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《2024年 GOLD 慢性阻塞性肺疾病诊断、管理及预防全球策略》更新要点解读



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【摘要】 《2024年GOLD慢性阻塞性肺疾病诊断、管理及预防全球策略》(以下简称《GOLD 2024》)于2023-11-13重磅更新。总体来说,《GOLD 2024》与《2023年GOLD慢性阻塞性肺疾病诊断、管理及预防全球策略》大致相同,但其内容更加精炼,并对目前研究的热点问题如保留比值受损肺功能(PRIsm)、肺过度充气和慢性阻塞性肺疾病(COPD)的诊断、筛查、评估及戒烟等13个方面进行了扩充和新增。本文主要介绍《GOLD 2024》各部分要点及重点更新内容。

【关键词】 肺疾病, 慢性阻塞性; 诊断; 疾病管理; 疾病预防; 慢性阻塞性肺疾病全球倡议

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Interpretation of the Key Points of Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (2024 Report)

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【Abstract】 Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (2024 Report) (hereinafter referred to as GOLD 2024) has been updated significantly from November 13, 2023. Overall, GOLD 2024 is roughly the same as Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (2023 Report), but its content is more refined, and it expands and adds 13 new areas of current research hotspots such as preserved ratio impaired spirometry (PRIsm), pulmonary hyperinflation, diagnosis, screening and evaluation of chronic obstructive pulmonary disease (COPD), and smoking cessation. This article mainly introduces the key points and key updates of each part of GOLD 2024.

【Key words】 Pulmonary disease, chronic obstructive; Diagnosis; Disease management; Disease prevention; Global Initiative for Chronic Obstructive Lung Disease

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1998年慢性阻塞性肺疾病全球倡议（Global Initiative for Chronic Obstructive Lung Disease, GOLD）计划启动，其目标是根据现有的最佳科学信息提出慢性阻塞性肺疾病（chronic obstructive pulmonary disease, COPD）管理建议^[1]。第1版《慢性阻塞性肺疾病诊断、管理及预防全球策略》于2001年首次发布，每5年修订1次，并每年进行更新^[2]。《2024年GOLD慢性阻塞性肺疾病诊断、管理及预防全球策略》^[3]（以下简称《GOLD 2024》）于2023-11-13重磅更新。总体来说，《GOLD 2024》^[3]与《2023年GOLD慢性阻塞性肺疾病诊断、管理及预防全球策略》^[4]（以下简称《GOLD 2023》）大致相同，但其内容更加精炼，并对目前研究的热点问题如保留比值受损肺功能（preserved ratio impaired spirometry, PRISm）、肺过度充气和COPD的诊断、筛查、评估及戒烟等13个方面进行了扩充和新增。本文主要介绍《GOLD 2024》各部分要点及重点更新内容。

1 COPD概述及其重点更新内容

1.1 COPD概述

COPD是一种异质性肺部疾病，其特征是气道病变（支气管炎、细支气管炎）和/或肺泡异常（肺气肿）所致慢性呼吸道症状（呼吸困难、咳嗽、咳痰），且引起持续进行性加重的气流受限^[5]。COPD患者通常伴有呼吸困难、喘息、胸闷、疲劳、活动受限和/或咳嗽伴或不伴咳痰，并且可能发生上述呼吸症状的急性恶化，即慢性阻塞性肺疾病急性加重（acute exacerbation of chronic obstructive pulmonary disease, AECOPD），从而影响患者的预后^[3]。

COPD的危险因素可分为遗传因素、环境因素、全生命周期事件^[6]。迄今为止确定的与COPD最相关（但罕见）的遗传因素是SERPINA1基因突变导致 α 1抗胰蛋白酶缺乏，该基因突变与肺功能下降和COPD发生风险升高相关^[7]。研究显示，导致COPD的主要环境因素是吸烟及吸入有毒颗粒和气体^[6]。COPD是由生命周期内动态、累积和重复的基因-环境相互作用引起的，这些相互作用可损伤肺和/或改变其正常发育、衰老过程^[3]。

COPD是一种可防可治的疾病，肺功能检查提示存在不完全可逆的气流受限〔吸入支气管舒张剂后第1秒用力呼气容积（forced expiratory volume in one second, FEV₁）/用力肺活量（forced vital capacity, FVC）<0.7〕即可确诊COPD^[8]。但人们对其普遍认识不足且临床对其诊断不足^[9]，这导致患者常得不到及时治疗或治疗不当，故早期正确诊断COPD具有重要的公共卫生意义。

1.2 重点更新内容

1.2.1 扩充了PRISm的相关内容

《GOLD 2023》^[4]提出了新术语PRISm，即一秒率正常（吸入支气管舒张剂后FEV₁/FVC $\geq$ 0.7）但肺功能受损（吸入支气管舒张剂后FEV₁占预计值的百分比<80%）。《GOLD 2024》^[3]指出，PRISm并非一种稳定的表型，患者的肺功能可恢复正常，亦可出现阻塞性通气功能障碍。基于人群的研究显示，PRISm患病率为7.1%~11.0%；而在当前吸烟人群和既往吸烟人群中，PRISm患病率为10.4%~11.3%，且其与BMI、女性、肥胖等相关^[10-14]。PRISm还与心肺疾病、全因死亡率和心血管疾病死亡率、住院风险以及气流受限风险增加相关^[10-11, 13, 15-17]。据报道，随着时间推移，20%~30%的PRISm患者会发生阻塞性通气功能障碍，其预测因素为吸烟、女性以及肺功能复查中用力呼气时间（forced expiratory time, FET）延长^[11]。并非所有PRISm患者会发展为COPD，但由于其已出现呼吸症状和/或肺功能异常和/或肺结构异常，仍应注意给予其相应的护理干预和治疗，然而目前还没有证据证明其最好的治疗方法^[18]。尽管目前关于PRISm的文献报道越来越多，但其发病机制和治疗方面仍存在重大空白，还需要进一步研究。

1.2.2 病理生理部分增加了肺过度充气的内容

肺过度充气指肺内气体容积大于自然呼气末时参考范围上限^[19]，其可导致COPD患者发生呼吸困难^[20]、运动耐量受损^[21]、住院次数增加^[22]、呼吸衰竭^[23]和死亡率增加^[22]。研究显示，肺过度充气在COPD患者中很常见^[24]，而导致肺过度充气的因素为弹性回缩力下降和呼气流量受限^[25]。当通气需求增加和呼气时间缩短时，在静息状态下，肺气肿可导致肺弹性回缩丧失，进而导致静态肺过度充气；而在运动状态下，气流受限可导致动态肺过度充气^[19]。还有研究显示，支气管舒张剂^[26]、补充氧气^[27]、补充氮-氧混合气^[28]、肺康复^[29]、缩唇呼吸^[30]、吸气肌训练^[31]、在引起严重肺过度充气的肺气肿情况下的肺减容术^[32]、支气管镜肺减容术均可有效治疗肺过度充气^[33]。

2 COPD诊断和评估方面重点更新内容

2.1 肺活量检测部分增加关于吸入支气管舒张剂前肺功能检查的进一步说明

《GOLD 2024》^[3]指出，如果吸入支气管舒张剂前肺功能检查显示有COPD临床表现（呼吸困难、咳嗽、咳痰等）的患者不存在气道阻塞，则其无需进行吸入支气管舒张剂后的肺功能检查，除非临床上高度怀疑其存在COPD；反之，则应采用吸入支气管舒张剂后的肺功能检查指标来诊断COPD。此外，对于有COPD临床表现，但吸入支气管舒张剂前肺功能检查未显示

存在气道阻塞的患者,吸入支气管舒张剂后由于FVC增加,其 FEV_1/FVC 会小于0.7,此时需要进一步调查患者的病因,并要求其间隔一段时间后再次进行肺功能检查^[3]。研究发现,若患者吸入支气管舒张剂前 $FEV_1/FVC < 0.7$,而吸入支气管舒张剂后 $FEV_1/FVC \geq 0.7$,那么其未来发展为COPD的风险增加,应密切随访^[34]。

2.2 增加在目标人群中筛查COPD

2.2.1 不要对无症状的成年人进行COPD筛查

美国预防服务工作组(United States Preventative Service Task Force, USPSTF)基于对参加药物或非药物临床试验的无症状或轻度COPD患者数据的系统审查,建议不要对无症状的成年人进行COPD筛查,但该意见不适用于COPD高风险人群〔如每年接受低剂量计算机断层扫描(low-dose computed tomography, LDCT)以筛查肺癌的人群〕或胸部影像学检查(胸部X线检查或胸部CT检查)发现肺结构异常(如肺气肿、气道壁增厚、支气管扩张等)人群^[35]。

2.2.2 对肺癌高危人群进行胸部影像学检查以筛查COPD

USPSTF推荐肺癌高危人群〔年龄50~80岁且有吸烟史(吸烟量 ≥ 20 包/年)〕每年进行1次胸部LDCT检查以便早期发现肺癌^[3]。研究显示,在接受筛查的肺癌高危人群中,有34%~57%存在气流受限,68%~73%存在肺气肿,且67%此前未诊断为COPD^[36-38]。目前认为,肺癌和COPD有共同的危险因素,且COPD是肺癌的独立危险因素,是影响肺癌患者生存的主要共病^[39-41]。因此,对接受胸部LDCT检查的肺癌高危人群进行临床症状评估和肺功能检查可以同时筛查其是否存在未识别的COPD症状和气流受限。

2.2.3 对合并COPD危险因素的非肺癌人群进行胸部影像学检查以筛查COPD

《GOLD 2024》^[3]指出,除吸烟外,其他因素(如生长发育异常、遗传、环境暴露、儿童时期感染各种病原微生物等)也会增加COPD的发生风险,而针对存在上述危险因素的非肺癌人群,可进行胸部影像学检查来评估其呼吸道情况。与每年进行胸部LDCT检查的人群不同,存在上述其他因素的非肺癌人群从不吸烟或很少吸烟,且通常年龄较小,而胸部CT本身有助于识别非肺癌人群中的COPD高风险个体,因而临床医生应考虑为这些高风险个体进行肺功能检查^[42-47]。

2.3 增加关于嗜酸性粒细胞(eosinophil, EOS)计数的说明

COPD患者的平均EOS计数较高^[48]。大量研究表明,EOS计数可以帮助临床医生预估COPD患者在常规支气管舒张剂治疗的基础上加用吸入性糖皮质激素(inhaled corticosteroids, ICS)能否获得更好的疗

效^[49-54]。因此《GOLD 2024》^[3]建议将血EOS计数作为COPD患者是否使用ICS的参考指标之一。还有研究发现,在没有COPD的年轻个体中,较高的EOS计数与COPD发生风险增加相关^[55],提示临床医生要重视初诊COPD患者的EOS计数。

2.4 增加肺间质异常(interstitial lung abnormalities, ILA)相关内容

肺实质纤维化或炎症在吸烟者和非吸烟者的胸部CT检查中均常见,如果在非间质性肺疾病(interstitial lung disease, ILD)患者中偶然发现该情况时,被称为ILA^[56]。老年(>60岁)人群ILA患病率为4%~9%^[56]。COPD Gene研究共纳入了4 360例COPD患者,其中443例(10%)患有ILA〔其中239例(54%)符合疑似ILD的诊断标准(即CT检查显示存在肺实质纤维化,FVC低于预计值的80%或一氧化碳弥散量低于预计值的70%)〕;与不符合疑似ILD诊断标准的ILA患者相比,符合疑似ILD诊断标准的ILA患者呼吸道症状更明显且死亡率更高^[57]。此外,纤维性ILA(即合并牵拉性支气管扩张、结构扭曲和蜂窝样变)更有可能进展为COPD^[58]。

3 COPD预防和管理方面重点更新内容

3.1 修订戒烟部分

戒烟是所有持续吸烟的COPD患者的关键干预措施。医疗保健提供者在提供戒烟信息和干预措施方面至关重要,应鼓励患者抓住一切机会戒烟。研究显示,尽管知道自己患有COPD,但仍有相当一部分患者继续吸烟(约40%的COPD患者仍吸烟),这种行为对疾病的预后和进展有负面影响^[59]。对于患有COPD的吸烟者来说,戒烟可能比没有COPD的吸烟者更具有挑战性,因为其对尼古丁的依赖性更大,自我效能感更低,自尊心更低^[60-62]。此外,据报道,抑郁症在COPD吸烟者中更常见,这可能导致戒烟失败^[63]。尽管存在这些不利条件,但戒烟对COPD的自然病程影响最大,其能改善患者症状^[64],并降低AECOPD频率^[65]。

对于COPD患者的戒烟治疗应根据个人需求和烟草依赖程度进行调整。有证据表明,咨询和药物治疗相结合是COPD患者最有效的戒烟治疗方法^[66-68]。戒烟过程的复杂性在很大程度上取决于尼古丁成瘾性。因此,应对所有患者进行尼古丁依赖性评估。尼古丁高度依赖的指标包括:起床后30 min内吸烟、夜间吸烟、吸烟 ≥ 20 支/d、Fagerström量表评分为7~10分或重度吸烟指数评分为5~6分^[69]。除了个人戒烟方法外,立法禁烟在提高戒烟率和减少二手烟暴露方面也很有效^[70]。

3.2 更新疫苗接种建议

COPD患者应接种当地相关指南推荐的所有疫苗。

3.2.1 流感疫苗

接种流感疫苗可以降低COPD患者严重疾病（如需要住院治疗的下呼吸道感染）发生率^[71]和死亡率^[72]。一项基于人群的研究结果表明，COPD患者，特别是老年患者，每年接种流感疫苗后其缺血性心脏病发生风险降低^[73]。

3.2.2 肺炎球菌疫苗

肺炎球菌结合疫苗（pneumococcal conjugated vaccine, PCV）和肺炎球菌多糖疫苗（pneumococcal polysaccharide vaccine, PPSV）获批用于≥65岁的老年人^[3]。虽然关于PCV和PPSV对COPD患者影响的具体数据有限，但目前的研究表明，接种肺炎球菌疫苗可降低AECOPD风险^[74]。

3.2.3 呼吸道合胞病毒疫苗

美国疾病控制与预防中心（Centers for Disease Control and Prevention, CDC）、免疫实践咨询委员会（Advisory Committee on Immunization Practices, ACIP）和欧盟委员会建议60岁及以上的稳定期COPD患者接种新型呼吸道合胞病毒双价融合前F蛋白疫苗^[75]和融合前F蛋白疫苗^[76]。

3.2.4 其他疫苗

COPD患者应常规接种带状疱疹疫苗^[77]。COPD患者应按照国家建议接种COVID-19疫苗^[78]。

3.3 扩充吸入性治疗的管理部分

大多数用于治疗COPD的药物是吸入性的，因此适当使用吸入器装置对于优化吸入治疗的获益-风险比至关重要。

目前至少有33种不同的吸入疗法，包含不同的支气管舒张剂（短效和长效）和吸入性皮质类固醇（ICS）单独或联合使用^[3]。此外，至少有22种不同的吸入器装置可供选择，包括雾化器、带或不带单向阀储雾罐（valved holding chamber, VHC）的定量吸入器（metered dose inhalers, MDIs）、呼吸驱动型MDIs（breath-actuated MDIs, BAIs）、软雾吸入器（soft mist inhalers, SMIs）和干粉吸入器（dry powder inhalers, DPIs）^[79]。由于各吸入器装置的大小和便携性不同，在准备步骤、装载或驱动力、输送药物所需时间、清洁和维护的需要以及有效使用时所需的吸气动作方面也有所不同，此外，吸气流量、气流加速度和吸入量是患者成功将药物颗粒从吸入器装置吸入下呼吸道的重要因素^[79]。MDIs和SMIs需要缓慢而深的吸气，而DPIs则需要用力吸气。可以肯定的是，使用吸入器的步骤越繁琐，患者正确使用吸入器的可能性越低^[80]。故医生在开具吸入器装置处方时，必须提供个性化指导，确保患者掌握正确的吸入方法，并在每次就诊时重新检查患者是否能继续正确使用吸入器装置。

3.4 新增药物治疗的证据概述

3.4.1 新增戒烟药物治疗研究

一项荟萃分析纳入了4项分析药物对COPD患者戒烟率影响的高质量研究，结果显示，接受尼古丁替代疗法、安非他酮、去甲替林和伐尼克兰治疗的COPD患者长期戒烟率为14%~27%，明显高于接受安慰剂治疗的COPD患者（长期戒烟率为5%~9%）^[70]。还有研究显示，与接受尼古丁贴片（38.2%）治疗的COPD患者相比，接受伐尼克兰（58.3%）和安非他酮（55.6%）治疗的COPD患者治疗第9~24周持续戒烟率更高^[79]。

3.4.2 新增可潜在减少AECOPD的新药物研究

一项RCT显示，度普利尤单抗可以明显降低伴有慢性支气管炎、基线血EOS计数≥300个/ μ l且有AECOPD史的COPD患者急性加重年发生率，升高FEV₁，减轻呼吸道症状，提高健康相关生活质量^[80]。因此，关注血EOS计数增多的COPD患者，并针对性研发多种生物制剂，对于COPD的治疗具有重要意义。

4 COPD合并症方面重点更新内容

4.1 增加心血管疾病（cardiovascular diseases, CVD）相关研究

一项大型初级保健人群研究发现，无CVD史的COPD患者主要不良心血管事件（包括急性心肌梗死、卒中或心源性死亡）的校正风险较有CVD史者增加25%^[81]。

4.2 增加阻塞性睡眠呼吸暂停（obstructive sleep apnea, OSA）相关研究

OSA是一种以反复发作的上气道闭合为特征的睡眠障碍^[82]。COPD合并OSA患者的预后比单纯COPD患者和单纯OSA患者差^[83]。COPD患者合并OSA与较高的门诊就诊率和住院率相关^[84]。

4.3 增加衰弱相关研究

一项荟萃分析结果显示，衰弱和衰弱前期与COPD患者的全因死亡、急性加重和住院相关^[85]。欧洲呼吸学会发表了一篇关于成年慢性呼吸系统疾病患者衰弱治疗的综述，其中包括老年护理、康复、营养、药物以及心理治疗等临床管理方案^[86]。

5 COVID-19与COPD方面重点更新内容

与《GOLD 2023》^[4]相比，《GOLD 2024》^[3]增加了对于疑似或确诊为COVID-19的COPD患者的药物治疗，患者如果有雾化指征（如COVID-19重症患者），可以使用雾化治疗，而提供治疗者应佩戴适当的个人防护用品。除此之外，还可以采用抗病毒药物、糖皮质激素、免疫调节治疗等治疗COVID-19^[87-88]。

6 小结

综上所述，与《GOLD 2023》^[4]相比，《GOLD

2024》^[3]在COPD概述方面,扩充了PRISm的相关内容,病理生理部分增加了肺过度充气的内容;在COPD诊断和评估方面,肺活量检测部分增加了关于吸入支气管舒张剂前肺功能检查的进一步说明,增加了在目标人群中筛查COPD(指出不要对无症状的成年人进行COPD筛查,应对肺癌高危人群进行胸部影像学检查以筛查COPD,应对合并COPD危险因素的非肺癌人群进行胸部影像学检查以筛查COPD)、关于血EOS计数的说明及ILA相关内容;在COPD预防和管理方面,修订了戒烟部分,更新了疫苗接种建议(包括流感疫苗、肺炎球菌疫苗、呼吸道合胞病毒疫苗等),扩充了吸入性治疗的管理部分,新增了药物治疗的证据概述(新增了戒烟药物治疗研究及可潜在减少AECOPD的新药物研究);在COPD合并症方面,增加了CVD、OSA、衰弱相关研究;在COVID-19与COPD方面,增加了对于疑似或确诊为COVID-19的COPD患者的药物治疗。

作者贡献:王妍进行论文的构思与设计,并撰写论文;王妍、张昊天进行文献/资料收集与整理;闫巍进行文章的可行性分析及修订,负责文章的质量控制及审校,并对文章整体负责、监督管理。

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