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慢性阻塞性肺疾病急性加重并发呼吸衰竭危险因素研究现况

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摘　要

慢性阻塞性肺疾病(COPD)是一种具有异质性的慢性疾病。随着全球人口老龄化的持续加剧，COPD的发病率显著增加，现已成为全球第四大死亡原因，对公共卫生和社会经济造成了巨大负担。慢阻肺患者在疾病急性加重阶段常伴发呼吸衰竭，这不仅直接导致患者高死亡率，还与其远期预后密切相关。因此，明确影响呼吸衰竭的危险因素并针对性地进行治疗与预防，对于降低患者死亡率及改善长期生存率具有重要意义。本研究对相关文献进行了系统地检索和分析，总结了慢性阻塞性肺疾病急性加重期发生呼吸衰竭的相关危险因素。为临床实践中促进早期识别疾病高危患者、实施个体化干预措施及优化治疗策略提供支持。

关键词

慢性阻塞性肺疾病，AECOPD，呼吸衰竭，危险因素

Risk Factors of Acute Exacerbation of Chronic Obstructive Pulmonary Disease Complicated with Respiratory Failure

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Abstract

Chronic obstructive pulmonary disease (COPD) is a heterogeneous chronic disease. With the continuous increase in global population aging, the incidence of COPD has significantly risen, making it now the fourth leading cause of death worldwide. It has imposed a substantial burden on public health and the socioeconomy. During the acute exacerbation phase of COPD, patients often suffer from respiratory failure, which not only directly leads to a high mortality rate but is also closely related to their long-term prognosis. Therefore, identifying the risk factors for respiratory failure and providing targeted treatment and prevention are of great significance for reducing mortality and improving long-term survival rates. This study systematically retrieved and analyzed relevant literature, summarizing the risk factors associated with respiratory failure during the acute exacerbation phase of COPD. It provides support for the early identification of high-risk patients in clinical practice, the implementation of individualized intervention measures, and the optimization of treatment strategies.

Keywords

Chronic Obstructive Pulmonary Disease, AECOPD, Respiratory Failure, Risk Factors

1. 引言

慢性阻塞性肺疾病(COPD)是一种复杂且异质性的肺部疾病，其主要特征在于由于气道异常(如支气管炎、细支气管炎)和/或肺泡破坏(如肺气肿)引起的持续性呼吸气流受限。这种气流受限通常具有进行性，并与慢性呼吸道症状共同表现。尽管 COPD 通常是可预防和可治疗的，但其急性加重和并发症显著影响患者的总体疾病严重程度[1]。

COPD 可被视作为个体在生命过程中基因与环境因素相互作用的累积结果[2]。主要危险因素包括环境暴露(例如吸烟、空气污染等)、遗传易感性、肺功能轨迹异常、肺发育和老化过程、社会经济状况、感染既往病史以及哮喘等。

临床上，COPD 患者常表现为呼吸困难、喘息、胸闷、乏力、慢性咳嗽伴痰液分泌以及运动耐力下降等症状。此外，COPD 患者可能经历呼吸系统症状的急性加重(简称 AECOPD)。AECOPD 被定义为：“在不超过 14 天内，患者出现以呼吸困难和/或咳嗽、咳痰为主的症状急性加重，通常伴随呼吸急促和/或心动过速，这种加重通常与气道感染、污染或其他气道刺激因素引发的局部与全身炎症反应有关”[3]。这种状态往往需要针对性的预防策略和治疗措施。

慢性阻塞性肺疾病(COPD)患者通常伴有多种合并症，不仅严重影响患者的临床状况及预后，同时复杂的临床表现也增加了 COPD 的诊断及治疗难度。目前，全球范围内 COPD 相关死亡人数的增加主要与人口增长及老龄化趋势有关，而死亡率在约 65 岁时达到高峰[4]。

COPD 急性加重时，首先表现出肌肉负荷增加、肌肉功能恶化和气体交换效率降低的现象。当上述生理现象达到临界点时，可能引发呼吸肌(泵)衰竭。同时，肺部排气不畅导致空气潴留进一步加重，而气道及血管功能异常则致使通气/血流比值(V/Q)下降，气体交换功能受损。过度充气的肺区压迫相对健康的

肺组织，进一步恶化了 V/Q 比值[5]-[7]。这些病理生理过程相互作用，最终导致了呼吸衰竭的发生，而这正是 COPD 患者高短期及长期死亡率的主要原因之一。除高死亡率外，低氧性呼吸衰竭还与显著的再住院风险密切相关[8]。

研究表明，为患者提供及时而充分的呼吸支持可显著改善病情进展，降低并发症发生率，缩短住院时间，并减少院内及长期死亡率[9] [10]。因此，在 COPD 急性加重的管理中，呼吸支持治疗尤为关键。

2. 方法

本文就慢性阻塞性肺疾病急性加重期呼吸衰竭的危险因素进行综述，我们通过检索 PubMed、EMBAS，Cochrane 等数据库，以阐述目前的相关研究进展，检索了从建库到 2024 年 12 月 10 日的 AECOPD 呼吸衰竭危险因素的文章，检索关键词包括呼吸功能不全、呼吸衰竭、低氧血症性呼吸衰竭、高碳酸血症性呼吸衰竭、COPD、AECOPD、危险因素等。此外，最初纳入的文章的参考文献也用于系统检索，以防止遗漏并全面报告 AECOPD 患者呼吸衰竭的危险因素。

3. 结果

3.1. 年龄与性别

老年人被认为是慢性阻塞性肺疾病(COPD)急性加重并发生呼吸衰竭的独立危险因素。研究表明，男性患 COPD 急性加重并伴发呼吸衰竭的比例更高[11]-[13]。这一性别差异可能部分归因于男性更高的吸烟率及肥胖情况，这与其肺功能较快下降密切相关。此外，中老年人群的研究发现，肺功能指标及限制性通气障碍与肌肉力量和肌肉质量的比值显著相关，提示通过肌肉训练改善群体肺功能可能具有潜在益处[14] [15]。总体而言，较大年龄与 COPD 的不良预后密切相关[12]。

3.2. 肺功能

研究表明，COPD 的风险增加与特定基因变异相关，这些变异可能导致从儿童期到成年期肺功能的持续下降[16]。较低的 FEV1 水平显著增加了 COPD 急性加重并发呼吸衰竭的风险[17] [18]。此外，动脉血氧饱和度的下降与年龄、性别及肺功能之间存在线性相关[19]。功能残气量和静息心率被认为是发作性低氧血症的重要独立预测因子[20]。随着气流受限程度的加重，气道阻塞进一步引发通气/灌注(V/Q)比率紊乱，并加剧肺部气体交换异常。此外，功能残气量的增加可能反映过度通气，从而进一步影响气体交换效率。

3.3. 白蛋白水平

低白蛋白血症往往是慢性疾病患者炎症反应的结果，同时也与蛋白质及热量摄入不足有关。研究发现，血清白蛋白水平的降低与肺炎的发病率及死亡率风险增加显著相关[21]。此外，低白蛋白血症是 COPD 患者发生呼吸衰竭的主要危险因素之一，每年白蛋白补充剂量的年均值高于 13.8 g 的患者，发生呼吸衰竭的风险更高[11] [22]。营养状况被认为是慢性呼吸衰竭的可靠标志物，同时也是患者死亡的独立预后因素[23]。在急性加重期并发呼吸衰竭的 COPD 患者中，贫血、低白蛋白血症及肌钙蛋白水平升高均为需要有创机械通气(IMV)的危险因素[24]。

3.4. 营养及代谢因素

预后营养指数(PNI)已被证实可独立预测 AECOPD (慢性阻塞性肺病急性加重)患者的呼吸衰竭，其中 PNI 较高被视为慢性阻塞性肺病(COPD)患者呼吸衰竭的保护性因素[13]。PNI 作为一种客观的营养评估

指标，在呼吸系统疾病预后中的重要性不可忽视。此外，低尿酸水平被认为是 COPD 患者发生呼吸衰竭的危险因素，这可能与机体炎症状态的加重有关。尿酸能够清除氧自由基，有助于缓解氧化应激反应[22]。同时，糖尿病的存在也与呼吸衰竭风险的增加密切相关，而甘油三酯－葡萄糖(TyG)指数被视为胰岛素抵抗的有效标志物，其升高与 AECOPD 患者不良临床结局的高风险独立相关[25]。对于 COPD 及慢性呼吸衰竭患者而言，营养状况是死亡的重要独立预测因素之一，体重指数(BMI)也显著影响低氧血症性呼吸衰竭患者的 1 年死亡风险[26]。

3.5. 细菌

研究表明，在高碳酸血症性呼吸衰竭患者中，肺炎克雷伯菌和铜绿假单胞菌的检出率更高[27]。细菌性支气管肺炎常常造成弥漫性肺泡损伤、肺水肿及肺泡出血，是诱发呼吸衰竭的重要原因之一。这种情况在老年患者中表现得尤为明显[28] [29]。

3.6. 血液成分

对于 AECOPD 合并呼吸衰竭的患者，血细胞比容(HCT)被认为是高碳酸血症性呼吸衰竭的独立预测因子[13]。同时，贫血、低白蛋白血症以及肌钙蛋白水平升高均与需要有创机械通气(IMV)的风险相关[24]。贫血可能是住院期间死亡的危险因素，而高于贫血诊断阈值的血红蛋白水平则与慢性呼吸衰竭患者的长期生存率改善相关[30] [31]。此外，中性粒细胞计数、血红蛋白浓度和 C-反应蛋白水平也与低氧血症性呼吸衰竭患者的 1 年死亡风险显著相关[26]。

3.7. 其他因素

研究显示，肺表面活性蛋白内含子 4 (SP-B4)变异[32]、蛋白尿[28]以及日常生活活动能力[13]可能与 COPD 中急性呼吸衰竭风险的增加相关。过度充气和碱剩余在慢性高碳酸血症性呼吸衰竭中被视为可靠且一致的标志物，并且是预测死亡的重要独立因素[23]。此外，类固醇治疗、生活区域的城市化程度较低、合并终末期肾病、糖尿病、帕金森病以及中风均与急性呼吸衰竭风险的升高相关[12]。既往高碳酸血症性呼吸衰竭的病史亦是 COPD 患者高碳酸血症的重要相关因素之一[18]。

4. 讨论

慢性阻塞性肺病是一种常见的慢性气道疾病，在其发病过程中，肺功能的下降不仅影响呼吸衰竭的发生，还对疾病进展和患者预后有重要影响。现有研究表明，肺力学异常通过改变通气/灌注比例和死腔/潮气量比值，直接影响呼吸动态模式。患者的气流受限导致肺部压力增加、呼吸肌功能减弱，进一步加重病情[33]。

目前，从婴儿期至成年阶段肺功能的发育与 COPD 发病之间的潜在关系尚未深入研究。COPD 的发展受遗传与环境因素共同作用，针对早期肺功能异常的研究可能为疾病的诊断与预防提供新方向。

在 COPD 急性加重(AECOPD)的研究领域，种族、经济地位、生活环境等异质性依然带来研究结果的差异。因此，大样本、多中心的研究对于明确相关危险因素至关重要。同时，新型生物标志物的探索有助于评估疾病进展与治疗反应。

未来研究需要重点解决如何改善肺部力学异常、促进气道修复及增强呼吸肌功能等问题。通过揭示病理机制并紧密结合临床实践，COPD 的精准医疗发展将得到进一步推动。

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