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## Cardiopulmonary exercise test in patients with post SARS-CoV-2 sequelae: need to create a multicenter working group. Response



### Prueba de esfuerzo cardiopulmonar en pacientes con secuelas tras el SARS-CoV-2: necesidad de crear un grupo de trabajo multicéntrico. Respuesta

#### To the Editor,

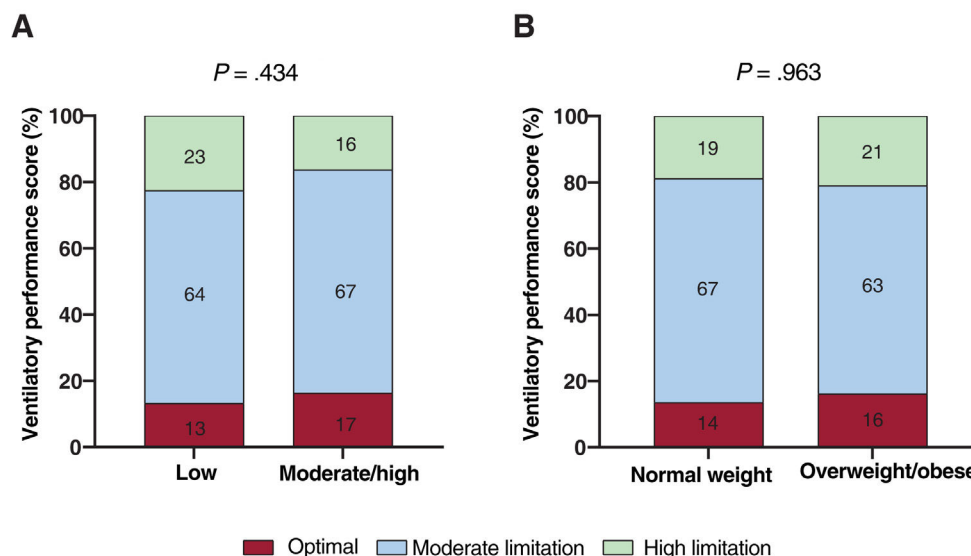
We have read with interest the comments by Vannini et al. regarding our scientific letter<sup>1</sup> on ventilatory response during exercise testing in a population of patients with persistent COVID-19 symptoms. We thank the authors for their observations and comments.

In the assessment of oxygen consumption, we understand the relevance of including spirometry data with diffusing capacity for carbon monoxide ( $D_{LCO}$ ) testing, given that 43% of patients with SARS-CoV-2 sequelae have been reported to have a  $D_{LCO}$  of less

than 80% of the predicted capacity.<sup>2</sup> We are aware of this limitation in our work and welcome the comment by Vannini et al. on future improvements to our research.

Regarding the absence of a subgroup analysis (eg, obese vs nonobese, or trained vs untrained) in explaining our previous findings,<sup>1</sup> the figure 1 presented again shows that ventilatory inefficiency is independent of nutritional status or physical activity levels. We disagree that the protocol used in our study “may be poorly tolerated by less trained patients with symptoms of chronic fatigue”, suggesting adaptations to achieve better exercise tolerance. As previously mentioned,<sup>1</sup> the mean exercise test time was 13.0 minutes and this small difference still preserves the relationship between  $VO_2$ , workload, and heart rate during cardiopulmonary exercise testing.

We agree that the pathophysiological mechanisms of COVID-19 sequelae remain uncertain, and we believe that rehabilitation, based on physical exercise, is a mainstay for the treatment of various persistent symptoms, as recently demonstrated.<sup>3</sup> Indeed, this was the motive prompting our study.<sup>4</sup>



**Figure 1.** Comparison of physical activity levels (A) and nutritional status by BMI (B) and ventilatory performance categories. The ventilatory performance criteria score is derived from the sum of the abnormal criteria, then classified as follows: no ventilatory limitation (no abnormal criteria), moderate limitation (1-2 abnormal criteria), and high limitation (more than 3 abnormal criteria). Values are expressed as No. (%). Differences were determined using the chi-square contingency test. BMI, body mass index.

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## AUTHORS' CONTRIBUTION

All authors have contributed substantially to the drafting, review, and intellectual content of the manuscript.

## CONFLICTS OF INTEREST

None declared.

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## New research avenues for the prognostic value of the Tpeak-Tend interval in patients with different morphological variants of tako-tsubo syndrome



## Nuevas vías de investigación para el valor pronóstico del intervalo onda Tpeak-Tend en pacientes con diferentes variantes morfológicas del síndrome de tako-tsubo

### To the Editor,

I was delighted to read the interesting study by Rosa et al.,<sup>1</sup> in which the authors evaluated the prognostic value of the corrected global (mean of the 12-lead electrocardiogram [ECG] values) Tpeak-Tend interval (Tpeak-Tend) at 48 hours from admission in 87 consecutive patients, aged  $72 \pm 12$  years, with tako-tsubo syndrome (TTS). The authors found that a Tpeak-Tend of  $> 108$  ms was an independent predictor of subacute (beyond 48 hours after admission) ventricular arrhythmias (VAs), defined as premature ventricular contractions  $\geq 2000$  within a 24-hour window of telemetry monitoring, ventricular fibrillation, sustained ventricular tachycardia (VT), polymorphic VT, and nonsustained VT. Such VAs, detected during a median of 8 days of hospitalization, were found to be associated with greater in-hospital mortality. The predictive performance of Tpeak-Tend was found to be superior to that of the standard corrected QT interval (QTc), currently used in patients monitored after TTS.<sup>1</sup> The authors emphasize the advantages of employing all 12 ECG leads, rather than the limb or the precordial leads, in calculating the Tpeak-Tend; they also allude to the hypothesis that myocardial edema (ME) may be at the root of the repolarization aberrations and subacute VAs, via a re-entry or afterdepolarization mechanism due to delayed and dispersed ventricular apico-basal, interventricular and transmural repolariza-

tion gradients,<sup>1</sup> as previously proposed.<sup>2–4</sup> Unfortunately, cardiac magnetic resonance data to evaluate ME were available in only 21% of their patients, and thus the authors could not evaluate the relationship of repolarization aberrations (Tpeak-Tend and QTc) and VAs with the inflammatory ME.<sup>1</sup>

I would appreciate the authors' response to the following points: a) the calculation of T-peak-Tend is labor-intensive; perhaps the global Tpeak-Tend can be electronically calculated, since many other ECG calculations (eg, QT) are currently automatically available upon ECG recording in many commercially available contemporary electrocardiographs; b) to evaluate the feasibility of such an undertaking, perhaps the authors could compare their QTc values, as manually measured, with those calculated by their ECG recording equipment (EL 280 Resting Electrocardiograph, Welch Allyn, United States), as has been done previously; c) although the authors carried out an impressively comprehensive analysis, using a very large array of variables,<sup>1</sup> there is no information on the different morphological variants (ie, apical, mid-ventricular, basal/inverse, or focal) encountered in their 87 patients with TTS; d) the topography of ME would most probably be expected to differ in intensity in the apical and the basal/inverse TTS morphological phenotypes; indeed, in mid-ventricular TTS, it has been found to be more intense in the mid-lateral wall, with corresponding T-wave inversion/QTc prolongation confined to the lateral ECG leads<sup>3</sup>; e) accordingly, it would be of interest for the authors<sup>1</sup> to explore whether the global Tpeak-Tend and QTc differed in patients with apical vs basal/inverse TTS; f) of even greater interest is the question of whether the Tpeak-Tend and QTc, derived from limb, or precordial, or individual (eg, lateral)<sup>3</sup> ECG leads, were more prolonged in patients with apical, basal/inverse, or mid-ventricular TTS.