

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active. In fact, in the pattern ground-glass opacification/opacity, the response is very quickly correlated with  $\dot{V}/\dot{Q}$ matching or edema formation. Still, this benefit should disappear immediately when the patient is repositioned in the supine position, as shown in Retucci et al's work.<sup>1</sup> Rather than improvements in V/Q matching, no variation of the lung ultrasound pattern before and after prone noninvasive ventilation has been detected in the study.<sup>2</sup> In the consolidative pattern, the response is unpredictable, especially if the thickened areas are peripheral and posterior. The pronation may interrupt the process of progressive basilar atelectasis and rapid deterioration.<sup>3</sup> However, this could be challenging in COVID-19 patients with obesity. An approach to overcome this issue is a pregnancy massage pillow, which is essentially an inflatable pillow with a cut-out to allow for a protuberant abdomen. In the prone position, this support allows release of abdominal pressure on the chest.

Another clinical problem is the patient's prone position compliance and interface use. The helmet is the most advantageous and safest interface to give a CPAP, but it is difficult to use in prone patients.<sup>3</sup> The most likely complications caused by prone positioning (eg, vomiting or nausea in patients with pancreatic or abdominal problems in general) would have been clinically evident. In the last period, during low-pressure CPAP use, there is a lot of pneumomediastinum and pneumothorax incidence. It is a real problem for the change of position and prone position, especially during nondrained pneumomediastinum and the placement of any drainages in patients who would require the prone position should be carefully evaluated.

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FINANCIAL/NONFINANCIAL DISCLOSURES: None declared. CORRESPONDENCE TO: Giuseppe Fiorentino, MD; e-mail: giuseppefiorentinol@gmail.com

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# Response

#### To the Editor:

We thank Dr Fiorentino and coworkers for their interest in our recently published experience on prone and lateral positioning in spontaneously breathing patients with COVID-19 pneumonia undergoing noninvasive helmet CPAP treatment.<sup>1</sup> Noninvasive ventilation (NIV) and noninvasive CPAP have been extensively used during the COVID-19 pandemic, as documented by several observational studies published over the past few months, although no randomized controlled studies have been designed to investigate their safety and efficacy in this specific population.<sup>2,3</sup> Different clinical challenges of prone and lateral positioning in spontaneously breathing patients with COVID-19 pneumonia undergoing NIV/CPAP treatment should be acknowledged, including an adequate patients' selection and the correct use of the interface. First, Dr Fiorentino and coworkers accurately underlined the crucial role of both radiology and lung ultrasounds in identifying potential responders. However, we should also acknowledge potential difficulties in performing chest CT scans in patients with severe COVID-19 as well as the low specificity of lung ultrasounds in deeply characterizing the interstitial pattern of a COVID-19 pneumonia. Second, the identification of a positive physiological response to the application of positive end-expiratory pressure during helmet CPAP treatment along with optimal levels of positive end-expiratory pressure is of paramount importance. Recent data documented a successful lung recruitability test in fewer than 30% of COVID-19 patients undergoing CPAP, and these tests also should be considered in clinical practice in patients undergoing prone and lateral positioning to document safety and efficacy of this intervention.<sup>4</sup> Third, the management of the interface, either facemask or helmet, during NIV/ CPAP should be optimized during prone and lateral

positioning, as anticipated by Dr Fiorentino and coworkers. A 180-degree rotation of the helmet during CPAP/NIV treatment is crucial to have the safety (antiasphyxia) valve free from any possible obstruction. The use of armpit braces could be avoided to improve patients' tolerance during prone or lateral positioning, and rolled sheets or pillows could be used to prevent skin lesions caused by ischemia, shearing forces, or mechanical stress because of the pressure of the helmet collar on the patient's neck.<sup>5</sup> Patients also should be trained to safety move their arms or legs and identify a comfortable position during prone/lateral positioning. Finally, prone/lateral positioning in spontaneously breathing patients with COVID-19 pneumonia undergoing CPAP/NIV treatment should always be planned in a safe environment with very-well-trained staff.

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**DOI:** https://doi.org/10.1016/j.chest.2021.01.021

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# Chronic Beryllium Disease Finding Requires Reexamination

## To the Editor:

We read with interest the article by Frye et al<sup>1</sup> published in *CHEST* (March 2021). We believe the evidence presented to justify an environmental beryllium exposure as causative of beryllium sensitization (BeS) and chronic beryllium disease (CBD) requires reexamination in light of the nonstandard beryllium lymphocyte proliferation test (BeLPT) methods.

Of primary concern is the admission by Frye et al<sup>1</sup> that the prevalence of 27% BeS in this small population was unusually high, then failing to examine their BeLPT method as a causative factor. A 27% rate is two to five times higher than what has been found in berylliumprocessing operations. This should have been a huge red flag for the authors.

After consultation with BeLPT experts, we offer the following comments. This study BeLPT method is used rarely. The use of bromodeoxyuridine incorporation to measure cell proliferation is a colorimetric test and is not based on the same principal as the standard tritiated thymidine incorporation. A traditional stimulation index is not appropriate for this assay, in that each individual served as their own control in an effort to have a specific cutoff because the authors did not have a population-based cutoff for this assay. Use of a mean optical density plus 3 SDs is a highly conservative cutoff. The values within 3 SDs follow the empirical rule, meaning that 99.7% of the data in the distribution would fall within this range, thus any values over the 3 SDs would be clearly outside the expected distribution of results and would result in an abnormal result. It is our opinion that this likely accounts for the high BeS rate and CBD diagnosis.

Absent space to provide details, we also take issue with the following items:

- Authors did not consider the relevant BeS studies of beryllium miners,<sup>2</sup> gem cutters,<sup>3</sup> the general population,<sup>4</sup> and studies of the accuracy of the BeLPT.<sup>5,6</sup>
- The use of three of five downwind cases as "evidence" is speculative, absent upwind/downwind air samples.
- Referencing community studies around beryllium production sites as evidence is extremely speculative, absent actual exposure data.

