

肺通气功能检测小气道功能参数在哮喘诊断及评估中的应用

杨靖溢^{1,2,3,4}, 罗征秀^{1,2,3,4*}

¹重庆医科大学附属儿童医院呼吸科, 重庆

²国家儿童健康与疾病临床医学研究中心, 重庆

³儿童发育疾病研究教育部重点实验室, 重庆

⁴儿科学重庆市重点实验室, 重庆

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摘要

支气管哮喘是常见慢性气道炎症性疾病, 小气道是哮喘气道炎症及阻塞关键部位, 与哮喘发生发展密切相关。肺通气功能检测作为运用最广泛的肺功能检测手段, 对小气道功能评估具有较高灵敏性及特异性, 本文就肺通气功能检测小气道功能参数在哮喘诊断、评估中的作用进行综述, 以期提高临床工作者对小气道功能的认识及重视, 推动哮喘精准化管理及治疗。

关键词

肺通气功能, 小气道, 支气管哮喘

The Application of Pulmonary Ventilation Function Testing of Small Airway Function Parameters in the Diagnosis and Evaluation of Asthma

Jingyi Yang^{1,2,3,4}, Zhengxiu Luo^{1,2,3,4*}

¹Department of Respiratory, Children's Hospital of Chongqing Medical University, Chongqing

²National Clinical Research Center for Child Health and Disorders, Chongqing

³Ministry of Education Key Laboratory of Child Development and Disorders, Chongqing

⁴Chongqing Key Laboratory of Pediatrics, Chongqing

*通讯作者。

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Abstract

Bronchial asthma is a common chronic inflammatory disease of the airways, and the small airways are the key site of airway inflammation and obstruction in asthma, which is closely related to the occurrence and development of asthma. As the most widely used pulmonary function test, pulmonary ventilation function test has high sensitivity and specificity in the assessment of small airway function. This article reviews the role of pulmonary ventilation function test in the diagnosis and assessment of asthma in order to improve the understanding and attention of clinical workers to small airway function, and to promote the accurate management and treatment of asthma.

Keywords

Pulmonary Ventilatory Function, Small Airways, Bronchial Asthma

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1. 前言

支气管哮喘作为一种常见的慢性气道炎症性疾病,其发病率在全球范围内逐年呈上升趋势[1],不仅对患者身体健康产生影响,同时也给家庭和社会带来了沉重精神和经济负担[2] [3]。近年来,研究对小气道功能在哮喘等气道阻塞性疾病中的应用更加重视。研究显示,哮喘患者小气道阻力可达总气道阻力的50%~90%,小气道炎症、阻塞、重塑是导致气流受限和阻塞的关键因素[4],对哮喘控制及远期预后具有重大影响[5]。肺通气功能检测具有无创、准确、操作简单等特点,大量研究证明,其在哮喘诊断、评估病情严重程度和控制水平方面具有重要意义[3] [5] [6],相关参数不仅可以了解大气道情况,对小气道功能评估也具有一定价值[7]。本文对肺通气功能检测小气道功能参数及其在哮喘诊断、评估中的价值进行综述,以期促进临床工作者对小气道功能的深入了解,早期识别并治疗小气道功能障碍,从而更好地帮助哮喘患者实现疾病的控制和管理。

2. 肺通气功能的小气道功能参数定义

在肺通气功能检查中,FEF50% (呼出50%肺活量时的呼气流速)、FEF75% (呼出75%肺活量时的呼气流速)、FEF25%~75% [也称为最大呼气中段流量(MMEF)]是主要用于评估小气道功能的参数。FEF25%~75%不仅可以反映气道阻塞,也是评价小气道功能障碍的重要指标[7]。然而,研究发现小气道参数下降并不等同于小气道功能障碍。一些学者将 $FEF25\% \sim 75\% < 65\%$ 预测值定义为小气道功能受损[8] [9] [10]。在无通气功能障碍前提下(即当FVC、FEV1、FEV1/FVC、PEF在正常范围),FEF50%、FEF75%、FEF25%~75%三个小气道指标中有两项低于正常值下限<65%预计值,可诊断小气道功能障碍(Small airways dysfunction, SAD) [11]。

3. 小气道功能与哮喘诊断

哮喘发病机制为气道阻塞和可逆性气流受限。指南推荐[1] [3]将第一秒用力呼气容积(FEV1)和一秒率

(FEV1/FVC)作为评估气道阻塞指标,但这主要反映大中气道阻塞情况,不能全面评估整个气道。Yi, L等人[12]分析 851 例学龄前哮喘患儿肺通气功能发现,绝大多数(91.5%)学龄前哮喘患儿无阻塞性通气功能障碍,提示在哮喘发病早期,尤其在儿童期,使用 FEV1、FEV1/FVC 评估气道阻塞可能存在局限性。

有研究发现 FEF25%~75%与 FEV1/FVC、FEV1 呈正相关,且先于 FEV1 出现变化,推测哮喘患者小气道功能变化出现在大气道功能障碍前[13]。Lutfi, M.F.等[14]运用 ROC 曲线评估肺通气功能参数诊断哮喘效能,结果显示,FEF50%、FEF25%~75%对哮喘诊断能力优于 FEV1。既往研究表明[15],FEF25%~75% < 65%时预测气道高反应性(AHR)的特异性高达 92%。近期一项为期 10 年的前瞻性研究发现,以 FEF25%~75%改善大于 30%作为舒张试验阳性指标时,可显著提高儿童哮喘诊断的敏感性[16],这无疑有助于 FEV1 正常的哮喘患儿的诊断。而在咳嗽变异性哮喘(CVA)人群中,至少一半以上患者合并 SAD,同时发现 FEF50%是早期识别 SAD 的简单可行指标[17][18],提示小气道功能参数下降对不典型哮喘同样具有早期识别作用。

慢性炎症可累积哮喘整个气道,但以中小气道为主,尤其是小气道[19],研究者[20][21][22]从严重哮喘患者肺叶切除手术标本中获得数据表明,小气道中嗜酸性粒细胞和 CD4⁺Th2 细胞聚集较大气道明显增加,提示小气道炎症与 2 型炎症有关且较大气道严重。在临床中,支气管激发试验是通过一定方法诱发气道平滑肌痉挛收缩,以尚未完全在最高浓度吸入后 FEV1 较基础值下降 $\geq 20\%$ 来判断是否存在 AHR 及其程度。研究表明,与 FEV1%相比,小气道功能参数能更好预测 AHR 存在[12][23]。尤其对轻度哮喘儿童,使用激发剂后,FEF25%~75%、FEF50%下降速度比 FEV1 更快、幅度更大,对气道反应程度较低或无反应状态的患者有一定预测价值[24][25][26]。因此,在患者不配合或激发风险较大情况下,可通过小气道功能参数推测 AHR 及严重程度,适合在基层医院推广。

4. 小气道功能与哮喘症状及评估

在哮喘急性发作期,大小气道均存在不同程度功能障碍[27][28][29]。大气道指标呼气峰值流量(PEF)、FEV1 呈轻中度损害为主,小气道指标 FEF50%、FEF75%则更多呈现中重度损害,且重度哮喘患者中存在小气道功能异常比例显著高于轻中度患者[30],提示小气道功能损害较大气道更重并与哮喘严重程度密切相关。

一项关于成人大型队列研究显示,FEF50%和 FEF25%~75%与哮喘控制、急性发作、生活质量密切相关[31],儿童研究结果也表明,三个小气道功能指标均能较好预测哮喘未完全控制,其中 FEF50%、FEF25%~75%诊断价值尤为突出,最佳截断值分别为 70.2、73.25 [32]。对哮喘重度发作患儿,与 FEV1/FVC 降低患儿比较,FEF25%~75%降低者哮喘急性发作风险、急诊就诊率、住院率和激素使用率更高[16],提示小气道功能指标在监测哮喘临床症状和疾病控制方面似乎优于大气道参数。

此外,小气道功能异常与哮喘长期持续存在相关[33]。研究发现[34],在 CVA 患者中,MMEF 是其转变为典型哮喘的独立危险因素。部分哮喘患者即使处于症状缓解期,仍存在小气道阻塞[35][36]。SAD 持续存在与哮喘病程及严重程度有关,有哮喘控制不良及预后不佳风险[37]。

由此可见,小气道功能无论是对于评估哮喘患者病情严重程度、预测哮喘未完全控制等方面都具有一定作用。重要的是,Postma, D.S.等人发现[38],在生命后期,哮喘患者发生慢性阻塞性肺疾病(COPD)的风险更大。同时,大量病理学、影像学、临床数据表明[13][39][40],小气道病变是导致早期 COPD 气道阻塞的关键因素,COPD 患者小气道阻力显著增加。因此,哮喘患者 SAD 是否会进展为固定气流阻塞甚至慢性阻塞性肺疾病仍是未来重要关注点[41],定期检测哮喘患者小气道功能变化至关重要。

5. 肺通气功能评估小气道功能的局限性

肺通气功能检测是评估小气道功能最常用的诊断手段,但其临床应用也存在一些问题。首先,老年

人或儿童在进行常规肺通气功能检查时, 配合程度较差, 易受呼气不足或用力程度不足影响[42], 故在使用该参数评价小气道功能时, 需注意检查质量。其次, 小气道功能指标参考值设定存在争议。目前国内使用 $<65\%$ 预计值作为异常[9]。由于 FVC 下降, 即使没有气道阻塞, FEF $25\% \sim 75\%$ 也会随之下降。因此, 一些学者提出只有在 FVC 正常时, 才能更有意义地解读 FEF $25\% \sim 75\%$ 观测结果[43]; 在对儿童患者进行研究时, 虽然 FEF $25\% \sim 75\%$ 较其他常规肺功能参数能更好的反映小气道功能, 但仍是大小气道的综合指标, 不能够精准区分大小气道功能[44]。

6. 结论

肺通气功能检测小气道功能参数对哮喘诊断及评估有提示及指导意义, 临床需提高对 FEF 50% 、FEF 75% 、FEF $25\% \sim 75\%$ 三个小气道指标的认识和重视, 早期识别 SAD, 提升哮喘控制水平。未来还需探讨针对 SAD 的新型诊断和治疗方法, 以期更精准应对哮喘挑战。

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