时间间隔为观察间隔。主要评估内容包括孕前最后1次

CT扫描图像中GGN的大小(取CT肺窗轴位图像中的最大直径)、性质(纯磨玻璃结节、异质性磨玻璃结节和部分实性结节)、实性成分大小(取CT纵隔窗轴位图像中实性成分的最大直径)、Lung-Rads分级、位置、形状、边界(是否清晰)、内部及周围特征(毛刺征、胸膜牵拉、空泡征、支气管充气征及血管穿行征),以及GGN是否满足生长定义。其中纯磨玻璃结节(pure ground glass nodule, PGGN)是指GGN在肺窗及纵隔窗均未观察到固体成分,异质性磨玻璃结节(heterogeneous ground glass nodule, HGGN)是指GGN仅在肺窗中检测到的固体成分,部分实性结节(part-solid nodule, PSN)是指GGN可以在纵隔窗检测到固体成分^[11]。评估孕前最后1次CT图像时参照Lung-Rads 2022版本^[12]对每个GGN进行危险度分级。

1.2.3 病理诊断

对于接受肺部GGN手术的患者,手术后病理标本经由10%福尔马林固定,石蜡包埋,切片,HE染色,并根据国际肺癌研究协会/美国胸科学会/欧洲呼吸学会肺癌国际多学科分类进行组织学分类^[13]。

1.3 统计学方法

所有的数据分析均基于SPSS26.0。在分析患者的临床特征与GGN的放射学特征时,符合非正态分布的连续性变量使用中位数(四分位数)[$M(P_{25}, P_{75})$]表示,分类变量则使用百分比表示。

2 结果

2.1 患者特征

共纳入44例患者,孕前最后1次CT检查时的年龄中位数为31岁(范围20~42岁),分娩时的年龄中位数为32岁(范围23~43岁)。她们初次接受胸部CT检查的原因为健康体检(19例,43.2%),存在呼吸道症状(13例,29.5%)或胸部不适(12例,27.3%)。其中,25例(56.8%)为初产妇,19例(43.2%)为经产妇。17例(38.6%)患者在此次妊娠过程中患有妊娠相关并发症,包括妊娠期糖尿病(12例,27.3%)和甲状腺功能异常(6例,13.6%),6例甲状腺功能异常的患者中包含了4例甲状腺功能减退患者以及2例亚临床甲状腺功能减退患者。24例(54.5%)患者经历了自然分娩,20例(45.5%)接受了剖宫产。值得注意的是,本研究并没有患者存在吸烟史或家族癌症病史(表1)。

2.2 GGN的放射学特征

在44例患者中,共检测到70个GGN。其中,患

表1 研究患者的临床特征

Table 1 Clinical characteristics of the study patients	
Characteristic	Number of cases(<i>n</i> =44)
Age(the last CT scan before pregnancy) [years, <i>M</i> (<i>P</i> ₂₅ , <i>P</i> ₇₅)]	31(28, 33)
Age(delivery)[years, <i>M</i> (<i>P</i> ₂₅ , <i>P</i> ₇₅)]	32(30, 34)
Reason for taking chest CT[<i>n</i> (%)]	
Health examination	19(43.2)
Respiratory symptoms	13(29.5)
Chest discomfort	12(27.3)
Parturient categories[<i>n</i> (%)]	
Primipara	25(56.8)
Multipara	19(43.2)
Pregnancy complications[<i>n</i> (%)]	
Diabetes	12(27.3)
Hypertension	0(0)
Thyroid dysfunction	6(13.6)
Hypothyroidism	4(9.1)
Subclinical hypothyroidism	2(4.5)
Smoking history[<i>n</i> (%)]	0(0)
Family cancer history[<i>n</i> (%)]	0(0)
Presentation[<i>n</i> (%)]	
Spontaneous labor	24(54.5)
Caesareansection	20(45.5)
Nodules per patient[<i>n</i> (%)]	
1	30(68.2)
2	9(20.5)
≥3	5(11.4)
Observing interval[d, <i>M</i> (<i>P</i> ₂₅ , <i>P</i> ₇₅)]	779(608, 1 170)

有单个GGN的患者有30例,2个GGN的患者有9例,3个GGN的患者有2例,5个GGN的患者有2例,还有1例患者有6个GGN。研究纳入的GGN中,有66个(94.3%)为PGGN,其余4个为HGGN。在这70个GGN中,43个直径<6 mm,22个直径6.0~7.9 mm,4个直径8.0~9.9 mm,1个直径>10 mm。最终,在779 d(范围337~2 795 d)的中位观察间隔内,没有GGN出现生长(表2)。

在纳入的44例患者中,有1例患者最初于2014年6月接受胸部CT扫描,发现左肺上叶1枚直径为8 mm的PGGN;2018年6月,接受了第2次CT检查,这枚GGN增长到11 mm;没有立即接受手术治疗,而是选择继续随访。2018年10月—2019年6月,经历了1次妊娠。分娩结束2个月后,胸部CT检查结果与2018年6月相比并没有明显变化。随后,该患者接受了手术治疗,术后GGN的组织学结果显示为

表2 孕前最后1次CT扫描时GGN的影像学特征

Table 2 Radiologic characteristics of GGN on the last CT scan before pregnancy	
Characteristic	Number of nodules(<i>n</i> =70)
Type	
Pure GGN	66(94.3)
Heterogeneous GGN	4(5.7)
Part solid nodule	0(0)
Size	
<6.0 mm	43(61.4)
6.0~7.9 mm	22(31.4)
8.0~9.9 mm	4(5.7)
≥10.0 mm	1(1.4)
Lung-Rads category	
Lung-Rads 2	68(97.1)
Lung-Rads 3	2(2.9)
Location	
RUL	15(21.4)
RML	3(4.3)
RLL	18(25.7)
LUL	19(27.1)
LLL	15(21.4)
Shape	
Round or oval	64(91.4)
Irregular	6(8.6)
Well defined margin	45(64.3)
Spiculation	0(0)
Pleural retraction	1(1.4)
Bubble lucency	3(4.3)
Air bronchogram	0(0)
Vessel sign	49(70.0)

GGN: ground glass nodule; RUL: right upper lobe; RML: right middle lobe; RLL: right lower lobe; LUL: left upper lobe; LLL: left lower lobe.

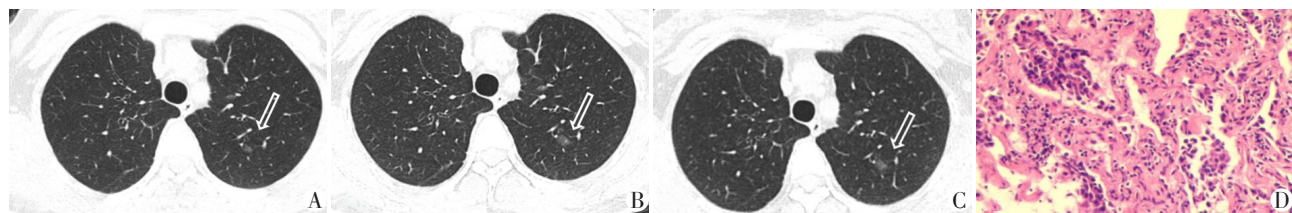
微浸润腺癌(图1)。这位患者同时接受了10L及12L组的淋巴结采样术,采样的3枚淋巴结未发现肿瘤转移。

2.3 切除GGN的病理结果

在本研究中,除上述患者外,还有1例患者也接受了手术治疗(图2)。该患者GGN的病理结果为原位腺癌。这位患者接受了10R组的淋巴结采样术,采样的1枚淋巴结未发现肿瘤转移。

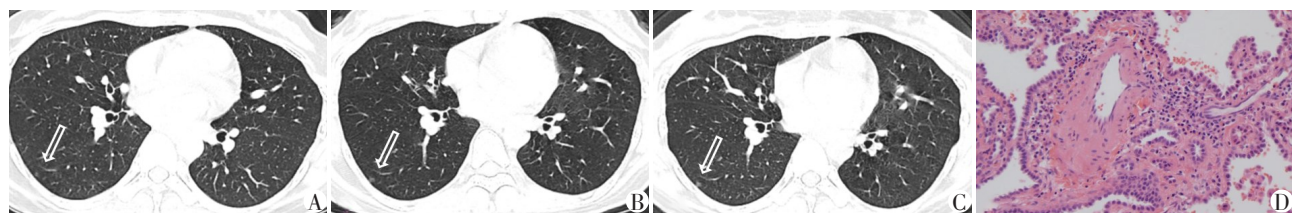
3 讨论

目前,对于偶然发现的风险较低的GGN,首先会建议进行定期规律随访。若在随访期间发现GGN有生长趋势,则通常建议考虑手术切除^[5-6]。在



A: A physical examination revealed an 8 mm ground-glass nodule in the upper lobe of the left lung. B: A follow-up CT scan after 2 years showed that the GGN had grown to 11 mm. The patient chose to continue monitoring and become pregnancy 5 months later. C: A follow-up CT scan 2 months after delivery showed that no significantly change in the GGN compared to the pre-pregnancy scan. D: A pathological examination revealed minimally invasive adenocarcinoma(HE, ×100).

图1 女31岁左肺上叶磨玻璃结节
Figure 1 One 31 years-old female patients with left pGGN



A: The patient had chest discomfort, and a CT scan revealed a 4 mm GGN in the right lower lobe. She became pregnant a month later and had thyroid dysfunction during pregnancy. B: Four years later, the patient had a second CT scan. Although the GGN had grown to 5 mm, it did not meet the criteria for GGN growth. C: Four months later, a follow-up CT scan showed no significant change in the GGN. D: Pathological examination revealed adenocarcinoma in situ(HE, ×100).

图2 女26岁右肺下叶磨玻璃结节
Figure 2 One 26 years-old female patients with right pGGN

过去的研究中,GGN的生长被定义为直径和固体成分的增加,这常被视为GGN病理侵袭性增加的影像学表现^[14-16]。因此,GGN的生长情况是临床实践中值得深入研究的重要原因。

Matsuguma等^[17]研究指出,在一般人群中,非实性结节和部分实性结节的生长率在2年时分别为13%和38%,在5年时分别上升至23%和55%。即使GGN在短期内保持稳定,随着观察时间的延长,仍存在生长的可能性。一份基于GGN的分析报告称,GGN稳定5年后的生长概率仍可达到13%^[18]。此外,一项荟萃分析显示,男性、有肺癌病史、年龄超过65岁、GGN直径超过10 mm以及结节密度较高是导致PGGN生长的独立危险因素^[19]。

妊娠是一个复杂的生理过程,对孕妇的生殖、内分泌和循环系统等方面都有显著影响。先前的研究已经报道了妊娠与肺部疾病,如哮喘、结节病、淋巴管平滑肌瘤病和肺癌等疾病之间的关联^[7-8,20]。尽管少数研究认为妊娠可能会加速晚期肺腺癌的进展,但妊娠与磨玻璃样早期肺癌生长情况之间的关系仍未得到明确的结论^[21-22]。此前,Bai等^[9]研究虽然指出了妊娠与GGN生长之间似乎没有明显的关联,但由于其研究样本量较为有

限,因此结论的可靠性有所限制。而本研究则基于更多的样本量再次证实了这一点,即妊娠不太可能导致肺部GGN的生长。此外,先前的研究已证实,孕妇的焦虑状态可能会增加不良产科及妊娠结局的发生概率。本研究的结论有助于减轻部分患有GCN的孕妇群体的焦虑,从而可能改善她们的妊娠结局^[23]。

本研究也存在一定局限性。首先,这是一项在单个中心进行的回顾性研究,因此潜在的选择偏倚是不可避免的。其次,在本研究中,大多数GGN属于PGGN,且直径大多数位于10 mm以下,这些特征都不是GGN生长的危险因素。最后,由于本研究并未观察到阳性结果,因此并未设立对照组。扩充更大的样本量并与无妊娠患者进行对照比较,是未来的研究方向。

总之,本研究发现,在779 d(范围337~2 795 d)的中位观察间隔内并没有GGN显示出增长,因此得出结论,认为妊娠不太可能导致肺部直径较小的PGGN生长。对于计划妊娠的育龄期女性患者来说,他们无需过分担心此类GGN的生长问题。

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