·专家共识·

中国慢性阻塞性肺疾病急性加重中西医诊治专家共识（2021）

国家卫生健康委员会急诊医学质控中心 中华医学会急诊医学分会 中国医师协会急诊医师分会 世界中医药学会联合会急症专业委员会 中华中医药学会肺系病分会 中国中西医结合学会重症医学专业委员会

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【摘要】 慢性阻塞性肺疾病急性加重（AECOPD）是指慢性阻塞性肺疾病（COPD）呼吸道症状的急性恶化，包括呼吸困难加重、咳嗽加剧、痰量增多和（或）痰液呈脓性，导致患者需要改变用药方案及增加额外治疗措施。AECOPD已成为COPD患者住院和死亡的最重要原因，严重影响患者预后，同时造成较大的经济和社会负担。为了早期预防并规范治疗AECOPD，国家卫生健康委员会组织国内众多专家就AECOPD的预防和中、西医治疗撰写了《中国AECOPD中西医诊治专家共识（2021）》，以期为AECOPD的临床诊疗和预防提供参考。

【关键词】 慢性阻塞性肺疾病急性加重； 中西医结合； 临床治疗； 专家共识

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Expert consensus of Chinese and Western medicine treatment on acute exacerbation of chronic obstructive pulmonary disease in China (2021)

National Health Commission Emergency Medical Quality Control Center, Emergency Medical Branch of Chinese Medical Association, Chinese Medical Doctor Association Emergency Medical Branch, World Federation of Chinese Medicine Societies Emergency Professional Committee, Pulmonary Disease Academy of China Association of Chinese Medicine, Chinese Society for Integrated Chinese and Western Medicine Intensive Medicine Specialized Committee

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【Abstract】 Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is defined as an acute worsening of respiratory symptoms including worsening dyspnea and cough, increased sputum volume, and/or purulent sputum, resulting in additional treatments. AECOPD has become a major cause of hospitalization and death in COPD patients, leading to a large economic and social burden. In order to prevent and standardize the early treatment of AECOPD, the National Health Commission organized many domestic experts to write the Chinese expert consensus on the prevention and the integrated traditional Chinese and Western medicine of treatment for AECOPD to provide reference for clinicians.

【Key words】 Acute exacerbation of chronic obstructive pulmonary disease; Integrated traditional Chinese and Western medicine; Clinical therapeutics; Expert consensus

Fund program: National Key Research and Development Program of China (2018YFC1705900); Inheritance and Innovation of Traditional Chinese Medicine Millions of Talent Projects (Qihuang Project) of State Administration of Traditional Chinese Medicine of China (2018-12)

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慢性阻塞性肺疾病（chronic obstructive pulmonary disease, COPD）是以持续存在的呼吸系统症状和气流受限为特征的疾病[1]。据全球疾病负担研究估计，2017年全球COPD发病率为3.9%，全球每年每10万人中有41.9人因COPD死亡[2]，是病死率最高的慢性呼吸道疾病。中国肺部健康研究（the China Pulmonary Health study，CPH study）中指出，我国≥20岁人群COPD发病率为8.6%[3]。慢性阻塞性肺疾病急性加重（acute exacerbation of chronic obstructive pulmonary disease，AECOPD）是指呼吸道症状急性恶化，包括呼吸困难加重、咳嗽加剧、痰量增多和（或）痰液呈脓性，导致患者需要改变用药方案及额外增加治疗措施[4-5]。AECOPD患者症状不具有特异性，当出现以上症状时需排除肺炎、肺结核、哮喘、气胸、胸腔积液、肺栓塞、心源性肺水肿及心房颤动等疾病。病毒感染、细菌感染及空气污染均可诱发AECOPD，导致气道炎症加剧、黏液分泌增多以及气流严重受限。

重度 AECOPD 患者由于急性呼吸衰竭的发生需住院治疗，已成为 COPD 患者死亡的最重要原因，严重影响患者预后，同时造成较大的经济和社会负担[6]。为了科学认识 AECOPD，早期预防，规范治疗，国家卫生健康委员会组织国内众多专家撰写了《中国慢性阻塞性肺疾病急性加重期中西医诊治专家共识（2021）》，经过反复讨论和修改，该共识主要从 AECOPD 治疗及预防逐一论述，供广大同行参考。证据等级和推荐意见采用推荐分级的评价、制定与评估（Grades of recommendations assessment, development and evaluation, GRADE）方法，应用 GRADEpro 工具进行评估[7]。对于不能进行 GRADE 分级的强推荐，采取“最佳实践声明”推荐。

1　AECOPD 治疗

因 AECOPD 住院的患者远期预后较差，5 年生存率仅为 50%[8]。与 AECOPD 预后不良相关的独立危险因素包括：高龄、低体质量指数（body mass index, BMI）、合并症（如心血管疾病、肺癌）、既往因 AECOPD 住院治疗、重度 AECOPD 以及出院后需要长期氧疗[9-11]；另外，呼吸道症状反复出现、生活质量差、肺功能差、运动耐力差、CT 显示肺密度减低和支气管壁增厚以及寒冷季节等均可增加 AECOPD 患者死亡风险[12-13]。因此，AECOPD 的治疗目标是使本次急性加重的影响最小化，并预防急性加重事件的再次发生[14]。

1.1　AECOPD 患者住院治疗指征：轻度 AECOPD 患者只需要予以短效支气管扩张剂（short-acting bronchodilator, SABD）治疗；中度 AECOPD 患者需给予 SABD+ 抗菌药物和（或）口服激素治疗；重度 AECOPD 患者需要住院治疗。当 AECOPD 患者出现以下情况时推荐住院治疗：① 严重的症状，如静息状态下呼吸困难突然加重，呼吸频率增快，血氧饱和度降低，意识障碍，嗜睡；② 急性呼吸衰竭；③ 出现新的体征，如发绀、外周水肿；④ 初始治疗失败；⑤ 有严重的合并症或伴随疾病需要住院治疗，如心力衰竭、新发的心律失常等；⑥ 家庭氧疗支持不足。以上指征还需考虑当地医疗条件。当 AECOPD 患者出现以下情况时推荐收入重症监护病房（intensive care unit, ICU）治疗：① 对初始急诊治疗反应差的重度呼吸衰竭；② 意识改变（意识模糊、昏睡、昏迷）；③ 持续性或进行性低氧血症〔动脉血氧分压（arterial partial pressure of oxygen, PaO_2）<5.3 kPa 或 40 mmHg, 1 mmHg=0.133 kPa〕，尽管进行氧疗和无创机械通气（non-invasive mechanical ventilation, NIV），但仍存在严重 / 进行性加重的呼吸性酸中毒（pH<7.25）；④ 需要有创机械通气（invasive mechanical ventilation, IMV）；⑤ 血流动力学不稳定，需使用血管活性药物。

1.2　药物治疗：治疗 AECOPD 常用支气管扩张剂、糖皮质激素、抗菌药物及祛痰药物 4 类药物[15-17]。

1.2.1　支气管扩张剂

推荐意见 1：AECOPD 患者初始治疗为单用短效 β2 受体激动剂（short-acting β2 receptor agonist, SABA），或者 SABA 联合短效抗胆碱能药物（short-acting muscarinic antagonist, SAMA）（最佳实践声明），推荐优先选用空气驱动（强推荐，中级证据质量）。

AECOPD 支气管扩张剂的初始治疗仍为单用 SABA，或者 SABA 联合 SAMA[18]。关于 SABD 给药途径的系统回顾分析显示，雾化吸入与定量吸入气雾剂（metered-dose inhalation aerosol, MDI）对第 1 秒用力呼气容积（forced expiratory volume in one second, FEV1）的影响无显著差异，但雾化吸入对较衰弱的患者更容易接受[19-20]。针对未持续使用雾化吸入而使用 MDI 的患者推荐剂量为每小时 1 剂，共 2～3 剂，然后根据患者的反应，每 2～4 h 吸入 1 剂。如果选用压力喷雾剂来递送支气管扩张剂，推荐 AECOPD 患者优先选用空气驱动。若由氧气驱动，患者可能因吸入氧浓度过高而引起呼吸抑制，二氧化碳潴留[21]。

推荐意见 2：不推荐静脉使用甲基黄嘌呤类药物（茶碱或氨茶碱）作为一线支气管扩张剂（强推荐，高级证据质量）[22-23]。

一项有关茶碱和吸入糖皮质激素（theophylline with inhaled corticosteroids, TWICS）的随机对照试验（randomized controlled trial, RCT）研究纳入了 1 567 例接受吸入激素治疗且 1 年内发生急性加重事件超过 2 次的 COPD 患者，其中 791 例患者接受持续 1 年的低剂量茶碱（200 mg、每日 1 次或每日 2 次），以维持茶碱 1～5 mg/L（由理想体质量和吸烟状况确定）的血药浓度；其余 787 例患者使用安慰剂。经过 1 年随访后证实，在有急性加重风险的 COPD 成人患者中，加用低剂量茶碱并未降低 1 年内 AECOPD 的发生率[24]。

1.2.2　糖皮质激素

推荐意见 3：中重度 AECOPD 患者可从全身使用糖皮质激素中获益，推荐使用泼尼松 40 mg/d，疗程 5 d（强推荐，高级证据质量）。

一系列研究数据证实，AECOPD 患者使用全身激素可缩短恢复时间并改善肺功能和氧合[25-28]，降低早期复发及治疗失败的风险[29]，以及缩短住院时间[30]。口服泼尼松的疗效与静脉治疗相同[31]。近期一项研究证实，AECOPD 患者长期口服激素会增

加肺炎和死亡风险[32]。一项针对 18～64 岁门诊患者的研究显示，与未服用激素的患者相比，口服激素（时间＜30 d）的患者 30 d 内发生脓毒症、静脉血栓及骨折的风险更高[33]。因此，在全身使用激素时需确认 COPD 患者是否出现急性发作，如出现急性发作，推荐使用泼尼松 40 mg/d，疗程 5 d[34]。

推荐意见 4：推荐无酸中毒、轻中度及非住院 AECOPD 患者单独使用布地奈德雾化治疗，4～8 mg/d（弱推荐，高级证据质量）。上呼吸道感染的 AECOPD 患者，建议强化吸入糖皮质激素（inhaled corticosteroid，ICS）/ 长效 β2 受体激动剂（long-acting β2 receptor agonist, LABA）治疗以减少重度急性加重的风险（弱推荐，高级证据质量）。

单独使用布地奈德雾化可能是治疗某些 AECOPD 患者（如无酸中毒的 AECOPD 患者、轻中度 AECOPD 患者以及非住院 AECOPD 患者）的合适选择[35-36]，并且单独使用布地奈德雾化（2 mg、每日 3 次）可提供与静脉注射甲泼尼龙（40 mg、每日 1 次）相似的获益，然而这些措施的选择可能取决于当地的医疗成本问题[37]。一项多中心、随机、双盲、安慰剂对照试验证实，与安慰剂组相比，ICS/LABA 组虽然不能降低由上呼吸道病毒感染引起的 AECOPD，但可使重度急性加重风险降低 72%[38]。

1.2.3 抗菌药物

推荐意见 5：推荐 AECOPD 患者有指征地使用抗菌药物（强推荐，高级证据质量）。

引起 AECOPD 感染的病原菌可能是病毒或细菌[39-40]，有指征地使用抗菌药物可缩短恢复时间，降低早期复发风险，减少治疗失败及缩短住院时间。有证据支持，当 AECOPD 患者存在细菌感染的临床症状（如脓痰）时，应使用抗菌药物[41-42]。一项系统回顾研究证实，相对于安慰剂，抗菌药物使用可使短期死亡风险降低 77%，治疗失败风险降低 33%，脓痰发生风险降低 44%[43]。该研究为抗菌药物治疗中度或重度 AECOPD、咳嗽增加及黄脓痰提供了理论依据。推荐 AECOPD 患者接受抗菌药物治疗的指征为：① AECOPD 同时出现呼吸困难加重、痰量增多和痰液变脓这 3 个症状中的 2 个，且其中包括痰液变脓这一症状；② 需要机械通气（无创或有创）[44]。

1.2.4 祛痰药物

推荐意见 6：AECOPD 患者进行祛痰治疗（最佳实践声明）。

AECOPD 时痰量增多，且痰液为脓痰时，痰液中细菌载量会增多[44-46]。因此，祛痰药物在 AECOPD 的治疗中至关重要。

祛痰制剂种类繁多，按主要机制分类为：① 黏液溶解剂：例如 N- 乙酰半胱氨酸为巯基化合物，能使痰液中二硫键断裂，从而降低痰液黏稠度。目前吸入用 N- 乙酰半胱氨酸溶液是我国食品药品监督管理总局唯一批准的雾化吸入祛痰剂。② 黏液调节剂：例如羧甲司坦可调节支气管腺体的分泌，使痰液黏滞性降低，易于咳出。③ 黏液动力药：例如氨溴索可促进呼吸道内黏稠分泌物的排出及减少黏液的滞留，从而促进排痰。④ 除痰剂：例如高渗盐水可引起黏蛋白 5AC 的合成和分泌，促进黏液外排。

1.2.5 辅助治疗

推荐意见 7：推荐 AECOPD 住院患者评估维生素 D 水平，并对严重维生素 D 缺乏（维生素 D＜25 nmol/L 或＜10 μg/L）患者进行补充维生素 D 治疗（弱推荐，高级证据质量）。

近年来，维生素 D 在 AECOPD 中的疗效越来越受到学者的关注。近期一项荟萃分析显示，在整体人群中维生素 D 并不影响中重度 AECOPD 事件的发生，但在维生素 D＜25 nmol/L 的人群中，可减少中重度急性加重事件的发生[47]。

除此之外，应根据患者临床情况，维持适当的液体平衡，有临床指征者可使用利尿剂、抗凝治疗、合并症治疗及营养治疗等。考虑到 AECOPD 住院患者是发生深静脉血栓及肺栓塞的高危人群[48-49]，补充维生素 D 可采取措施预防血栓形成。

1.3 呼吸支持

1.3.1 氧　疗

推荐意见 8：推荐 AECOPD 患者血氧饱和度维持在 0.88～0.92；吸氧装置推荐选择文丘里面罩（强推荐，高级证据质量）。

氧疗是 AECOPD 患者住院治疗中的一个关键部分。调节吸入氧浓度从而改善患者低氧血症，使血氧饱和度维持在 0.88～0.92[50]。一旦氧疗开始，应密切监测血气分析以保证满意的氧合指数，且不出现二氧化碳潴留和（或）加重酸中毒。关于血气分析标本的选择，近期一项研究表明：与动脉血气相比，以静脉血气来评估碳酸氢根和 pH 值水平也是准确的[51]。但该项研究中纳入的大多数患者采样时 pH＞7.30，通过静脉血与动脉血测定的二氧化碳分压是不同的，且气流受限的严重程度也未报道。因此仍需要更多的数据来证实静脉血气分析在急性呼吸衰竭中对临床决策的价值。在吸氧装置的选择上，推荐使用文丘里面罩（高流量装置），文丘里面罩比双导管给氧更精确，也更容易控制氧流量[18]。

1.3.2 经鼻导管高流量氧疗（high-flow nasal cannula oxygen therapy, HFNC）

推荐意见 9：发生呼吸衰竭的 AECOPD 患者，

推荐使用 HFNC（强推荐，高级证据质量）。

对于急性低氧血症型呼吸衰竭患者，HFNC 可能作为标准氧疗或无创正压通气的替代措施，推荐气体流量成人最高 60 L/min，婴儿最高 8 L/min[52]。对于存在低氧血症性急性呼吸衰竭的患者，HFNC 可以减少插管率和病死率[53]。一项随机交叉试验表明，HFNC 可以改善 COPD 患者氧合并减少高碳酸血症的发生[54]，还可缓解轻中度 AECOPD 患者膈肌疲劳[55]。在急性呼吸衰竭人群中，HFNC 可以改善患者氧合[56]。同时，HFNC 可减少有稳定高碳酸血症的 COPD 患者发生高碳酸血症的风险，改善患者生活质量[57-58]。然而目前的研究都是在存在严重基础疾病、需要氧疗的 COPD 患者中进行的。未来仍需进一步设计良好的、多中心 RCT 研究来证实 HFNC 在 AECOPD 患者，尤其是在因 AECOPD 所致急性呼吸衰竭患者中的作用。

1.3.3　机械通气

推荐意见 10：AECOPD 合并Ⅱ型呼吸衰竭患者机械通气首选 NIV；对于存在 IMV 指征的 AECOPD 患者，应尽早行 IMV（强推荐，高级证据质量）。

AECOPD 患者的机械通气支持可以是无创的（如鼻罩或面罩），也可以是有创的（如经口气管插管或气管切开）。对于伴有急性呼吸衰竭的 COPD 患者，若无 NIV 绝对禁忌证，则应将 NIV 作为首选治疗。

1.3.3.1　NIV

对于 AECOPD 住院患者，治疗其急性呼吸衰竭的初始通气模式更倾向于使用 NIV 而不是 IMV。多项 RCT 研究数据显示，AECOPD 患者使用 NIV 的成功率在 80%～85%[59-63]，且使用 NIV 可提升患者 pH 值并降低二氧化碳分压，从而改善氧合，纠正急性呼吸性酸中毒。此外，NIV 还可以降低呼吸频率、呼吸肌作功以及呼吸困难的严重程度，并减少并发症（如呼吸机相关性肺炎）以及缩短住院时间。更重要的是，NIV 也可降低病死率及插管率[64-66]。关于撤机时机，有研究者指出：一旦患者病情好转，并且能够耐受至少 4 h 的无辅助呼吸，可以直接停用无创辅助通气，无需“撤机”期[67]。

NIV 使用适应证（至少符合以下 1 个条件）：① 呼吸性酸中毒〔动脉血二氧化碳分压（arterial partial pressure of carbon dioxide，$PaCO_2$）≥6 kPa 或 45 mmHg，和动脉血 pH≤7.35〕；② 严重呼吸困难合并提示呼吸肌疲劳、呼吸功增加的临床症状，例如应用辅助呼吸机呼吸出现胸腹矛盾运动或者肋间隙肌群收缩；③ 虽然持续氧疗，但仍然有低氧血症。

1.3.3.2　IMV

IMV 指征：① 能够耐受 NIV 或 NIV 治疗失败（或不适合 NIV）；② 呼吸或心搏骤停；③ 意识障碍，需使用镇静剂；④ 严重误吸或持续呕吐；⑤ 长期不能排出呼吸道分泌物；⑥ 严重的血流动力学不稳定，对液体疗法和血管活性药物无反应；⑦ 严重的室性心律失常；⑧ 威胁生命的低氧血症且不能耐受 NIV。

一旦初始 NIV 治疗失败而接受 IMV 治疗，则会增加患者病死率，延长住院时间[61]。极重度 COPD 患者 IMV 的使用会受到以下因素的影响，即急性加重诱因的可逆性、患者的自身意愿以及是否具备重症监护设施[61]。IMV 的主要危害包括：呼吸机相关性肺炎发生风险增加（特别是有多重耐药病原菌流行时），气压伤和容积伤，气管切开，以及呼吸机依赖风险增加。

因 AECOPD 所致呼吸衰竭而进行机械通气的患者，急性期病死率低于因非 COPD 因素而进行机械通气的患者[68]。大型研究报道，发生急性呼吸衰竭的 COPD 患者院内病死率为 17%～49%，若患者行气管插管前肺功能差（FEV1＜30% 预计值）、存在肺外合并症或无法外出，则会增加出院后 12 个月内的死亡风险[69]。

2　AECOPD 的预防

COPD 患者过去 1 年内急性加重的次数可以预测将来急性加重发生的频率[70]，急性加重次数越多，死亡风险越大[71]。除此之外，AECOPD 复发与急性加重后首次住院病情及治疗有关，肺功能降低与脑卒中及心力衰竭发生风险增高有关[72-73]。因此，减少急性加重次数是 COPD 患者稳定期管理的重要措施。在急性加重发生后，应立即启动相应的预防措施防止 AECOPD 再次发生。预防 AECOPD 的干预措施见表 1。

表 1　预防 AECOPD 的干预措施

干预种类	干预方法
支气管扩张剂	LABA、LAMA、LABA+LAMA
含激素的治疗方案	LABA+ICS、LABA+LAMA+ICS
抗炎（非激素类）	罗氟司特
预防感染	疫苗、长期大环内酯类
黏液调节剂	N- 乙酰半胱氨酸、羧甲司坦
其他	戒烟、肺康复、肺减容

注：AECOPD 为慢性阻塞性肺疾病急性加重，LABA 为长效 β2 受体激动剂，LAMA 为长效抗胆碱能拮抗剂，ICS 为吸入糖皮质激素

2.1　支气管扩张剂联合 ICS

推荐意见 11：对于有 COPD 急性发作入院史或 1 年内有≥2 次中度 COPD 急性发作事件且存在重度或以上气流受限者，稳定期推荐使用含有

ICS/长效抗胆碱能拮抗剂(long-acting muscarinic antagonist, LAMA)/LABA 的三联治疗。若有不推荐使用 ICS 的因素存在,则推荐使用 LABA/LAMA 联合用药(强推荐,高级证据质量)。

LABA 和 LAMA 可有效改善肺功能、呼吸困难及健康状况,并降低 COPD 患者急性加重发生率,但 LAMA 比 LABA 更能使患者获益。LAMA 较 LABA 更能有效降低急性加重发生率和住院率[74];噻托溴铵可提高肺康复治疗的有效性[75]。LABA/LAMA 联合用药在增加 FEV1、减轻症状及减少 COPD 急性加重发生率方面均优于单药使用[76]。

相比 ICS/LABA、LABA/LAMA 及 LAMA 单药使用,ICS/LABA/LAMA 三联治疗可以更好地改善 COPD 肺功能,改善健康状况,减少急性加重次数及降低死亡风险[77-80]。在 ICS/LABA 基础上加入 LAMA 可以改善 COPD 患者肺功能和结局,尤其是急性加重风险[81-84]。对于 FEV1<50%、有症状、有急性加重史的 COPD 患者,三联治疗比噻托溴铵可以使患者更加获益[85]。近期几项双盲 RCT 研究报道,在不同人群中 ICS/LABA/LAMA 三联治疗比 LABA/LAMA 联合治疗有更大的益处,并在不同人群中证实三联治疗可降低全因病死率[86-89]。两项大型 RCT 研究证实了对频繁和(或)有重度急性加重史的 COPD 患者,ICS/LABA/LAMA 三联治疗比 LABA/LAMA 联合治疗可降低死亡风险及中重度 COPD 急性发作风险[90-91]。由此说明,含有 ICS 的三联药物优于双联支气管扩张剂的作用。

血嗜酸粒细胞计数可预测 ICS(在规律支气管扩张剂维持治疗基础上)在预防急性加重事件的作用[92-94]:血嗜酸粒细胞计数<100×10^6/L,含有 ICS 的治疗方案获益较少或无获益;血嗜酸粒细胞计数>300×10^6/L,含有 ICS 的治疗方案有明显获益。因此,ICS 的使用应结合血嗜酸粒细胞计数进行判断。① 强烈推荐长效支气管扩张剂可联合 ICS 使用的患者:有因 COPD 急性发作入院史;1 年中有≥2 次中度 COPD 急性发作事件;血嗜酸粒细胞计数>300×10^6/L;有哮喘史或急性发作合并哮喘。② 可以考虑使用长效支气管扩张剂联合 ICS 的患者:1 年中有 1 次中度 COPD 急性发作事件;血嗜酸粒细胞计数(100~300)$\times10^6$/L。③ 不能联合使用 ICS 的患者:复发性肺炎;血嗜酸粒细胞计数<100×10^6/L;有分枝杆菌感染史。

2.2 疫 苗

推荐意见 12:推荐 COPD 患者每年接种流感疫苗和每 5 年接种肺炎链球菌疫苗(强推荐,高级证据质量)。

流感疫苗可减少 COPD 患者因呼吸道感染而需要住院的次数、急性加重次数及降低病死率[95-98]。因此推荐每年接种流感疫苗以预防 AECOPD 的发生[99]。一项纳入 12 项 RCT 研究的 Meta 分析显示,接种肺炎链球菌疫苗可减少 AECOPD 事件发生[100]。23 价肺炎球菌多糖疫苗可降低小于 65 岁 COPD 患者的社区获得性肺炎发生率[101];13 价肺炎球菌多糖结合疫苗可预防大于 65 岁 COPD 患者脓毒症及社区获得性肺炎的发生[102]。同时也建议青少年时期未接种过百白破疫苗的 COPD 患者,可补种百白破疫苗以预防百日咳、白喉及破伤风。

2.3 免疫调节剂

推荐意见 13:推荐 COPD 稳定期患者使用免疫调节剂(强推荐,高级证据质量)。

细菌溶解产物(OM-85)可缩短 AECOPD 患者住院时间及减少急性发作次数[103-104]。Li 等[105]证实,OM-85 还可以改善 COPD 合并慢性支气管炎患者呼吸道症状及降低痰培养阳性率。

2.4 黏液调节剂

推荐意见 14:推荐 COPD 稳定期患者使用黏液调节剂(强推荐,高级证据质量)。

对于未使用 ICS 的 COPD 患者,规律使用黏液调节剂(如厄多司坦、羧甲司坦和 N-乙型半胱氨酸)可以减少急性加重事件及改善患者健康状况[106-108];近期一项研究也证实,厄多司坦和 N-乙型半胱氨酸可缩短 AECOPD 发作时间[109]。但由于患者异质性,在使用羧甲司坦和 N-乙型半胱氨酸时应注意剂量个体化治疗[111]。

2.5 戒 烟

推荐意见 15:推荐吸烟的 AECOPD 患者戒烟(最佳实践声明)。

强烈建议所有吸烟者戒烟。在医务工作者指导及家属和社会参与下,帮助患者实施戒烟。

2.6 肺康复

推荐意见 16:COPD 稳定期患者推荐肺康复治疗(强推荐,高级证据质量)。

肺康复可改善稳定期 COPD 患者呼吸困难、健康状态和运动耐受力;降低近期(上次出院后 4 周内)有急性加重患者的再入院率。同时,肺康复可降低 COPD 患者焦虑和抑郁的发生风险[111]。

2.7 患者教育和自我管理

推荐意见 17:推荐 AECOPD 患者进行基于医务工作者沟通的自我管理(弱推荐,中级质量证据)。

AECOPD 患者进行包括与医务工作者沟通在内的多元自我管理可减少急性加重住院时间,降低病死率[112],降低再入院及死亡风险[113]。

3　中医治疗

COPD 属于中医学“咳嗽”“肺胀”“喘病”等范畴，早在 3 000 余年前的《黄帝内经》就有有关该病的记载。中医认为，肺脏感邪，迁延失治，痰瘀停留，损伤正气，肺、脾、肾虚损，正虚卫外不固，外邪易反复侵袭，诱使本病发作，其病理变化为本虚标实[114-115]。AECOPD 的基本病机为痰阻（痰热、痰浊）或痰瘀互阻，常兼气虚或气阴两虚、水凌心肺，其中痰瘀互阻为病理关键。中医治疗多以疏风散邪、清热解毒、宣肺平喘、豁痰宽胸、温阳利水为基本法则，方剂多以麻杏石甘汤、银翘散、千金苇茎汤、三拗汤、瓜蒌薤白半夏汤、清金化痰汤、桔梗汤、二陈汤、葶苈大枣泻肺汤、真武汤为主方[116-118]，作为不同中医证型时加减的主要单位用药。AECOPD 也可以静脉使用中成药，临床应用循证研究较多的药物有喜炎平注射液、痰热清注射液、热毒宁注射液、参附注射液等。喜炎平注射液的主要成分为穿心莲内酯磺化物，具有抗病毒、抗炎、解热、抗菌的药理作用[119-120]，临床及 Meta 分析提示，在常规治疗上联合应用喜炎平注射液能够有效缓解 AECOPD 的临床症状，改善肺功能，缩短住院时间，减少抗菌药物使用[121-122]。苏黄止咳胶囊和银马解毒颗粒是临床常用的中药制剂。苏黄止咳胶囊能够抑制 AECOPD 患者血清炎性细胞因子水平，改善血气分析指标，提高患者肺功能，改善症状，疗效确切[123-124]。银马解毒颗粒常用于痰热壅肺证 AECOPD 伴有一定程度的腑实兼证患者，研究表明，其联合西医基础治疗可明显缓解咳、痰、炎、喘，改善患者腹胀、大便干结等腑气不通的症状，提高患者生活质量[125]。柴芩清宁胶囊主要成分为黄芩苷、柴胡、人工牛黄，具有退热、抗炎的药理作用[126]。研究提示，柴芩清宁胶囊可有效缓解发热症状，退热时间明显提前，其配伍成分影响体内代谢过程，延长退热作用时间，可有效改善发热、咽痛等感染引起的不适症状，明显改善中医证候积分[127]。清解退热颗粒为中医治疗温热病传统方剂升降散的现代制剂，具有抗炎、调节免疫功能、抗病毒、抗气道炎症等作用，该方主要针对肺胃郁热而设，具有宣展肺气、通络祛瘀、祛除痰热、通利三焦气机的功效[128]。清咳平喘颗粒可用于 AECOPD 痰热壅肺证的治疗，其有效成分具有广谱抗病毒、抗菌、退热、改善气道炎症等作用，研究表明其联合西医常规治疗能够明显缓解咳、痰、喘症状，改善患者肺功能，提高生活质量[129-130]。传统中药六神丸 / 胶囊具有清凉解毒、消炎止痛的功效，药理研究表明其具有抗呼吸道病毒、细菌感染的作用，并可抑制病毒、细菌引发的气道炎症；对于风热犯肺证 AECOPD 患者，六神丸 / 胶囊联合基础治疗能提高临床疗效，增强抗炎活性，具有较高安全性[131-132]。

中医药治疗 AECOPD 应遵循整体观念、辨证论治，重视标本兼治。中医药在 AECOPD 促进痰液引流、增强患者免疫力、提高患者生活质量、减少急性发作等方面优势显著[133-136]。同时，因个体化差异，中医药在治疗 AECOPD 的高质量 RCT 研究尚显不足，还需进一步加强中医药治疗 AECOPD 的循证研究。

4　展　望

目前 COPD 患者发病率高，急性加重事件已成为 COPD 患者住院和死亡的最重要原因，严重威胁公众健康。随着对 AECOPD 的进一步研究和探索，针对该病的治疗和预防措施也在不断完善，其治疗方案也根据不同患者的临床特征而趋于个体化。针对 AECOPD 患者管理的重要措施可减少急性加重事件的发生次数，因此在每次 AECOPD 发生后，应立即启动相应的预防措施防止其再次发生。然而，目前仍需要大量研究探讨不同治疗和预防方案在不同人群中的疗效及作用机制，为 AECOPD 的精准治疗、个体化治疗提供理论依据。

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利益冲突　所有作者均声明不存在利益冲突

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