Measurement of PETCO2 at Anaerobic Threshold: A Best Prognostic Marker in Patients with Cardiac Resynchronization Therapy?

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Short Editorial related to the article: Predictive Ability of Cardiopulmonary Exercise Test Parameters in Heart Failure Patients with Cardiac Resynchronization Therapy

The cardiopulmonary exercise test (CPET) is a consolidated tool in the functional and prognostic assessment of patients with heart failure[1] with reduced ejection fraction (HFrRF), being a cornerstone in the evaluation for the indication of advanced therapies in HFrEF.[1,2] Cardiac resynchronization therapy (CRT), in addition to reducing mortality, can improve cardiorespiratory fitness, leading to an increase in peak oxygen consumption (VO_2 peak) and a reduction in the slope of the respiratory equivalent CO2 ratio (VE / VCO2 slope).[3-5] In recent years, with the evolution of treatments, general mortality and the risk of the sudden death of patients with HFpEF have been reduced.[6,7] In this context, reviewing the prognosis and the values associated with a higher risk among the CPET variables in patients undergoing CRT becomes important.

The measurement of end-tidal carbon dioxide pressure (PETCO2) during CPET, both at rest,[8] and at the first ventilatory threshold or anaerobic threshold ($P_{ET}CO2_{LA}$),[9] has a well-established prognostic value in heart failure.[8,9] The increase of dead space ventilation, caused by the impairment of the ventilation/perfusion (V/Q) ratio, for example, in patients with left ventricular dysfunction, leads to a reduction in alveolar CO2 and, consequently, in $P_{ET}CO_2$. It is expected that there will be an increase in its measurement up to the anaerobic threshold, which is correlated with an increase in cardiac output.

In this issue of *Arquivos Brasileiros de Cardiologia*, Reis et al.[10] present an interesting analysis of the prognostic role of CPET in a cohort of 450 patients, 114 of whom underwent CRT.[10] The patients were followed up for 2 years, and the evaluated outcome was cardiovascular mortality and the need for urgent transplantation. The classic evaluation studies for heart transplantation[9,11] involving CPET do not include patients with CRT, which makes it important to question how the behavior of prognostic variables would be in this context.[9,11] Knowledge of this scenario is scarce, and some evidence suggests a less important role of peak VO_2 in these patients in the selection for heart transplantation.[12]

In the study by Reis et al.,[10] VO_2 peak, VE/VCO2 slope, $_{PET}CO2$ and $P_{ET}CO2_{LA}$ were able to predict outcomes in patients with HF and CRT in uni- and multivariable analyses.[10] However, in the ROC curve analysis, $P_{ET}CO2_{LA}$ apparently showed superior accuracy for predicting events. Interestingly, the optimal cut-off point was 33 mmHg, lower than the 36 mmHg in previous studies that evaluated this variable.[8,13] On the other hand, the cut-off points for peak VO_2 (12 ml/kg/min) and VE/VCO2 slope (35) were similar to values previously described in the literature16, with no difference in patients with and without CRT.[14] It is important to emphasize that, in this observational study, there was no difference in the incidence of major cardiovascular events between patients with and without CRT.

A possible limitation of the study, already mentioned by the authors, is the presence of submaximal tests in a reasonable number of patients, which reduces the discriminatory power of peak VO^2 for predicting events. However, the evidence provided, in addition to consolidating the prognostic role of CPET in these patients, calls attention to the importance of routinely measuring $P_{ET}CO2_{LA}$ in these cases. This variable has excellent prognostic power and can add information to traditional CPET measurements. Its measurement has an excellent relationship with the increase in cardiac output on exertion, and an altered response (absence of increase up to the AT) characterizes a greater loss in the increase in output during exercise.

Studies with larger sample sizes, preferably multicenter, evaluating the prognostic power of $P_{ET}CO2_{LA}$ in patients with HF and comparing it to other prognostic measures are welcome. The replication of results in different populations strengthens the evidence found and expands the external validity of the findings.

Keywords

Ergoespyrometry/methods; Stroke Volume; Cardiac Resynchronization Therapy/methods; Heart Failure; Cardiac Output, High; Prognosis.

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References

1. Herdy AH, Ritt LEF, Stein R, Soares de Araujo CG, Milani M, Meneghelo RS, et al. Teste cardiopulmonar de exercício: fundamentos, aplicabilidade e interpretação. Arq Bras Cardiol. 2016;107(5):467-81. doi: 10.5935/abc.20160171.
2. Comitê Coordenador da Diretriz de Insuficiência Cardíaca. Diretriz Brasileira de Insuficiência Cardíaca Crônica e Aguda. Arq Bras Cardiol 2018;111(3):436-539. doi: 10.5935/abc.20180190.
3. Cleland JG, Daubert JC, Erdmann E, Freemantie N, Gras D, Kappenberger L, et al. Cardiac Resynchronization Heart Failure (CARE-HF) Study Investigators. The effect of cardiac resynchronization on morbity and mortality in heart failure. N Engl J Med. 2005;352(15):1539-49. doi: 10.1056/NEJMoa050496.
4. Gazzoni GF, Fraga MB, Ferrari AL, Soliz PC, Borges AP, Bartholomay E, et al. Preditores de mortalidade total e de resposta ecocardiográfica à terapia de ressincronização cardíaca: um estudo de coorte. Arq Bras Cardiol. 2017;109(6):569-78. doi: 10.5935/abc.20170171.
5. Vanderheyden M, Wellens F, Bartunek J, Verstreken S, Walraevens M, Geelen P, et al. Cardiac resynchronization therapy delays heart transplantation in patients with end-stage heart failure and mechanical dissynchrony. J Heart Lung Transplant. 2006;25(4):447-53. doi: 10.1016/j.healun.2005.11.454
6. Shen L, Jhund PS, Petrie MC, Claggett BL, Barlera S, Cleland JGF, et al. Declining risk of sudden cardiac death in heart failure. N Engl J Med. 2017;377(1):41-51. doi: 10.1056/NEJMoa1609758.
7. Marcondes-Braga FG, Moura LAZ, Issa VS, Vieira JL, Rohde LE, Simões MV, et al. Atualização de Tópicos Emergentes da Diretriz de Insuficiência Cardíaca – 2021. Arq Bras Cardiol. 2021;116(6):1174-212. doi: 10.36660/abc.20210367.
8. Arena R, Peberdy MA, Myers J, Guazzi M, Tevald M. Prognostic value of resting end-tidal carbono dioxide in patients with heart failure. Int J Cardiol. 2006;109(3):351-8. DOI: 10.1016/j.ijcard.2005.06.032
9. Matsumoto A, Itoh H, Eto Y, Kobayashi T, Kato M, Omata M, et al. End-tidal CO_2 pressure decreases during exercise in cardiac patients: association with severity of heart failure and cardiac output reserve. J Am Coll Cardiol. 2000;36(1):242-9. doi: 10.1016/s0735-1097(00)00702-6.
10. Reis JF, Gonçalves AV, Brás PG, Moreira RI, Rio P, Timóteo AT, et al. Capacidade preditiva dos parâmetros do teste de esforço cardiopulmonar em pacientes com insuficiência cardíaca em terapia de ressincronização Cardíaca. Arq Bras Cardiol. 2022; 119(3):413-423.
11. Osada N, Chaitman BR, Miller LW, Dyp D, Cishek MB, Wolford TL, et al. Cardiopulmonary exercise testing identifies low risk patients with heart failure and severely impaired exercise capacity considered for heart transplantation. J Am Coll Cardiol. 1998;31(3):577-82. doi: 10.1016/s0735-1097(97)00533-0.
12. Goda A, Lund LH, Mancini D. The Heart Failure Survival Score outperforms the peak oxygen consumption for heart transplantation selection in the era of device therapy. J Heart Lung Transplant 2011;30(3):315-25. doi: 10.1016/j.healun.2010.09.007.
13. Myers J, Gujja P, Neelagaru S, Hsu L, Vittorio T, Jakson-Nelson T, et al. End-tidal CO_2 pressure and cardiac performance during exercise in heart failure. Med Sci Sports Exerc 2009;41(1):19-25. doi: 10.1249/MSS.0b013e318184c945.
14. Mehra MR, Canter CE, Hannan MM, Semigram MJ, Uber PA, Baran DA, et al. The 2016 International Society for Heart Lung Tranplantation listing criteria for heart transplantation: 10-year update. J Heart Lung Transplant 2016;35(1):1-23. doi: 10.1016/j.healun.2015.10.023.

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