Jagadeesh.[3] However, this report in fact clearly states that "[n]o overt cardiovascular effects are known," and no specific reference to these phenomena is to be found within the article. Further confirmation is suggested from the review by Mishriky *et al.*,[4] but this systematic review and meta-analysis also fails to describe an effect of pregabalin on organ perfusion or function.

Competing Interests

The author declares no competing interests.

Sibtain Anwar, M.D., Ph.D., Barts Heart Centre, NIHR Biomedical Research Centre, St. Bartholomew's Hospital, London, United Kingdom. s.anwar@qmul.ac.uk

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Physiologic Effects of Pulmonary Artery Occlusion: Comment

To the Editor:

Langer *et al.* demonstrated that a regional pulmonary vascular occlusion is associated with a diversion of ventilation from nonperfused to perfused lung areas.[1] This compensation, due to hypocapnic bronchoconstriction, in combination with pneumo-constriction, limits the increase in dead-space ventilation, improves ventilation-perfusion matching, and thus may decrease the work of breathing during spontaneous ventilation. Wheezing occurs with acute pulmonary embolism in patients both with and without previous cardiopulmonary disease.[2] Wheezing due to bronchoconstriction thus may be just be a marker or consequence and not the cause of respiratory dysfunction. Since the bronchoconstriction may have beneficial effects, do the authors recommend not treating the wheezing associated with pulmonary embolus, particularly in patients with no previous cardiopulmonary disease, where the wheezing is likely to be caused solely by the hypocapnic bronchoconstriction reflex?

Competing Interests

The author declares no competing interests.

Jonathan V. Roth, M.D. Sidney Kimmel Medical College, Thomas Jefferson University, and Albert Einstein Medical Center, Philadelphia, Pennsylvania. jvroth1@aol.com

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Physiologic Effects of Pulmonary Artery Occlusion: Reply

In Reply:

We thank Dr. Roth for the interest in our experimental study, in which we described the changes in blood flow

and ventilation secondary to a controlled regional pulmonary vascular occlusion.[1] These physiologic compensations likely occur through an increase in airway resistance (bronchoconstriction) in the nonperfused lung areas. As a result, ventilation of nonperfused alveoli is reduced, limiting the increase in dead space fraction and preserving the ventilation-perfusion matching. Bronchoconstriction, and therefore wheezing, are thus possible symptoms of pulmonary embolism[2,3] and might (rarely) be so pronounced to be mistaken for severe asthma.[4]

Given these premises, Dr. Roth asks if bronchoconstriction (wheezing) secondary to pulmonary embolism should be treated, as an effective resolution of bronchoconstriction could cause an increase in dead space fraction, thus increasing the required minute ventilation to exhale the produced carbon dioxide load. Again, we thank him for the very interesting and clinically relevant question.

It is our opinion that, once pulmonary embolism is diagnosed (or highly suspected) in a wheezing patient, the choice whether to use bronchodilators should be made according to the specific clinical condition and keeping in mind the particular pathophysiology of bronchoconstriction.

For instance, in case of a patient with diffuse wheezing leading to severe air trapping, increased intrathoracic pressure and *hemodynamic impairment*, we think that pharmacologic bronchodilation might be a reasonable option in order to improve the associated hemodynamic derangement. In particular, it is reasonable to assume that such a patient would be intubated and mechanically ventilated. In this context, therefore, the need to increase mechanical ventilation due to the worsening ventilation-perfusion matching would not be of great concern, as the ventilator would carry out at least part of the additional work of breathing.

On the other hand, in case of a spontaneously breathing, *hemodynamically stable* patient, the treatment of bronchoconstriction might paradoxically *increase*, rather than decrease, the work of breathing, due to the increased dead space fraction. According to this pathophysiologic reasoning, in this setting, *i.e.,* a condition likely caused by regional (not diffuse) bronchoconstriction, bronchodilators could therefore be used with caution, or even be avoided.

Overall, the treatment of pulmonary embolism should of course have the priority. Indeed, the restoration of blood flow to previously nonperfused lung regions will reestablish carbon dioxide delivery to the alveoli and in exhaled air, thus reverting hypocapnic bronchoconstriction and the ensuing wheezing.[3]

Competing Interests

Dr. Pesenti reports advisory board membership at Fresenius AG (Germany) and medical advisory board membership at Baxter (Italy). The other authors declare no competing interests.

Thomas Langer, M.D., Alessandro Santini, M.D., Alberto Zanella, M.D., Antonio Pesenti, M.D. University of Milan-Bicocca, Monza, Italy; and Niguarda Ca' Granda, Milan, Italy (T.L.). Thomas.Langer@unimib.it

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