



## LETTER TO THE EDITOR

### Takotsubo cardiomyopathy and chronic obstructive pulmonary disease – Reply



### Miocardiopatia Takotsubo e doença pulmonar obstrutiva crónica – Resposta

We read with interest the comments by Dr. Dias and Dr. Franco on our recently published case report “Stress-induced cardiomyopathy associated with ipratropium bromide in a patient with chronic obstructive pulmonary disease” (COPD).<sup>1</sup> We agree with Dr. Dias and Dr. Franco that factors such as the presence of pneumonia may have contributed to the clinical picture. The point of divergence is the most likely acute trigger for the stress cardiomyopathy. As we state in the text, we think that the time-course of the association between the administration of ipratropium bromide and Takotsubo cardiomyopathy is suggestive of a causal role, and this view is strengthened by the second episode of bronchospasm.<sup>1</sup>

Epidemiological studies are generally speaking unable to provide proof of causality (only showing that an association exists). Causality can only be established in the context of controlled studies, such as a controlled clinical trial.<sup>2</sup> However, from a practical standpoint, it is important to evaluate the possible causal role of a given drug in a possible adverse drug reaction scenario, since the same patient, as well as others, may be treated in the future in the same type of context and with the same drug. Several methods have been put forward for this purpose, although most have shortcomings.<sup>3</sup>

The time-course, the temporal relation between drug administration and the suspected reaction, is critical in evaluating an adverse drug reaction – and the time course, in this particular case, in our view suggests that ipratropium bromide had a causal role. The parameters of temporal sequence, pattern of response, withdrawal and re-exposure<sup>4</sup> may be seen as favoring our view.

Previous reports of stress cardiomyopathy in COPD patients have described the use of ipratropium, namely the case reported by Pham et al.<sup>5</sup> and one of the cases by White and Stewart.<sup>6</sup> However, it can be argued that this falls short of establishing that there are previous conclusive reports of this reaction.<sup>4</sup>

Concerning drugs that act on adrenergic mechanisms, Sharkey et al. described a series of 136 patients with stress cardiomyopathy, including 13 patients treated with adrenergic agonists that could have acted as triggers.<sup>7</sup> However, 25 patients of the same series were taking beta-blockers,<sup>7</sup> raising doubts concerning the role of adrenergic mechanisms in this setting.

In conclusion, the association between ipratropium bromide use and stress cardiomyopathy in the case we reported was quite clear, and we think that it is reasonable to suggest that ipratropium bromide had a causal role in this case. Since ipratropium bromide use has been associated to stress cardiomyopathy in several individual COPD patients, a more systematic evaluation of this association could be justified.

### Conflicts of interest

The authors have no conflicts of interest to declare.

### References

1. Melao F, Nunes JPL, Vasconcelos M, et al. Stress-induced cardiomyopathy associated with ipratropium bromide therapy in a patient with chronic obstructive pulmonary disease. *Rev Port Cardiol.* 2014;33:175e1–4e.
2. Nunes JPL. Medical therapeutics: from induction to scientific evolution. *Perspect Biol Med.* 2013;56:568–83.
3. Macedo AF, Marques FB, Ribeiro CF, et al. Causality assessment of adverse drug reactions: comparison of the results obtained from published decisional algorithms and from the evaluations of an expert panel. *Pharmacoepidemiol Drug Safety.* 2005;14:885–90.
4. Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther.* 1981;30:239–45.

DOI of original article:

<http://dx.doi.org/10.1016/j.repc.2014.04.003>

<http://dx.doi.org/10.1016/j.repc.2014.09.004>

0870-2551/© 2014 Sociedade Portuguesa de Cardiologia. Published by Elsevier España, S.L.U. All rights reserved.

5. Pham JL, Bruhl SR, Sheikh M. COPD exacerbation with concurrent stress cardiomyopathy: a case of double dyspnoea. *Br J Medical Practitioners*. 2011;4.
6. White JM, Stewart RA. Troponin elevation during exacerbations of chronic obstructive airways disease due to stress cardiomyopathy. *Int J Cardiol*. 2012;160:206–7.
7. Sharkey SW, Windenburg DC, Lesser JR, et al. Natural history and expansive clinical profile of stress (tako-tsubo) cardiomyopathy. *J Am Coll Cardiol*. 2010;55:333–41.

Filipa Melão<sup>a</sup>, José Pedro L. Nunes<sup>b,\*</sup>

<sup>a</sup> *Department of Cardiology, Hospital São João, Porto, Portugal*

<sup>b</sup> *Faculdade de Medicina da Universidade do Porto, Porto, Portugal*

\* Corresponding author.

*E-mail address:* [jplnunes@med.up.pt](mailto:jplnunes@med.up.pt) (J.P.L. Nunes).