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Matthew A. Fuglestad

Hernan Hernandez MD

Yue Gao

Henamari Ybay hybay@unomaha.edu

Molly Schieber University of Nebraska at Omaha, mschieber@unomaha.edu

See next page for additional authors

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Authors

Matthew A. Fuglestad, Hernan Hernandez MD, Yue Gao, Henamari Ybay, Molly Schieber, Katyarina E. Brunette, Sara A. Myers, George P. Casale, and Iraklis Pipinos

Reply

We thank Lanéelle et al for their interest in our recent article.¹ We also want to commend the authors for their excellent publication demonstrating the ability of trans- cutaneous oxygen pressure (TcPO₂) of the calf and buttock, applied during a treadmill exercise test, to identify patients who have significant lower extremity atherosclerotic burden as measured by computed tomography angiography.² Both TcPO₂ and near-infrared spectroscopy (NIRS) represent exciting methods to measure the balance of oxygen delivery, demand, and utilization in the legs of patients with peripheral artery disease (PAD) in real time. We agree with the authors that the provocative insights offered by these technologies elicit challenging questions that warrant further study. What are we to do with the, often asymptomatic, patients who experience significant, exercise-induced skeletal muscle ischemia (as measured by NIRS/TcPO₂) but have mild (<30% stenosis) atherosclerotic disease by computed tomography angiography, which is traditionally considered hemodynamically insignificant? Should these patients be treated conservatively or with a more aggressive approach? Furthermore, can the measurements obtained by NIRS/TcPO₂ help us to decide on the type of therapy (revascularization, exercise, medication, observation) that is most appropriate for each individual PAD patient?

Our group and others have demonstrated that patients with PAD have pathologic changes in their lower extremity affecting their myofibers, mitochondria, and metabolic, inflammatory, and fibrosis-related pathways.^{3,4} It remains unclear if these skeletal muscle pathologies, better known as PAD myopathy, are reversible with the current treatment strategies. However, there are many experts who are concerned that first-line treatment options, such as supervised exercise treadmill training, may induce further skeletal muscle damage in the ischemic limbs because of the ischemia-reperfusion produced by repeated cycles of exercise to moderate to severe pain.⁵ We believe it is a matter of little time before these technologies become more widely used to improve diagnosis of patients with PAD who have a resting ankle-brachial index of greater than 0.90. However, we must also test their potential to better understand the long-term outcomes in patients with PAD who demonstrate pathologic patterns of lower extremity oxygenation during mild, moderate, or heavy exercise. For example, it may be that patients who demonstrate prompt and significant desaturation during even mild exercise will benefit from a revascularization- first approach or a modified exercise program that limits the duration and severity of lower extremity ischemia as measured by NIRS or TcPO₂.

Ultimately, guiding treatment decisions based on NIRS, TcPO₂, and other tests evaluating pathophysiology-based end points in PAD may promote both the functional recovery and long-term muscle integrity in patients with PAD. We challenge authors familiar with these technologies to investigate their use as a diagnostic adjunct, a guide for selection of the most appropriate treatment strategy, and a monitor of treatment response.

Matthew Fuglestad, MD Department of Surgery University of Nebraska Medical Center Omaha, Neb

Hernan Hernandez, MD Department of Surgery University of Nebraska Medical Center Omaha, Neb

Yue Gao, MD Department of Surgery University of Nebraska Medical Center Omaha, Neb

Henamari Ybay Department of Biomechanics University of Nebraska at Omaha Omaha, Neb

Molly Schieber, MS Department of Biomechanics University of Nebraska at Omaha Omaha, Neb

Katyarina E. Brunette, PhD Department of Surgery University of Nebraska Medical Center Omaha, Neb

Sara Myers, PhD Department of Biomechanics University of Nebraska at Omaha Omaha, Neb

George Casale, PhD Department of Surgery University of Nebraska Medical Center Omaha, Neb

Iraklis Pipinos, MD Department of Surgery University of Nebraska Medical Center Omaha, Neb

Department of Biomechanics University of Nebraska at Omaha Omaha, Neb

Department of Surgery Veterans Affairs Medical Center Omaha, Neb

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