

· 临床研究 ·

F-V 曲线吸气平台的慢性阻塞性肺疾病患者临床特征探讨

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[摘要] 目的: 研究合并流量-容积(flow-volume, F-V)曲线吸气平台的中重度稳定期慢性阻塞性肺疾病(chronic obstructive pulmonary disease, COPD)患者的临床与肺功能特点、急性加重风险及其相关性。方法: 选取2022年1月—2024年7月南京医科大学第一附属医院肺功能检查中第1秒用力呼气容积占预计值百分比(forced expiratory volume in the first second as a percentage of predicted value, FEV₁%pred)<60%、用力肺活量(forced vital capacity, FVC)≥正常值下限的中重度稳定期COPD患者109例, 按是否伴吸气平台分为吸气平台组53例及FEV₁%pred匹配的非吸气平台组56例。收集并比较两组患者基本资料、吸入药物的种类、急性加重情况、胸部CT影像表现、肺功能参数以及临床合并疾病。采用多因素Logistic回归分析F-V曲线吸气平台的相关因素, 构建诊断中重度稳定期COPD患者合并吸气平台的模型, 用Hosmer-Lemeshow检验进行校正, 用受试者工作特征曲线的曲线下面积(area under the curve, AUC)进行判别。卡方检验初步探索中重度稳定期COPD患者合并吸气平台与各类合并症的关系。结果: ①两组间肺功能分级占比差异无统计学意义($P > 0.05$)。②吸气平台组呼气峰值流量占预计值百分比、吸气峰值流量(peak inspiratory flow, PIF)、肺总量占预计值百分比、肺泡容量占预计值百分比均低于非吸气平台组, 呼气峰值流量(peak expiratory flow, PEF)与PIF的比值(PEF/PIF)、第1秒用力呼气容积(forced expiratory volume in the first second, FEV₁)与PEF的比值(FEV₁/PEF)、5 Hz下的阻力(resistance of 5 Hz, R₅)占预计值百分比、20 Hz下的阻力(resistance of 20 Hz, R₂₀)占预计值百分比、R₅与R₂₀的差值(R₅-R₂₀)、中心气道阻力(resistance of central airway, R_{central})均高于非吸气平台组, 差异有统计学意义($P < 0.05$)。③两组急性加重情况差异无统计学意义($P > 0.05$), 但吸气平台组急性加重率升高, 住院率也略高。④由PIF、PEF/PIF、FEV₁/PEF和R_{central}构成诊断模型, 该模型中影响因素的最佳阈值为PIF≤3.91 L/s、PEF/PIF≥0.830、FEV₁/PEF≥0.369 s和R_{central}≥1.905 cmH₂O/(L·s)。该模型的AUC为0.945, 模型判别能力强, Hosmer-Lemeshow拟合度检验 $P=0.957$, 模型校正良好。⑤与非吸气平台组相比, 吸气平台组上气道狭窄及中央型肺恶性肿瘤患病率更高, 差异有统计学意义($P < 0.05$)。结论: F-V曲线呈现吸气平台的中重度稳定期COPD患者多伴气道阻力的整体增高, 并提示可能存在上气道及周围相关疾病。因此, 中重度稳定期COPD肺功能报告中应关注是否有吸气平台, 通过PIF、PEF/PIF、FEV₁/PEF和R_{central}构建的多参数模型识别, 以便尽早筛查COPD合并疾病。

[关键词] 慢性阻塞性肺疾病; 流量-容积曲线; 吸气平台; 肺功能检查; 早期诊断

[中图分类号] R563

[文献标志码] A

[文章编号] 1007-4368(2026)05-673-12

doi: 10.7655/NYDXBNSN251251

Clinical characteristics of chronic obstructive pulmonary disease patients with inspiratory plateau in flow-volume curve

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[Abstract] **Objective:** To investigate the clinical and pulmonary function characteristics, risk of acute exacerbation, and associated correlations in moderate-to-severe stable chronic obstructive pulmonary disease (COPD) patients with inspiratory plateau on the flow-volume (F-V) curve. **Methods:** A total of 109 patients with moderate-to-severe stable COPD [forced expiratory volume in the first

[基金项目] 癌症、心脑血管、呼吸和代谢性疾病防治研究国家科技重大专项(2023ZD0506300)

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second as a percentage of predicted value ($FEV_1\% \text{ pred}$) $< 60\%$ and forced vital capacity (FVC) \geq lower limit of normal] who underwent pulmonary function tests at the First Affiliated Hospital of Nanjing Medical University from January 2022 to July 2024 were enrolled. Patients were divided into inspiratory plateau group ($n=53$) and non-inspiratory plateau group matched for $FEV_1\% \text{ pred}$ ($n=56$) based on the presence or absence of inspiratory plateau. Demographic data, types of inhaled medications, acute exacerbation, chest CT findings, pulmonary function parameters, and clinical comorbidities were collected and compared between the two groups. Multivariate logistic regression identified factors associated with the F-V curve inspiratory plateau. A diagnostic model for identifying the inspiratory plateau in patients with moderate-to-severe stable COPD was constructed and calibrated using the Hosmer-Lemeshow test, and evaluated using the area under the receiver operating characteristic curve (AUC). Chi-square test was used to preliminarily explore the association between inspiratory plateau and various comorbidities in patients with moderate-to-severe stable COPD. **Results:** ① The difference in the proportion of pulmonary function stages between the two groups was not statistically significant ($P > 0.05$). ② The inspiratory plateau group exhibited significantly lower values for peak expiratory flow as a percentage of predicted value, peak inspiratory flow (PIF), total lung capacity as a percentage of predicted value, and alveolar volume as a percentage of predicted value, but significantly higher values for the ratios of peak expiratory flow (PEF) to PIF (PEF/PIF), the ratios of forced expiratory volume in the first second (FEV_1) to PEF (FEV_1/PEF), resistance at 5 Hz (R_5) as a percentage of predicted value, resistance at 20 Hz (R_{20}) as a percentage of predicted value, the difference between R_5 and R_{20} ($R_5 - R_{20}$), and resistance of central airway (R_{central}) compared to the non-inspiratory plateau group ($P < 0.05$). ③ No statistically significant difference was found in the rate of acute exacerbation between groups ($P > 0.05$), although the inspiratory plateau group exhibited a higher acute exacerbation rate and slightly higher hospitalization rate. ④ A diagnostic model was constructed using PIF, PEF/PIF, FEV_1/PEF and R_{central} . The optimal thresholds for the influencing factors within this model were $PIF \leq 3.91$ L/s, $PEF/PIF \geq 0.830$, $FEV_1/PEF \geq 0.369$ s and $R_{\text{central}} \geq 1.905$ cmH₂O/(L·s). This model demonstrated strong discriminatory power with an AUC of 0.945. The Hosmer-Lemeshow goodness-of-fit test yielded a P -value of 0.957, indicating good model calibration. ⑤ Compared with the non-inspiratory plateau group, the inspiratory plateau group had higher prevalences of upper airway stenosis and central pulmonary malignancy, and the differences were statistically significant ($P < 0.05$). **Conclusion:** Moderate-to-severe stable COPD patients with inspiratory plateau in the F-V curve frequently exhibit increased overall airway resistance, suggesting potential upper airway and surrounding disorders. Therefore, the presence of an inspiratory plateau should be carefully evaluated in pulmonary function reports of moderate-to-severe stable COPD. A multi-parameter model incorporating PIF, PEF/PIF, FEV_1/PEF , and R_{central} may be utilized for identification, facilitating early detection of comorbidities in COPD patients.

[Key words] chronic obstructive pulmonary disease; flow-volume curve; inspiratory plateau; pulmonary function testing; early diagnosis

[J Nanjing Med Univ, 2026, 46(05): 673-684]

慢性阻塞性肺疾病(chronic obstructive pulmonary disease, COPD)是一种以持续性呼吸道症状和不完全可逆性气流受限为特征的异质性疾病,居全球死因第三位^[1]。其核心病理改变集中于小气道及肺泡结构,肺功能表现为小气道主导的阻塞性通气功能障碍,特征包括:第1秒用力呼气容积(forced expiratory volume in the first second, FEV_1)下降、 FEV_1 与最大用力肺活量(forced vital capacity, FVC)的比值(FEV_1/FVC)下降,流量-容积(flow-volume, F-V)曲线呼气下降支呈凹型^[2],严重时伴有呼气下降支夹角的出现^[3-4]。上述特征表明COPD的气流受限评估核心在于呼气相。然而,临床实践中发现部分COPD患者肺功能检查中除典型的呼气相受限外,同时伴有吸气相平台。现有研究明确提示吸气平台是中央或上气道阻塞(upper airway obstruction, UAO)的特征性征象,阻

塞部位涵盖胸内气道段(胸腔内气管和主支气管)或胸外气道段(咽部、喉部和胸腔外气管)^[5-6]。我国肺功能指南中也指出吸气平台提示UAO,并依据阻塞部位对胸内压变化的动力学差异,将其分类为可变胸内型、可变胸外型 and 固定型UAO^[7]。目前,COPD患者合并吸气平台这一兼具病理生理与临床意义的重要征象,尚缺乏系统性研究,其临床价值未获得充分重视,导致常规诊疗中易被忽略。为此,本研究深入分析F-V曲线吸气平台对中重度稳定期COPD患者的病情评估和急性加重风险的预测价值,并进一步探究出现此肺功能特征的潜在病理机制与病因。

1 对象和方法

1.1 对象

筛选2022年1月—2024年7月在南京医科大学

第一附属医院进行肺功能检查的FEV₁占预计值百分比(FEV₁ as a percentage of predicted value, FEV₁%pred)<60%、FVC≥正常值下限的阻塞性通气功能障碍304例。其中满足《慢性阻塞性肺疾病全球防治倡议2025年报告》(global initiative for chronic obstructive lung disease 2025 report, GOLD 2025)中COPD诊断标准的有217例,排除合并哮喘23例和肺功能研究数据不全者(缺失弥散功能、肺容量和脉冲振荡数据)63例,再根据是否伴吸气平台分组,排除两组间FEV₁%pred无法匹配的22例,最终纳入53例为吸气平台组,56例为FEV₁%pred匹配的非吸气平台组。纳入标准:①年龄50~85周岁,性别不限;②符合GOLD 2025指南中稳定期COPD的诊断标准;③肺通气功能符合30%≤FEV₁%pred<60%且FVC≥正常值下限。排除标准:①COPD近1个月有急性加重;②既往诊断合并哮喘;③合并未有效控制或功能失代偿的其他呼吸系统疾病、严重心脑血管系统疾病;④合并残疾、认知障碍、言语交流及精神障碍;⑤肺功能研究数据不全;⑥F-V曲线无可重复性,肺功能质量评估为D级、F级。本研究经南京医科大学第一附属医院伦理委员会批准(编号:2024-SR-843)。

1.2 方法

1.2.1 资料收集

收集受试者的基本资料[年龄、性别、吸烟指数、体重指数(body mass index, BMI)]、临床资料(吸入药物的种类、急性加重情况、胸部CT影像表现、肺功能参数以及临床合并疾病)。对COPD患者的吸入药物情况进行如下分类:Ⅰ表示未用或未规律应用吸入药物;Ⅱ表示应用1种吸入型长效支气管扩张剂[长效β₂受体激动剂(long-acting β₂-agonist, LABA)、长效抗胆碱能药物(long-acting muscarinic antagonist, LAMA)];Ⅲ表示应用2种吸入型长效支气管扩张剂;Ⅳ表示联合应用吸入性糖皮质激素和1~2种吸入型长效支气管扩张剂。通过门诊病历或电话随访统计两组COPD患者在过去1年内的急性加重人数、急性加重的发作次数以及急性加重导致住院人次及住院次数。

1.2.2 肺功能测定

运用德国耶格Master Screen IOS脉冲震荡肺功能仪,在吸入支气管舒张剂(沙丁胺醇400 μg)后,检测FEV₁、FEV₁%pred、FVC、呼气峰值流量(peak expiratory flow, PEF)、吸气峰值流量(peak inspiratory flow, PIF)等肺功能指标,绘制F-V曲线。肺功能检

查参照欧洲呼吸协会(European Respiratory Society, ERS)/美国胸科学会(American Thoracic Society, ATS)肺功能指南和中华医学会呼吸病学分会肺功能指南的质量控制要求完成^[7-11]。肺功能指标判断标准:通气功能指标采用2012年全球肺功能倡议(Global Lung Function Initiative, GLI)的东南亚人群肺功能正常预计值方程,其余指标采用欧洲胸科协会推荐的预计值——欧洲煤钢共同体1993年标准(European Community for Coal and Steel 1993, ECCS93)。FEV₁、FVC、FEV₁/FVC、PEF、最大中期呼气流量(maximum mid-expiratory flow, MMEF)、肺一氧化碳弥散量(diffusing capacity of the lung for carbon monoxide, D_LCO)、肺总量(total lung capacity, TLC)、5 Hz下的阻力(resistance of 5 Hz, R₅)、20 Hz下的阻力(resistance of 20 Hz, R₂₀)等取实测值占预计值的百分比,其中,FEV₁、FVC、PEF、MMEF、D_LCO占预计值的百分比≥80%为正常,FEV₁/FVC占预计值的百分比≥92%为正常^[9-12]。

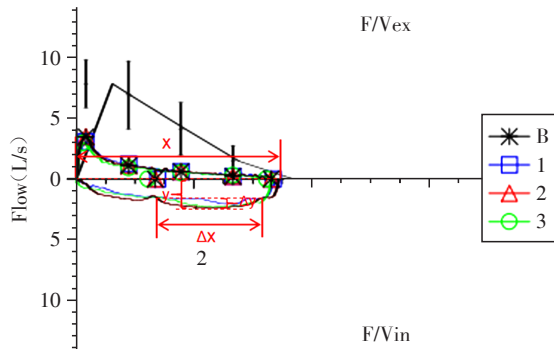
1.2.3 F-V曲线吸气平台判读

根据肺功能指南中吸气平台的定义,并通过Image J软件测量满足以下条件者纳入吸气平台组:①PIF下降^[5-7];②吸气环平坦处在横轴持续范围≥50% FVC;③平台段内流量波动幅度<20% PIF。具体测量过程如下:将肺功能检测获得的F-V曲线导入Image J软件。基于已知参考标尺校准空间比例尺,然后依次测量F-V环与横轴所形成的两交点之间的距离(x)、吸气环最低点(即PIF点)到横轴的垂直距离(y),经PIF点作横轴的平行线,取平台段位置沿上方再作1条横轴的平行线,其与吸气环形成2个交点,两交点之间的距离为Δx,两平行线之间的垂直距离为Δy。测量精度为0.001 cm。计算Δx/x与Δy/y。以上图形均至少有3个可重复的最大用力吸气和用力呼气F-V曲线。判读由2名经肺功能检查规范化培训合格的初级医师独立完成,当出现判读报告结果不一致时,再次讨论并最终由1名有肺功能培训导师资格的高级医师进行审核仲裁。2名医师判读的一致性Kappa值为0.98。

根据吸气平台定义,若满足Δx/x≥50%且Δy/y<20%,则纳入吸气平台组。吸气平台测量见图1。F-V曲线吸气平台的分组示意图2。

1.3 统计学方法

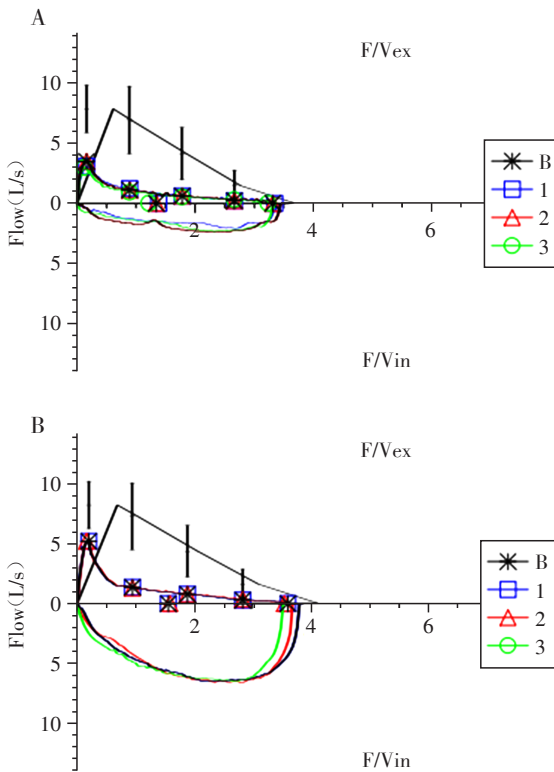
采用SPSS 27.0统计软件进行数据处理和分析,正态分布数据用均数±标准差($\bar{x} \pm s$)描述,采用独立样本t检验比较两组间差异,非正态分布的计量资



The X-axis of the flow-volume loop is the volume, and the Y-axis is the flow. F/Vex represents the expiratory phase of F-V loop, while F/Vin represents the inspiratory phase of F-V loop. The numbers 1 to 3 in the graph correspond to the F-V curves of patients with repeated measurements; B in the graph represents the best and clinically adopted F-V curve.

图1 吸气平台测量

Figure 1 Measurement of inspiratory plateau



A: The inspiration plateau group. B: The non-inspiration plateau group.

图2 F-V曲线吸气平台的分组示意

Figure 2 Schematic diagram of grouping for the F-V curve inspiratory plateau

料以中位数(四分位数)[$M(P_{25}, P_{75})$]表示,采用秩和检验进行组间比较;计数资料采用例数(百分率)[$n(\%)$]表示,采用卡方检验、校正卡方检验或Fisher确切概率法比较组间差异。采用多因素 Logistic 回

归分析 F-V 曲线吸气平台的相关因素,构建诊断中重度稳定期 COPD 患者合并吸气平台的模型,用 Hosmer-Lemeshow 检验进行校正,用受试者工作特征(receiver operating characteristic, ROC)曲线的曲线下面积(area under the curve, AUC)进行判别。卡方检验初步探索中重度稳定期 COPD 患者合并吸气平台与各类疾病的关系。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 吸气平台组和非吸气平台组一般资料比较

受试者基本资料见表1。两组在年龄、性别、身高、体重、BMI、吸烟指数、吸入药物种类和肺功能分级占比上差异均无统计学意义($P > 0.05$)。

2.2 吸气平台组和非吸气平台组肺通气功能比较

所有受试者肺通气功能情况见表2。两组 PEF 占预计值百分比(PEF as a percentage of predicted value, PEF%pred)、PIF、PEF/PIF、FEV₁/PEF 差异均有统计学意义(P 均 < 0.05)。吸气平台组的 PEF%pred、PIF 值均显著低于非吸气平台组,PEF/PIF、FEV₁/PEF 明显高于非吸气平台组。其余指标两组间差异无统计学意义($P > 0.05$)。

2.3 吸气平台组和非吸气平台组肺弥散功能及肺容量比较

所有受试者肺弥散功能及肺容量情况见表3。两组 TLC 占预计值百分比(TLC as a percentage of predicted value, TLC%pred)、肺泡容量占预计值百分比(V_A as a percentage of predicted value, V_A %pred)差异均有统计学意义(P 均 < 0.05)。吸气平台组的 TLC%pred、 V_A %pred 值均显著低于非吸气平台组。其余指标两组间差异无统计学意义($P > 0.05$)。

2.4 吸气平台组和非吸气平台组脉冲振荡数据比较

所有受试者脉冲振荡数据见表4。吸气平台组的 R_5 %pred、 R_{20} %pred、 R_5-R_{20} 、 $R_{central}$ 值均显著高于非吸气平台组,差异均有统计学意义(P 均 < 0.05)。其余指标两组间差异无统计学意义($P > 0.05$)。

2.5 中重度稳定期 COPD 患者 F-V 曲线出现吸气平台的多因素 Logistic 回归分析及相应模型构建

通过共线性分析检验各候选变量的独立性。经检验得:PEF%pred 和 PIF、TLC%pred 和 V_A %pred、 R_5 %pred 和 R_5-R_{20} 存在多重共线性($VIF > 10$),剔除 PEF%pred、 V_A %pred 和 R_5-R_{20} 后再次进行共线性分析,显示所有变量均 $1 < VIF$ 值 < 5 ,视为可接受。最终 PIF、PEF/PIF、FEV₁/PEF、TLC%pred、 R_5 %pred、

表1 吸气平台组和非吸气平台组的一般资料比较

Table 1 Comparison of general information between the inspiratory plateau group and the non-inspiratory plateau group

| Characteristic | Inspiratory plateau group (n=53) | Non-inspiratory plateau group(n=56) | $t/\chi^2/Z$ | P |
|--|-------------------------------------|--|--------------|-------|
| Age(years, $\bar{x} \pm s$) | 68.28 \pm 6.20 | 67.61 \pm 6.10 | -0.574 | 0.567 |
| Sex[n(%)] | | | 0.015 | 0.904 |
| Male | 44(83.02) | 46(82.14) | | |
| Female | 9(16.98) | 10(17.86) | | |
| Height(cm, $\bar{x} \pm s$) | 166.30 \pm 6.67 | 166.95 \pm 7.88 | 0.460 | 0.647 |
| Weight(kg, $\bar{x} \pm s$) | 62.72 \pm 11.80 | 64.86 \pm 10.17 | 1.013 | 0.313 |
| BMI[kg/m ² , M(P ₂₅ , P ₇₅)] | 23.51(19.72, 24.71) | 22.52(20.67, 25.13) | -0.700 | 0.484 |
| Smoking index [packs·years, M(P ₂₅ , P ₇₅)] | 35.00(20.00, 40.00) | 30.00(16.25, 45.00) | -0.649 | 0.516 |
| Inhaled drugs[n(%)] | | | 1.930 | 0.667 |
| I | 42(79.25) | 39(69.64) | | |
| II | 1(1.89) | 3(5.36) | | |
| III | 1(1.89) | 1(1.79) | | |
| IV | 9(16.98) | 13(23.21) | | |
| Pulmonary function stages[n(%)] | | | 0.155 | 0.694 |
| GOLD stage 2 | 37(69.81) | 41(73.21) | | |
| GOLD stage 3 | 16(30.19) | 15(26.79) | | |

I : no use or irregular use of inhaled medications; II : use of one inhaled long-acting bronchodilator[long-acting β_2 -agonist(LABA) or long-acting muscarinic antagonist(LAMA)]; III : use of two inhaled long-acting bronchodilators; IV : combination of inhaled corticosteroids and 1-2 inhaled long-acting bronchodilators.

表2 吸气平台组和非吸气平台组的肺通气功能比较

Table 2 Comparison of pulmonary ventilation function between the inspiratory plateau group and the non-inspiratory plateau group

| Characteristic | Inspiratory plateau group (n=53) | Non-inspiratory plateau group(n=56) | Z/t | P |
|---|-------------------------------------|--|--------|--------|
| FEV ₁ %pred[% , M(P ₂₅ , P ₇₅)] | 54.50(48.50, 58.00) | 53.80(49.65, 56.90) | -0.349 | 0.727 |
| FEV ₁ /FVC%pred[% , M(P ₂₅ , P ₇₅)] | 61.40(54.85, 67.90) | 60.10(55.93, 63.80) | -0.843 | 0.399 |
| FVC%pred[% , M(P ₂₅ , P ₇₅)] | 83.70(81.40, 89.10) | 86.60(82.63, 90.10) | -1.886 | 0.059 |
| FEF ₅₀ %pred[% , M(P ₂₅ , P ₇₅)] | 15.80(13.25, 19.85) | 15.20(12.30, 18.75) | -0.916 | 0.360 |
| MMEF%pred[% , M(P ₂₅ , P ₇₅)] | 16.20(14.00, 20.10) | 16.30(13.48, 18.78) | -0.725 | 0.469 |
| PEF%pred[% , M(P ₂₅ , P ₇₅)] | 43.10(35.60, 51.10) | 53.05(43.33, 59.73) | -4.187 | <0.001 |
| PIF[L/s, M(P ₂₅ , P ₇₅)] | 3.07(2.48, 3.60) | 4.87(4.01, 5.67) | -7.121 | <0.001 |
| PEF/PIF[M(P ₂₅ , P ₇₅)] | 1.04(0.85, 1.22) | 0.79(0.70, 0.94) | -5.259 | <0.001 |
| FEV ₁ /PEF(s, $\bar{x} \pm s$) | 0.47 \pm 0.11 | 0.37 \pm 0.08 | -5.046 | <0.001 |
| VCmax%pred[% , M(P ₂₅ , P ₇₅)] | 86.00(81.20, 93.10) | 87.75(84.20, 92.65) | -1.022 | 0.307 |

FEF₅₀%pred: forced expiratory flow at 50% of FVC as a percentage of predicted value; VCmax%pred: maximal vital capacity as a percentage of predicted value.

R₂₀%pred、R_{central}纳入多因素 Logistic 回归方程,分析吸气平台的相关因素,构建诊断中重度稳定期 COPD 患者合并吸气平台的多因素 Logistic 回归模型。通过向后回归得出的多因素回归模型包括 PIF、PEF/PIF、FEV₁/PEF 和 R_{central},而排除 TLC%pred、R₅%pred、R₂₀%pred。Hosmer-Lemeshow 拟合优度检验得到的 P 值为 0.957,表明由预测概率获得

的期望频数与观察频数之间的差异无统计学意义,即模型拟合度较好,模型校正良好。结果发现,PIF 对中重度稳定期 COPD 患者合并吸气平台的诊断具有统计学意义(OR=0.406, 95%CI: 0.180~0.914, P=0.030)。PEF/PIF 对中重度稳定期 COPD 患者合并吸气平台的诊断具有统计学意义(OR=1.073, 95%CI: 1.029~1.119, P < 0.001)。FEV₁/PEF 对中重

表3 吸气平台组和非吸气平台组的弥散功能及肺容量比较

Table 3 Comparison of diffusion function and lung capacity between the inspiratory plateau group and the non-inspiratory plateau group

| Characteristic | Inspiratory plateau group (n=53) | Non-inspiratory plateau group(n=56) | t/Z | P |
|--|----------------------------------|-------------------------------------|--------|-------|
| D _l CO%pred(% , $\bar{x} \pm s$) | 56.30 ± 20.20 | 53.90 ± 20.22 | -0.621 | 0.536 |
| D _l CO/V _A %pred(% , $\bar{x} \pm s$) | 67.53 ± 21.47 | 62.53 ± 22.78 | -1.178 | 0.242 |
| D _l COc%pred(% , $\bar{x} \pm s$) | 56.79 ± 20.02 | 53.93 ± 20.21 | -0.741 | 0.461 |
| D _l COc/V _A %pred(% , $\bar{x} \pm s$) | 68.14 ± 21.26 | 62.58 ± 22.77 | -1.316 | 0.191 |
| FRC%pred[%, M(P ₂₅ , P ₇₅)] | 94.20(79.90, 109.80) | 97.70(80.95, 116.43) | -0.991 | 0.322 |
| RV/TLC%pred(% , $\bar{x} \pm s$) | 126.70 ± 19.70 | 127.92 ± 16.85 | 0.349 | 0.727 |
| RV%pred(% , $\bar{x} \pm s$) | 112.82 ± 30.73 | 118.63 ± 26.55 | 1.056 | 0.293 |
| TLC%pred[%, M(P ₂₅ , P ₇₅)] | 83.50(75.75, 92.60) | 90.05(80.78, 96.15) | -2.080 | 0.038 |
| V _A %pred[%, M(P ₂₅ , P ₇₅)] | 83.00(75.45, 92.30) | 89.65(80.45, 96.03) | -2.028 | 0.043 |

D_lCOc%pred: diffusing capacity of the lung for carbon monoxide corrected as a percentage of predicted value; FRC%pred: functional residual capacity as a percentage of predicted value; RV%pred: residual volume as a percentage of predicted value.

表4 吸气平台组和非吸气平台组的脉冲振荡数据比较

Table 4 Comparison of impulse oscillometry data between the inspiratory plateau group and the non-inspiratory plateau group

| Characteristic | Inspiratory plateau group (n=53) | Non-inspiratory plateau group(n=56) | Z | P |
|---|----------------------------------|-------------------------------------|--------|---------|
| R ₅ %pred[%, M(P ₂₅ , P ₇₅)] | 149.60(125.25, 183.50) | 129.80(97.00, 153.43) | -2.807 | 0.005 |
| R ₂₀ %pred[%, M(P ₂₅ , P ₇₅)] | 99.20(83.80, 120.55) | 89.55(80.05, 103.88) | -2.046 | 0.041 |
| X ₅ %pred[%, M(P ₂₅ , P ₇₅)] | 681.80(461.80, 1451.85) | 566.80(362.13, 1 152.60) | -1.285 | 0.199 |
| R ₅ -R ₂₀ [cmH ₂ O/(L·s), M(P ₂₅ , P ₇₅)] | 3.88(3.31, 4.78) | 3.38(2.72, 4.04) | -2.622 | 0.009 |
| Fres[Hz, M(P ₂₅ , P ₇₅)] | 21.95(17.49, 28.03) | 21.08(16.89, 23.25) | -1.413 | 0.158 |
| Rcentral[cmH ₂ O/(L·s), M(P ₂₅ , P ₇₅)] | 2.55(2.11, 2.96) | 1.99(1.25, 2.52) | -3.750 | < 0.001 |
| Rperipheral[cmH ₂ O/(L·s), M(P ₂₅ , P ₇₅)] | 4.08(2.55, 7.14) | 3.06(2.55, 5.48) | -1.637 | 0.102 |

X₅%pred: reactance at 5 Hz as a percentage of predicted value, which reflects peripheral elastic resistance; Fres: resonant frequency; Rperipheral: peripheral airway resistance.

度稳定期COPD患者合并吸气平台的诊断具有统计学意义(OR=1.172, 95%CI: 1.056~1.300, P=0.003)。Rcentral对中重度稳定期COPD患者合并吸气平台的诊断具有统计学意义(OR=2.790, 95%CI: 1.125~6.917, P=0.027, 表5)。

2.6 构建ROC曲线

采用ROC曲线判断以PIF、PEF/PIF、FEV₁/PEF和Rcentral构建的中重度稳定期COPD患者合并吸气平台模型的诊断价值(图3)。该模型AUC为0.945, 判别能力强, 其灵敏度为88.7%, 特异度为87.5%。该模型中影响因素的最佳阈值为PIF≤3.91 L/s、PEF/PIF≥0.830、FEV₁/PEF≥0.369 s和Rcentral≥1.905 cmH₂O/(L·s)(表6)。

2.7 F-V曲线吸气平台对中重度稳定期COPD患者过去1年急性加重的影响

两组急性加重情况差异无统计学意义(P>0.05),

表5 中重度稳定期COPD患者F-V曲线出现吸气平台的多因素Logistic回归分析

Table 5 Multivariate logistic regression analysis of the inspiratory plateau in F - V curve of patients with moderate-to-severe stable COPD

| Variate | β | S.E | P | OR | 95%CI |
|-----------------------|--------|-------|---------|-------|-------------|
| PIF | -0.901 | 0.414 | 0.030 | 0.406 | 0.180-0.914 |
| PEF/PIF | 0.070 | 0.021 | < 0.001 | 1.073 | 1.029-1.119 |
| FEV ₁ /PEF | 0.159 | 0.053 | 0.003 | 1.172 | 1.056-1.300 |
| Rcentral | 1.026 | 0.463 | 0.027 | 2.790 | 1.125-6.917 |

但吸气平台组急性加重率升高, 住院率也较非吸气平台组略高(表7)。

2.8 吸气平台组和非吸气平台组COPD合并症

经临床检查数据及诊断资料分析发现: 结构性气道狭窄(如气管插管/切开后狭窄、甲状腺/食管压迫性狭窄)和中央型肺恶性肿瘤的发生率两组间差

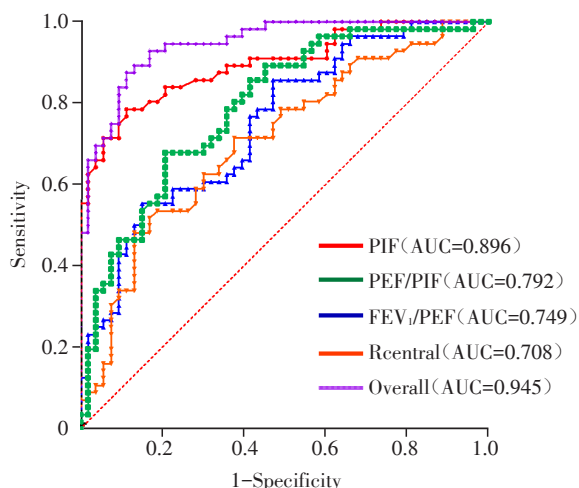


图3 不同变量对中重度稳定期COPD患者出现吸气平台的诊断价值的ROC曲线

Figure 3 ROC Curves for the diagnostic value of different variables in identifying inspiratory plateau in patients with moderate-to-severe stable COPD

异有统计学意义($P < 0.05$)。结构性气道狭窄(如气管插管/切开后狭窄、甲状腺/食管压迫性狭窄)和中

央型肺恶性肿瘤在吸气平台组的发生率显著高于非吸气平台组。其余疾病的发生率差异无统计学意义($P > 0.05$,表8)。

3 讨论

肺功能检查是临床重要检查项目,常用的检查包括肺容积检查、肺量计检查、支气管激发试验、支气管舒张试验、肺弥散功能检查、气道阻力检查及运动心肺功能检查等^[13];其中,肺量计检查因其满足临床诊断要求和可实施性,已成为临床普遍采用的一项肺功能检查方法,特别是在慢性气道疾病诊断与管理中应用最广泛。COPD是常见的慢性气道疾病,其特征性病理生理改变为持续性、不完全可逆的气流受限,其经典的F-V曲线表现为呼气下降支呈凹陷型下滑线。值得强调的是,我国2019年发布的肺功能检查报告规范指出,肺通气功能检查报告应包含通气功能参数及F-V曲线图形两方面内容^[12]。遵循该原则,我们在临床工作中观察到部分中重度稳定期COPD患者F-V曲线呼气相下降支呈

表6 模型及所含变量的诊断价值及界值

Table 6 Diagnostic value and thresholds of the model and its variables

| Variate | AUC | 95%CI | Optimal cutoff | Sensitivity (%) | Specificity (%) |
|-----------------------|-------|-------------|----------------|-----------------|-----------------|
| PIF | 0.896 | 0.837-0.954 | 3.910 | 88.7 | 78.6 |
| PEF/PIF | 0.792 | 0.708-0.876 | 0.830 | 79.2 | 67.9 |
| FEV ₁ /PEF | 0.749 | 0.659-0.839 | 0.369 | 84.9 | 55.4 |
| Rcentral | 0.708 | 0.611-0.805 | 1.905 | 86.8 | 48.2 |
| Overall | 0.945 | 0.907-0.984 | 0.417 | 88.7 | 87.5 |

Overall: combined diagnostic model incorporating PIF, PEF/PIF, FEV₁/PEF and Rcentral based on multivariate logistic regression.

表7 吸气平台组和非吸气平台组过去1年急性加重表现比较

Table 7 Comparison of acute exacerbations manifestations between the inspiratory plateau group and the non-inspiratory plateau group over the past year [n(%)]

| Acute exacerbation manifestation | Inspiratory plateau group(n=53) | Non-inspiratory plateau group(n=56) | χ^2 | P |
|---|---------------------------------|-------------------------------------|----------|-------|
| Number of patients with acute exacerbation | 21(39.62) | 19(33.93) | 0.380 | 0.538 |
| Number of acute exacerbations | | | 2.726 | 0.436 |
| 0 | 32(60.38) | 37(66.07) | | |
| 1 | 20(37.74) | 16(28.57) | | |
| 2 | 0(0) | 2(3.57) | | |
| 3 | 1(1.89) | 1(1.79) | | |
| Number of hospitalized patients with acute exacerbation | 10(18.87) | 10(17.86) | 0.019 | 0.892 |
| Times of hospitalizations for acute exacerbation | | | 1.072 | 0.585 |
| 0 | 43(81.13) | 46(82.14) | | |
| 1 | 10(18.87) | 9(16.07) | | |
| 2 | 0(0) | 1(1.79) | | |

表8 吸气平台组和非吸气平台组的疾病发生率比较

Table 8 Comparison of disease incidence between the inspiratory plateau group and the non-inspiratory plateau group

| Types of disease | Inspiratory plateau group(n=53) | Non-inspiratory plateau group(n=56) | χ^2 | P |
|---|---------------------------------|-------------------------------------|----------|-------|
| Airway narrowing ^a | 8(15.09) | 1(1.79) | 4.731 | 0.030 |
| Laryngeal and subglottic disorders ^b | 1(1.89) | 0(0) | - | 0.486 |
| Central pulmonary malignancies | 7(13.21) | 0(0) | 5.859 | 0.015 |
| Neuromuscular diseases ^c | 1(1.89) | 0(0) | - | 0.486 |
| Upper gastrointestinal disorders ^d | 6(11.32) | 9(16.07) | 0.518 | 0.472 |
| Snoring and sleep apnea syndrome | 0(0) | 3(5.36) | 1.261 | 0.261 |

a: including post-intubation/tracheostomy stenosis, extrinsic compression from thyroid/esophagus, etc.; b: including laryngeal carcinoma, vocal cord paralysis, vocal cord dysfunction, etc.; c: including myasthenia gravis, diaphragmatic paralysis, etc.; d: including gastroesophageal reflux disease, gastritis, etc.

凹陷型的同时伴有吸气平台。由于COPD的经典F-V曲线以呼气相凹陷型为特征,对呼气相图形关注度高,而吸气相图形判读常被忽略,易导致其潜在异常信息被忽视;同时,此前缺乏COPD患者F-V曲线吸气相图形研究。而既往F-V曲线图形分析显示,吸气平台特点是识别中央气道阻塞或UAO的一种简单且有效的无创方法。单纯吸气相平台样改变常提示可变胸外型UAO(气流受限主要发生在吸气相),单纯呼气相平台样改变常提示可变胸内型UAO(气流受限主要发生在呼气相),吸气相与呼气相均呈平台样改变则提示固定型UAO(气流受限主要发生在吸气相和呼气相)^[5-7,14]。吸气平台的形成机制可归因于两类情况:在可变胸外型UAO中,吸气时气道内压低于大气压,导致气管壁趋于闭陷,吸气阻力显著增加,从而引发吸气流量受限;而在固定型UAO中,阻塞部位的固定狭窄在吸气相和呼气相均对气流产生恒定限制,形成双相平台^[7]。故本研究关注了中重度稳定期COPD合并吸气平台患者,全面了解该部分COPD患者的临床与肺功能特点、疾病严重程度以及与疾病的相关性。

本研究纳入53例伴有吸气平台的COPD患者,并依据FEV₁%pred匹配56例不伴吸气平台的COPD患者。分析可知,两组间肺功能分级占比差异无统计学意义,但吸气平台组中GOLD 3级(气流阻塞严重程度更重)占比稍高于非吸气平台组。这表明吸气平台的存在与COPD气流阻塞严重程度无显著相关性。研究发现,两组的FEV₁和FVC差异无统计学意义,但吸气平台组PEF显著低于非吸气平台组,这与Stanojevic等^[5]报道的UAO患者肺功能特征一致。Pellegrino等^[6]在研究中提出FEV₁/PEF这一比值,该比值升高可作为UAO筛查指标,建议FEV₁/PEF

升高时需重复多次检测用力吸气和呼气流量容积环,以警惕UAO的发生,本研究支持该结论。同时,研究发现吸气平台组PIF显著低于非吸气平台组。PEF和PIF是评估气道通畅性及呼吸肌肉力量的关键参数,其下降对提示UAO、神经肌肉疾病等具有重要临床意义^[15-18]。Bode等^[19]在胸式呼吸伴通气不足的患者中发现吸气环扁平化伴PIF下降,这与本研究发现相互印证。

COPD患者常存在肺过度充气,表现为深吸气量(inspiratory capacity, IC)降低,残气量(residual capacity, RV)及TLC升高^[20]。这是由于肺泡壁破坏,肺弹性回缩力减弱,进而影响呼气时小气道塌陷,肺泡内气体滞留,造成静态肺过度充气^[21]。另外COPD患者因缺氧需通过增加呼吸频率来满足机体需求,而缩短的呼气时间难以使肺内的气体充分排空,残余气体长期积聚于肺泡内,使得呼气末肺容积逐渐增加,出现动态肺过度充气^[22]。但是在本研究中观察到COPD合并UAO组相较于单纯COPD组TLC及V_A减少,原因在于:上气道(喉、气管、主支气管)的狭窄(如肿瘤、瘢痕、异物、声带麻痹等)对吸气流量的限制远大于对呼气流量的限制,为了克服增大的吸气阻力,患者需要产生更大的胸腔负压,但在严重阻塞或呼吸肌疲劳时,不足以吸入足够的气体导致吸气流量受限^[7]。由于吸气受限,患者无法将肺部充分扩张到正常的最大容积,这导致TLC降低。同时由于吸入的总气体量减少,参与气体交换的V_A也相应减少。

本研究发现与非吸气平台组相比,吸气平台组的总气道阻力(R_S)、中心气道阻力(R₂₀)、外周气道阻力(R_S-R₂₀)以及中心阻力(R_{central})均增大,且两组间差异有统计学意义。脉冲震荡技术(impulse

oscillometry, IOS)可评估气道通畅性,精准判断阻力增高区域;吸气平台作为UAO的特征性表现,引起 R_5 、 R_{20} 、 R_{central} 显著升高,符合IOS对中心气道阻力增高的检测特性^[11]。COPD本质为小气道病变,主要表现为外周气道阻力增高,本研究也有一致性结果,体现在外周气道阻力指标 R_5 - R_{20} 也增大,可能与本研究纳入的是中重度COPD患者,且UAO导致的吸气受限加重COPD患者原有的气体陷闭有关。

通过一份肺功能报告的图形可初步判断COPD患者是否合并吸气平台。本研究在此提出基于肺功能参数构建中重度稳定期COPD患者合并吸气平台的客观诊断模型。该模型构建过程中剔除 R_5 - R_{20} 而纳入 $R_5\%$ pred指标,是由于 R_5 代表总气道阻力,更能反映COPD合并UAO所引起的总气道阻力和中心气道阻力的增加,代表外周气道阻力的 R_5 - R_{20} 反映COPD的典型特点,但无法反映合并UAO的影响。区别于传统图形判断方法,通过整合PIF、PEF/PIF、 FEV_1 /PEF和 R_{central} 量化指标构建判断中重度稳定期COPD患者合并吸气平台的模型,该模型的AUC为0.945,判别能力强,其灵敏度为88.7%,特异度为87.5%。当 $PIF \leq 3.91$ L/s、 $PEF/PIF \geq 0.830$ 、 $FEV_1/PEF \geq 0.369$ s和 $R_{\text{central}} \geq 1.905$ cmH₂O/(L·s)时,对判断中重度稳定期COPD患者合并吸气平台具有良好的指导意义;也便于后续人工智能判读推广应用。同时应注意,本模型为探索性诊断模型,需多中心前瞻性研究加以验证。

另外,本研究发现吸气平台的存在与中重度稳定期COPD患者急性加重风险无明确相关性,但吸气平台组急性加重率更高,住院率也较非吸气平台组略高。目前临床对COPD急性加重期的诊断仍主要依据患者的临床表现,即患者咳嗽咳痰和气喘等症状的变化^[23-24]。近年相关研究提出可将嗜酸性粒细胞、Clara细胞分泌蛋白、纤维蛋白原、C-反应蛋白等作为预测急性加重的生物标志物^[25-29]。而本研究中COPD伴吸气平台的患者其肺功能 $FEV_1\%$ pred平均在54.50%(48.50%~58.00%),吸气平台组的关键通气功能参数 FEV_1 、FVC、 FEV_1 /FVC以及MMEF等与非吸气平台组差异无统计学意义;而且吸气平台反映传导性UAO,并不直接参与炎症过程,因此观察结果未见到与COPD急性加重(acute exacerbation of COPD, AECOPD)有相关性;从呼吸流体力学角度也不支持其存在增加AECOPD风险。但本研究中可能存在Ⅱ类错误,按 $n=109$, $\alpha=0.05$,计算检测组间20%绝对差异的检验效能为55.76%,

低于80%的标准阈值,表明当前样本量不足以可靠识别目标效应量,需进一步扩大样本量提高检验效能。

早期研究发现,气管狭窄、气道肿瘤及双侧声带麻痹等病因所致胸内/外UAO,可表现为吸气曲线形态异常及吸气流量降低^[30-32]。后续研究进一步扩展UAO病因谱,发现喉部病变、神经肌肉疾病、气道灼伤、声带功能障碍、阻塞性和中枢性睡眠呼吸暂停、甲状腺肿、纵隔疾病及支气管术后狭窄等均可引发特征性吸气曲线改变^[33-38]。本研究观察到部分COPD合并吸气平台的患者确实存在结构性气道狭窄(气管插管/切开后狭窄、甲状腺/食管压迫性狭窄)和中央型肺恶性肿瘤,进一步验证了吸气平台的临床价值。烟草长期暴露往往与COPD和肿瘤的发病机制密切相关^[39-40];中央型肺恶性肿瘤可致主支气管狭窄/闭塞、纵隔及肺门淋巴结肿大、远端肺不张及阻塞性肺炎,多重机制加重吸气受限。中央型肺恶性肿瘤归属于固定型UAO,可同时导致吸气和呼气平台。因此,后续临床肺功能报告应同步关注吸气相图形,特别是F-V曲线存在吸气平台,需要在肺功能报告中标注,以便通过肺功能检查挖掘有效临床信息和诊断线索,尤其在COPD患者管理工作中定期肺功能检查需要予以关注,以防漏诊。另外,本研究喉及声门下疾病和神经肌肉疾病在两组之间差异无统计学意义,可能与本研究样本量不足有关,也可能与中重度稳定期COPD患者合并该类疾病的概率较低,临床不易收集有关。曾有研究认为反流酸吸入气道直接激活了气道迷走神经^[41],因此上消化道疾病可能通过反酸刺激气道或喉及声门下结构引发吸气平台,但本研究未发现两组差异,后续需更大样本验证。Krieger等^[36]研究揭示阻塞性睡眠呼吸暂停患者中67%存在胸腔外UAO,在中枢性睡眠呼吸暂停患者中该比例达71%。本研究3例患者都是觉醒状态下行肺功能检查,咽部肌肉张力代偿性增强,未表现吸气受限。

本研究仍具有一定局限性。首先,根据GOLD 2025指南,COPD患者的症状评分、近1年急性加重次数及肺功能评估在COPD临床管理中缺一不可^[42]。本研究缺乏症状评分,由于本研究为回顾性研究,临床工作少有完成8项症状评分[COPD评估测试(COPD assessment test, CAT)]任务,故收集既往资料过程中该项内容不完整,未纳入分析。此外,本研究为单中心横断面且针对中重度稳定期COPD患者的研究,所建模型未经外部验证,故后续研究将

建立多中心验证模型或前瞻性队列研究,进一步扩大样本量,完善症状评分(如CAT评分、改良版英国医学研究委员会呼吸困难量表评分),有条件纳入运动心肺功能检查中的指脉氧监测,以便全面评估患者呼吸生理功能状态,助力探索 COPD 治疗策略。“COPD 合并吸气平台”作为 COPD 一种肺功能特征,不同于现有的 COPD 临床分型,它从肺功能图形特点映射临床特征,适合甄别 COPD 患者是否存在合并症,有利于对患者的个体化整体性治疗提供临床线索。但是该肺功能特征是否独立? 仍需纵向研究验证其稳定性和治疗意义,以便进一步推广应用于临床实践。

综上所述,合并吸气平台的中重度稳定期 COPD 患者未见有急性加重风险增加,但关注吸气平台仍有临床价值。一旦中重度稳定期 COPD 患者肺功能检查合并可疑吸气平台,需要关注 PIF、PEF/PIF、FEV₁/PEF 和 R_{central} 指标,对多参数诊断模型识别出的合并吸气平台的中重度稳定期 COPD 患者,则应警惕是否存在合并上气道狭窄、中央型肿瘤等疾病,及时予以相应检查,以便合并疾病的早发现、早诊断、早治疗。

利益冲突声明:

全体作者声明没有利益冲突。

Conflict of Interests:

The authors declared no conflict of interests.

作者贡献声明:

徐小俊负责构思和设计实验、实施研究、采集数据、分析及解释数据、论文撰写;王诗绮、丁文秋、王懿涵、田薇、吴楨珍、宋玮负责采集和分析数据;孙培莉负责构思和设计实验、对文章的知识性内容作批评性审阅、研究经费支持。

Author's Contributions:

XU Xiaojun was responsible for conceiving and designing the experiments, conducting the study, collecting data, analyzing and interpreting the data, and writing the paper; WANG Shiqi, DING Wenqiu, WANG Yihan, TIAN Wei, WU Zhenzhen, and SONG Wei were responsible for collecting and analyzing data; SUN Peili was responsible for conceiving and designing the experiments, critically reviewing the intellectual content of the article, and research funding support.

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- (收稿: 2025-11-16; 修回: 2026-03-31; 录用: 2026-03-31)
(本文编辑: 蒋 莉)