**Advances in Clinical Medicine** 临床医学进展, 2024, 14(3), 1795-1800
Published Online March 2024 in Hans. https://www.hanspub.org/journal/acm
https://doi.org/10.12677/acm.2024.143909

Hans汉斯

# 心肺运动试验在慢性阻塞性肺疾病中的临床应用

**唐培希[1,2,3,4*]，姜英松[1,2,3,5#]**

[1]重庆医科大学，重庆
[2]中国科学院重庆绿色智能技术研究院，重庆
[3]中国科学院大学重庆学院，重庆
[4]重庆市人民医院呼吸与危重症医学科，重庆
[5]重庆市人民医院肾内科，重庆

收稿日期：2024年2月27日；录用日期：2024年3月21日；发布日期：2024年3月29日

## 摘　要

**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气流受限为主要特征的疾病。尽管肺功能测试是诊断COPD的基石，但由于疾病的异质性以及心脏、血管和肌肉骨骼系统等多系统的受累，它无法完全评估疾病的整体情况。心肺运动试验(Cardiopulmonary Exercise Testing, CPET)是评估多种临床疾病(包括慢性阻塞性肺疾病)的重要工具，可以评估各个系统的功能和储备能力。本文主要阐述CPET在COPD的病因、诊断、治疗、预后中的临床应用。**

## 关键词

**慢性阻塞性肺疾病，心肺运动试验，充气过度，运动受限**

# Clinical Application of Cardiopulmonary Exercise Testing in Chronic Obstructive Pulmonary Disease

**Peixi Tang[1,2,3,4*], Yingsong Jiang[1,2,3,5#]**

[1]Chongging Medical University, Chongqing
[2]Chongqing Institute of Green and Intelligent Technology, Chinese Academy of Sciences, Chongqing
[3]Chongqing School, University of Chinese Academy of Sciences, Chongqing
[4]Department of Respiratory and Critical Care Medicine, Chongqing General Hospital, Chongqing

[*]第一作者。
[#]通讯作者。

文章引用：唐培希，姜英松．心肺运动试验在慢性阻塞性肺疾病中的临床应用[J]．临床医学进展，2024，14(3): 1795-1800. DOI: 10.12677/acm.2024.143909

[5]Department of Nephrology, Chongqing General Hospital, Chongqing

Received: Feb. 27th, 2024; accepted: Mar. 21st, 2024; published: Mar. 29th, 2024

## Abstract

**Chronic obstructive pulmonary disease (COPD) is a disease mainly characterized by persistent respiratory symptoms and airflow obstruction. Although pulmonary function testing is the cornerstone of COPD diagnosis, it cannot fully assess the full extent of the disease due to the heterogeneity of the disease and the involvement of multiple systems including the heart, blood vessels, and musculoskeletal system. Cardiopulmonary exercise testing (CPET) is an important tool in the evaluation of a variety of clinical diseases, including chronic obstructive pulmonary disease, and can assess the function and reserve capacity of each system. This article mainly describes the clinical application of CPET in the etiology, diagnosis, treatment, and prognosis of COPD.**

## Keywords

**Chronic Obstructive Pulmonary Disease, Cardiopulmonary Exercise Testing, Hyperinflation, Exercise Limitation**



## 1. 引言

慢性阻塞性肺疾病(Chronic Obstructive Pulmonary Disease, COPD)是一种以气流受限为主要特征的疾病，可导致呼吸短促和功能受限[1]。肺功能检查(Pulmonary function testing, PFT)，特别是肺活量测定，是诊断 COPD 的关键标准。然而，PFT 有其局限性，根据肺活量测定，轻度 COPD 患者可能会出现与测试结果不符合的呼吸困难[2]。这往往可以反映 COPD 是一种累及全身系统的疾病。它不仅会影响呼吸系统，还会影响心血管和肌肉骨骼系统，对多器官功能造成损害。心肺运动试验(Cardiopulmonary Exercise Testing, CPET)是一种非侵入技术，可以评估最大限度运动期间呼吸系统、心血管系统、神经心理和代谢系统的功能，同时评估这些系统的储备能力[3]。对于 COPD 来说，呼吸困难和运动不耐受是其常见症状，并可在疾病的急性加重期间进一步恶化，目前心肺运动试验已被广泛用于 COPD 患者的诊疗和研究[4] [5]。本综述的目的是简要描述 CPET 各项指标的病理生理意义，同时总结 CPET 在慢性阻塞性肺疾病的病因鉴别、治疗指导、风险分层、合并症评估、预后评估中的临床应用。

## 2. 心肺运动试验

### 2.1. 心肺运动试验概述

心肺运动试验结合了运动通气量、肺气体交换(氧摄取量、氧气和二氧化碳排出量)和相关变量的测量，以及运动期间的心率、血压、血氧饱和度的测量。测试通常是用跑步机或自行车功率计进行的，运动功率逐渐增加，直到呼吸困难明显加重或运动不耐受。测试时屏幕可实时显示各项指标的变化趋势，数据将被记录于用于存储和分析的软件。

### 2.2. 心肺运动试验主要指标介绍

CPET 包括五个基础指标：每分钟通气量(VE)、摄氧量($VO_2$)、二氧化碳排出量($VCO_2$)、心率(HR)、血氧饱和度($SPO_2$)，衍生出来的指标主要包括以下三个方面：① 反映心功能和运动能力的指标：峰值摄氧量(peak oxygen uptake, peak-$VO_2$)、无氧阈(Anaerobic Threshold, AT)、心率储备与摄氧效率斜率(Oxygen Uptake Efficiency Slope, OUSE)等。② 反映肺组织通气功能的指标：呼吸储备(Breathing Reserve, BR)、最大通气量(Maximal Voluntary Ventilation, MVV)、峰值运动通气量(peak VE)等。③ 反映肺换气功能的指标：二氧化碳通气当量、动脉氧分压、动脉血二氧化碳分压等[6]。

### 2.3. 心肺运动试验重要指标与 COPD 的联系

峰值摄氧量(peak-$VO_2$)是在运动高峰时测得的最高摄氧量，是运动能力的重要衡量标准。在 COPD 中，peak-$VO_2$ 通常会降低，可能的机制是由于肺通气功能障碍导致的心血管系统供氧不足[7]。

无氧阈(AT)是乳酸阈值的无创估计值，高于此阈值时会发生代谢性酸中毒，乳酸会在血液中积聚[8]。由于代谢性酸中毒通常会出现呼吸代偿，因此在高于 AT 的运动期间，通气需求会放大，因此 AT 越低，因 COPD 导致呼吸能力低下的个体发生通气受限的速度就越快[8]。

摄氧效率斜率(OUSE)是 VE 相对于 $VO_2$ 的斜率(通过以 log10 表示 VE 进行线性化)，一项研究报告称 OUSE 与 peak-$VO_2$ 相关，且心力衰竭患者的 OUES 比慢性阻塞性肺病(COPD)更有可能降低[9]，这可能表明低 OUSE 的 COPD 患者存在额外的心血管损害。

呼吸储备(Breathing Reserve, BR)计算为最大通气量(MVV)与峰值运动通气量(Peak VE)之间的差值，在健康个体中，BR 通常是 MVV 的 15~40%。由于 MVV 较低以及 VE 需求过高，患有 COPD 的个体通常具有较低 BR。相比之下，由于低水平的运动限制，高 BR 经常出现在心血管疾病中[10]。一项研究报告称，无氧阈时的呼吸储备指数(VE/MVV)可以区分呼吸短促的原因是肺器质性病变还是心血管系统的限制[11]。

二氧化碳通气当量($VE/VCO_2$)：$VE/VCO_2$ 的比值通常被用来衡量 VE 排出 $CO_2$ 的效率，VE 与 $VCO_2$ 之间的变化关系可表示为 $\Delta VE/\Delta VCO_2$ 的斜率，$\Delta VE/\Delta VCO_2$ 斜率已经成为 CPET 的一个重要变量，因为它是包括慢性心力衰竭和肺动脉高压在内的许多心血管疾病的强大预后标志[12] [13]。有肺动脉高压的慢性阻塞性肺疾病患者 $\Delta VE/\Delta VCO_2$ 斜率较高，在静息和运动时的血氧饱和度也可能比不伴有肺动脉高压的患者低[14]。

## 3. 心肺运动试验的临床应用

临床上可将 CPET 指标用于 COPD 患者呼吸困难原因的鉴别、药物治疗的指导、术前风险的评估、心血管疾病合并症的评估、预后的评估。

### 3.1. 呼吸困难原因的鉴别

COPD 中呼吸困难的机制较为复杂，CPET 有助于确定呼吸困难的原因，从而进行针对性治疗[15] [16]。例如，没有通气受限证据的低 AT 预示着运动训练等传统疗法有很高的改善潜力。相比之下，动态过度充气和通气受限表明需要使用支气管扩张剂进行规律治疗，甚至支持使用侵入性干预措施[15]。

### 3.2. 指导 COPD 的药物治疗

动态过度充气是 CDPD 的一个主要特征[17]。它与症状严重程度和运动能力受限有关，导致身体不适和生活质量下降[18] [19] [20]。因此，稳定疾病的治疗旨在解决劳累症状并提高运动耐量[17]。6 分钟

步行试验和穿梭步行试验可用于测量运动能力，评估治疗干预后对运动的心肺功能，已广泛应用于评估COPD 治疗的临床试验中，被认为是评估 COPD 患者的宝贵工具[21]。然而，多项研究表明，高强度恒定负荷运动试验(耐力 CPET；ECPET)可全面评估 COPD 患者经过药物治疗后的运动耐量[22] [23]。因此，长效 $\beta$2 受体激动剂和长效抗胆碱能药物在临床试验中单独使用或作为双重支气管扩张剂均可通过ECPET 评估治疗后的效果[24] [25]。最常用的评估方法是使用自行车测力计评估治疗前后中耐力时间的变化。这表明在临床上我们可以通过 CPET 指标的动态变化调整患者的药物治疗方案，达到更好的治疗效果。

### 3.3. 患者手术前风险评估

CPET 可进行术前风险评估，因为它为围手术期风险分层提供了常规肺功能测定无法提供的重要预后信息[26]。对于准备接受手术的 COPD 患者，CPET 可以筛查无症状心肌缺血，并根据 peak-$VO_2$ 量化心血管系统储备[27]。在准备接受肺切除手术的患者中，研究表明，与峰值 $VO_2$ > 20 mL/kg/min 的相比，峰值 $VO_2$ < 20 mL/kg/min 的患者心脏和肺部并发症的发生率增加了 4 倍[27] [28]。一些证据建议在高风险个体进行重大选择性腹部手术之前进行术前 CPET，因为观察到 AT 可预测围手术期发病率和死亡率[29]。因此，CPET 已成为对具有围手术期风险的患者进行术前评估的有力工具。

### 3.4. COPD 心血管系统合并症的评估

慢性阻塞性肺病中最常见的合并症是心血管疾病(包括充血性心力衰竭、肺动脉高压和冠状动脉疾病) [30]。

(1) 有研究表明，患有冠状动脉疾病的 COPD 患者的运动能力明显受损，具体表现为较低的峰值工作率(WR)、较低的峰值摄氧量(peak-$VO_2$)、较低的峰值摄氧量(peak-$VO_2$)/峰值心率[31]。这些结果表明，慢性阻塞性肺病患者中存在冠心病进一步损害了他们的有氧能力和对运动的通气反应。

(2) 有研究认为，COPD 患者合并肺动脉高压(Pulmonary Hypertension, PH)会由于肺血管床的丧失引起无效腔通气，从而加重通气功能损害[32]。而另外一项更大规模的研究表明，COPD 患者中合并肺血管病变者具有较低的峰值摄氧量(peak-$VO_2$)和峰值功率，表明 CPET 可能有助于检测没有左心疾病临床症状的门诊 COPD 人群的肺动脉高压[33]。

(3) 充血性心力衰竭在 COPD 患者中发病率很高，运动能力受限、劳力性呼吸困难和疲劳是充血性心力衰竭的常见症状，也常见于 COPD 患者[30]。一项研究表明，患有充血性心力衰竭的 COPD 患者具有更低的 VE/VO2 截距，更高的 VE/$VCO_2$ 斜率[34]，提示这些患者的通气效率和运动能力受到更大的损伤。

### 3.5. 评估 COPD 患者的预后

目前普遍利用基础肺功能中的一秒率预计值(FEV 1% pred)对 COPD 患者的预后进行评估，但有研究表明其对死亡率影响较弱，而 CPET 中的峰值摄氧量(Peak-$VO_2$)是 COPD 死亡率的重要预测因子[35] [36]。此外，在 COPD 合并慢性心力衰竭的患者中，peak-$VO_2$ 的意义可用于选择心脏移植等高级干预措施[37]。

## 4. 结论

慢性阻塞性肺病是一种异质性疾病，身体功能可能通过多种机制受损。CPET 是评估 COPD 患者运动能力、运动限制的严重程度并确定其原因的宝贵工具。它提供了运动能力的客观衡量标准，可直接应用于风险分层和评估，可以指导药物治疗干预的建议，可以评估合并症的严重程度，此外，CPET 还提供重要的预后信息和有价值的数据。目前在我国，由于流程相对复杂、数据分析不够完善等各种原因，CPET 的实际应用仍然存在一定的局限性，检查方法、分析结果的统一标准也尚未构建完成，未来还需要更多更深入的研究。

## 参考文献


[1] Global Initiative for Chronic Obstructive Lung Disease (2019) 2020 Gold Reports. https://goldcopd.org/gold-reports

[2] Behnia, M., Wheatley, C., Avolio, A. and Johnson, B. (2017) Influence of Resting Lung Diffusion on Exercise Capacity in Patients with COPD. *BMC Pulmonary Medicine*, **17**, Article No. 117. https://doi.org/10.1186/s12890-017-0454-y

[3] Albouaini, K., Egred, M., Alahmar, A. and Wright, D.J. (2007) Cardiopulmonary Exercise Testing and Its Application. *Postgraduate Medical Journal*, **83**, 675-682. https://doi.org/10.1136/hrt.2007.121558

[4] Palange, P., Ward, S.A., Carlsen, K.H., Casaburi, R., Gallagher, C.G., Gosselink, R., Whipp, B.J., *et al*. (2007) Recommendations on the Use of Exercise Testing in Clinical Practice. *European Respiratory Journal*, **29**, 185-209. https://doi.org/10.1183/09031936.00046906

[5] Radtke, T., Crook, S., Kaltsakas, G., Louvaris, Z., Berton, D., Urquhart, D.S., Hebestreit, H., *et al*. (2019) ERS Statement on Standardisation of Cardiopulmonary Exercise Testing in Chronic Lung Diseases. *European Respiratory Reviews*, **28**, Article 180101. https://doi.org/10.1183/16000617.0101-2018

[6] Glaab, T. and Taube, C. (2022) Practical Guide to Cardiopulmonary Exercise Testing in Adults. *Respiratory Research*, **23**, Article No. 9. https://doi.org/10.1186/s12931-021-01895-6

[7] Broxterman, R.M., Hoff, J., Wagner, P.D. and Richardson, R.S. (2020) Determinants of the Diminished Exercise Capacity in Patients with Chronic Obstructive Pulmonary Disease: Looking Beyond the Lungs. *The Journal of Physiology*, **598**, 599-610. https://doi.org/10.1113/JP279135

[8] Poole, D.C., Rossiter, H.B., Brooks, G.A. and Gladden, L.B. (2021) The Anaerobic Threshold: 50+ Years of Controversy. *The Journal of Physiology*, **599**, 737-767. https://doi.org/10.1113/JP279963

[9] Barron, A.J., Medlow, K.I., Giannoni, A., Unsworth, B., Coats, A.J., Mayet, J., Francis, D.P., *et al*. (2010) Reduced Confounding by Impaired Ventilatory Function with Oxygen Uptake Efficiency Slope and VE/$VCO_2$ Slope Rather than Peak Oxygen Consumption to Assess Exercise Physiology in Suspected Heart Failure. *Congestive Heart Failure*, **16**, 259-264. https://doi.org/10.1111/j.1751-7133.2010.00183.x

[10] Wasserman, K., Hansen, J.E., Sue, D.Y., Whipp, B.J. and Froelicher, V.F. (1987) Principles of Exercise Testing and Interpretation. *Journal of Cardiopulmonary Rehabilitation and Prevention*, **7**, 189. https://doi.org/10.1097/00008483-198704000-00014

[11] Medoff, B.D., Oelberg, D.A., Kanarek, D.J. and Systrom, D.M. (1998) Breathing Reserve at the Lactate Threshold to Differentiate a Pulmonary Mechanical from Cardiovascular Limit to Exercise. *Chest*, **113**, 913-918. https://doi.org/10.1378/chest.113.4.913

[12] Sue, D.Y. (2011) Excess Ventilation during Exercise and Prognosis in Chronic Heart Failure. *American Journal of Respiratory and Critical Care Medicine*, **183**, 1302-1310. https://doi.org/10.1164/rccm.201006-0965CI

[13] Teopompi, E., Tzani, P., Aiello, M., Gioia, M.R., Marangio, E. and Chetta, A. (2014) Excess Ventilation and Ventilatory Constraints during Exercise in Patients with Chronic Obstructive Pulmonary Disease. *Respiratory Physiology & Neurobiology*, **197**, 9-14. https://doi.org/10.1016/j.resp.2014.03.002

[14] Holverda, S., Bogaard, H.J., Groepenhoff, H., Postmus, P.E., Boonstra, A. and Vonk-Noordegraaf, A. (2008) Cardiopulmonary Exercise Test Characteristics in Patients with Chronic Obstructive Pulmonary Disease and Associated Pulmonary Hypertension. *Respiration*, **76**, 160-167. https://doi.org/10.1159/000110207

[15] Wouters, E.F., Posthuma, R., Koopman, M., Liu, W.Y., Sillen, M.J., Hajian, B., Franssen, F.M., *et al*. (2020) An Update on Pulmonary Rehabilitation Techniques for Patients with Chronic Obstructive Pulmonary Disease. *Expert Review of Respiratory Medicine*, **14**, 149-161. https://doi.org/10.1080/17476348.2020.1700796

[16] Stickland, M.K., Neder, J.A., Guenette, J.A., O'Donnell, D.E. and Jensen, D. (2022) Using Cardiopulmonary Exercise Testing to Understand Dyspnea and Exercise Intolerance in Respiratory Disease. *Chest*, **161**, 1505-1516. https://doi.org/10.1016/j.chest.2022.01.021

[17] O'Donnell, D.E., Casaburi, R., Frith, P., Kirsten, A., De Sousa, D., Hamilton, A., Maltais, F., *et al*. (2017) Effects of Combined Tiotropium/Olodaterol on Inspiratory Capacity and Exercise Endurance in COPD. *European Respiratory Journal*, **49**, Article 1601348. https://doi.org/10.1183/13993003.01348-2016

[18] Garcia-Rio, F., Lores, V., Mediano, O., Blas Rojo, B., Hernanz, A., López-collazo, E. and Alvarez-Sala, R. (2009) Daily Physical Activity in Patients with Chronic Obstructive Pulmonary Disease Is Mainly Associated with Dynamic Hyperinflation. *American Journal of Respiratory and Critical Care Medicine*, **180**, 506-512. https://doi.org/10.1164/rccm.200812-1873OC

[19] Jones, P.W. (2007) Activity Limitation and Quality of Life in COPD. *COPD*: *Journal of Chronic Obstructive Pulmonary Disease*, **4**, 273-278. https://doi.org/10.1080/15412550701480265

[20] ZuWallack, R. (2007) How Are You Doing? What Are You Doing? Differing Perspectives in the Assessment of Indi-

viduals with COPD. *COPD*: *Journal of Chronic Obstructive Pulmonary Disease*, **4**, 293-297. https://doi.org/10.1080/15412550701480620

[21] Borel, B., Provencher, S., Saey, D. and Maltais, F. (2013) Responsiveness of Various Exercise-Testing Protocols to Therapeutic Interventions in COPD. *Pulmonary Medicine*, **2013**, Article ID: 410748. https://doi.org/10.1155/2013/410748

[22] O'Donnell, D.E., Elbehairy, A.F., Faisal, A., Webb, K.A., Neder, A.J. and Mahler, D.A. (2016) Exertional Dyspnoea in COPD: The Clinical Utility of Cardiopulmonary Exercise Testing. *European Respiratory Review*, **25**, 333-347. https://doi.org/10.1183/16000617.0054-2016

[23] Puente-Maestu, L., Palange, P., Casaburi, R., Laveneziana, P., Maltais, F., Neder, J.A., Ward, S., *et al*. (2016) Use of Exercise Testing in the Evaluation of Interventional Efficacy: An Official ERS Statement. *The European Respiratory Journal*, **47**, 429-460. https://doi.org/10.1183/13993003.00745-2015

[24] Maltais, F., Kirsten, A.M., Hamilton, A., De Sousa, D., Voß, F. and Decramer, M. (2016) Evaluation of the Effects of Olodaterol on Exercise Endurance in Patients with Chronic Obstructive Pulmonary Disease: Results from Two 6-Week Crossover Studies. *Respiratory Research*, **17**, Article No. 77. https://doi.org/10.1186/s12931-016-0389-5

[25] Tzani, P., Crisafulli, E., Nicolini, G., Aiello, M., Chetta, A., Clini, E.M. and Olivieri, D. (2011) Effects of Beclomethasone/Formoterol Fixed Combination on Lung Hyperinflation and Dyspnea in COPD Patients. *International Journal of Chronic Obstructive Pulmonary Disease*, **6**, 503-509. https://doi.org/10.2147/COPD.S23746

[26] Ha, D., Mazzone, P.J., Ries, A.J., Malhotra, A. and Fuster, M. (2016) The Utility of Exercise Testing in Patients with Lung Cancer. *Journal of Thoracic Oncology*, **11**, 1397-1410. https://doi.org/10.1016/j.jtho.2016.04.021

[27] Brunelli, A., Kim, A.W., Berger, K.I. and Addrizzo-Harris, D.J. (2013) Physiologic Evaluation of the Patient with Lung Cancer Being Considered for Resectional Surgery: Diagnosis and Management of Lung Cancer: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*, **143**, E166S-E190S. https://doi.org/10.1378/chest.12-2395

[28] Brunelli, A., Charloux, A., Bolliger, C.T., *et al*. (2009) ERS/ESTS Clinical Guidelines on Fitness for Radical Therapy in Lung Cancer Patients (Surgery and Chemo-Radiotherapy) (European Respiratory Journal (2009) 34 (17-41)). *European Respiratory Journal*, **34**, 782. https://doi.org/10.1183/09031936.50184308

[29] Levett, D.Z.H., Jack, S., Swart, M., Carlisle, J., Wilson, J., Snowden, C., Perioperative Exercise Testing and Training Society (POETTS), *et al*. (2018) Perioperative Cardiopulmonary Exercise Testing (CPET): Consensus Clinical Guidelines on Indications, Organization, Conduct, and Physiological Interpretation. *British Journal of Anaesthesia*, **120**, 484-500. https://doi.org/10.1016/j.bja.2017.10.020

[30] Negewo, N.A., Gibson, P.G. and McDonald, V.M. (2015) COPD and Its Comorbidities: Impact, Measurement and Mechanisms. *Respirology*, **20**, 1160-1171. https://doi.org/10.1111/resp.12642

[31] Thirapatarapong, W., Armstrong, H.F. and Bartels, M.N. (2014) Comparison of Cardiopulmonary Exercise Testing Variables in COPD Patients with and without Coronary Artery Disease. *Heart and Lung*: *The Journal of Critical Care*, **43**, 146-151. https://doi.org/10.1016/j.hrtlng.2013.12.005

[32] Divo, M., Cote, C., De Torres, J.P., Casanova, C., Marin, J.M., Pinto-Plata, V., BODE Collaborative Group, *et al*. (2012) Comorbidities and Risk of Mortality in Patients with Chronic Obstructive Pulmonary Disease. *American Journal of Respiratory and Critical Care Medicine*, **186**, 155-161. https://doi.org/10.1164/rccm.201201-0034OC

[33] Skjørten, I., Hilde, J.M., Melsom, M.N., Hisdal, J., Hansteen, V., Steine, K. and Humerfelt, S. (2017) Cardiopulmonary Exercise Test and $PaO_2$ in Evaluation of Pulmonary Hypertension in COPD. *International Journal of Chronic Obstructive Pulmonary Disease*, **13**, 91-100. https://doi.org/10.2147/COPD.S150034

[34] Arbex, F.F., Alencar, M.C., Aline Souza, A., Mazzuco, A., Sperandio, P.A., Rocha, A., Neder, J.A., *et al*. (2016) Exercise Ventilation in COPD: Influence of Systolic Heart Failure. *COPD*: *Journal of Chronic Obstructive Pulmonary Disease*, **13**, 693-699. https://doi.org/10.1080/15412555.2016.1174985

[35] Hiraga, T., Maekura, R., Okuda, Y., Okamoto, T., Hirotani, A., Kitada, S., Ogura, T., *et al*. (2003) Prognostic Predictors for Survival in Patients with COPD Using Cardiopulmonary Exercise Testing. *Clinical Physiology and Functional Imaging*, **23**, 324-331. https://doi.org/10.1046/j.1475-0961.2003.00514.x

[36] Oga, T., Nishimura, K., Tsukino, M., Sato, S. and Hajiro, T. (2003) Analysis of the Factors Related to Mortality in Chronic Obstructive Pulmonary Disease: Role of Exercise Capacity and Health Status. *American Journal of Respiratory and Critical Care Medicine*, **167**, 544-549. https://doi.org/10.1164/rccm.200206-583OC

[37] Mehra, M.R., Kobashigawa, J., Starling, R., Russell, S., Uber, P.A., Parameshwar, J., Barr, M., *et al*. (2006) Listing Criteria for Heart Transplantation: International Society for Heart and Lung Transplantation Guidelines for the Care of Cardiac Transplant Candidates—2006. *The Journal of Heart and Lung Transplantation*, **25**, 1024-1042. https://doi.org/10.1016/j.healun.2006.06.008