In Reply—Giant Cell Arteritis: The Place of 18F-FDG PET/CT and Serum Haptoglobin Level

To the Editor: We agree with Dr Yildiz1 regarding the ongoing need for identifying readily available, quantifiable blood biomarkers and noninvasive imaging modalities that provide validated assessment strategies to determine disease activity in large-vessel vasculitis, specifically in patients receiving tocilizumab. The findings by Unizony et al2 described by Dr Yildiz are noted and provide an area worthy of further investigation and confirmation. We chose to exclude guidance or suggestion of exploratory biomarkers in the recommendations of management because some proposed biomarkers are not commercially available to the practicing clinician. Serum haptoglobin is clinically available but has not yet been validated. Replicability of novel biomarkers across different giant cell arteritis cohorts has been a significant challenge, resulting in several preliminary and promising biomarkers from being used broadly.3 Thus, the overall utility of serum haptoglobin in the assessment of disease activity in patients with large-vessel vasculitis outside of the GiACTA trial is yet to be known and requires further investigation before routine use can be recommended.

The authors agree that 18F-fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) can provide additional information about the presence of arterial hypermetabolism in the large vessels of patients with giant cell arteritis. The diagnostic accuracy of PET/CT in the diagnosis of large-vessel vasculitis has a pooled sensitivity of 83.3% and specificity of 89.6%; however, the diagnostic value for monitoring activity while treatment is being received is lower, with a sensitivity of 77% and specificity of 71%.4 Whereas groups have reported that arterial hypermetabolism in some patients portends a higher risk of subsequent aortic complications,5 hypermetabolism can also be noted in patients with hypercholesterolemia6 as well as in vascular remodeling resulting from prior aortic injury7; therefore, interpretation of detectable arterial hypermetabolism in patients without clinical symptoms of disease activity must be done with caution. Large-scale prospective studies using systematically obtained noninvasive imaging are needed to understand the clinical applicability of advanced arterial imaging in the long-term management of patients with large-vessel vasculitis. Until such time, we agree with the current consensus recommendations that arterial imaging (such as PET/CT) is reasonable to use in patients for whom relapse is suspected, if imaging can assist in the confirmation of or exclusion of flare; however, advanced arterial imaging is not routinely recommended for patients in clinical and biochemical remission.8

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Exercise-Based Cardiopulmonary Rehabilitation: A Suitable Addition to Pharmacological Therapy for Pulmonary Hypertension

To the Editor: We read with great interest the article by Burger et al.1 The authors have conducted an intricate, focused review on the pathobiology and recent advances in the management of pulmonary arterial hypertension. The authors provide excellent insight toward the pathobiology of pulmonary arterial hypertension and focus on potential interventional targets and the basis for genetic predisposition.
They also summarize the published and ongoing trials on newer pharmacological approaches targeting the various classes of pulmonary hypertension (PH).

As this review outlines the modern interventional approaches, we would like to highlight the role of exercise-based cardiopulmonary rehabilitation (EBCR) for PH. Exercise intolerance, which is a hallmark of PH, is known to occur from a complex interplay of physiological mechanisms, of which a few have been known to respond to exercise training.1,2,3 Much of the exercise training programs to date have focused on either supervised or hybrid training (ie, supervised followed by home based) that include a combination of aerobic and resistance training, with only a few home-based programs.3 The recent statement by the European Respiratory Society wonderfully elucidates the process of exercise-based evaluations and exercise prescription through a systematic search of the available evidence.4 Overall, EBCR has shown improvements in 6-minute walk distance, peak oxygen consumption, and workload by 53 to 72 m, 1.5 to 2.2 mL/kg per minute, and 14.9 W, respectively.4 These changes have been accompanied by improvements in quality of life and cardiac index (at rest and maximal exercise), along with significant reductions in mean pulmonary arterial pressure and pulmonary vascular resistance at rest.4 These findings indicate that EBCR, among those stabilized with pharmacotherapy, would favorably affect functional capacity and quality of life in patients with PH. However, the long-term effects of EBCR on survival and disease progression are yet to be ascertained. In light of the current pandemic, there is a need to consider the use of alternate models of delivery of EBCR using technology-driven models.5

All things considered, we firmly believe that exercise-based interventions are imperative to the holistic management of patients with PH. As mentioned in the recent European Respiratory Society statement, “individually adjusted exercise training rehabilitation programs supervised by PH expert centres and rehabilitation professionals are likely to be safe for patients with PH who are stable on medical therapy,” with special emphasis on “stable medical therapy.”6,7 Once again, we commend the authors for their excellent work on this complex topic.

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In reply—Exercise-Based Cardiopulmonary Rehabilitation: A Suitable Addition to Pharmacological Therapy for Pulmonary Hypertension

I am thankful for kind comments by Babu et al1 regarding our recent focused review of pulmonary hypertension. They have also provided an argument favoring the addition of exercise-based cardiopulmonary rehabilitation to medical therapy for pulmonary arterial hypertension (PAH), noting that this topic was not addressed in the review. There was no intention to provide a comprehensive review, and omitted certain topics that seemed more appropriate for guideline statements or Task Force reviews as highlighted by Babu et al.

Current recommendations for treatment of PAH have considered structured exercise potentially beneficial, as measured most commonly by improvement in 6-minute walk distance. Indeed, the 2015 European Society Cardiology/European Respiratory Society guidelines recommended a supervised and closely monitored exercise and respiratory training program in specialized clinics as an add-on to medical therapy for stable patients with pulmonary hypertension (class II, level of evidence B), recognizing the limited published literature confirming benefits.2

More recently as noted by Babu et al, a literature review summary produced by a European Respiratory...