TO THE EDITOR: Boyer et al. (2) carefully investigate brachial artery (BA) perfusion in 15 polycythemic (P) and 13 normocytic (N) patients with chronic obstructive pulmonary disease, matched for age, sex, smoking, blood pressure, heart rate, lung function, and blood gases. P vs. N had not only higher mean hemoglobin concentrations ([Hb]: 17.4 vs. 14.3 g/dl) but also larger mean BA diameters (5.2 vs. 4.5 mm, \( P < 0.02 \)), which directly correlated with [Hb] (\( P < 0.01 \)). Wall shear was not significantly higher in P vs. N (despite greater blood viscosity), given the inverse relation between shear and vessel radius (2). P vs. N appeared to show greater brachial flow-mediated dilatation in response to hyperemia (FMD), with significantly reduced dilatation to acetylcholine, and similar responses to bradykinin, substance P, and \( \mathrm{N} \)-monomethyl-L-arginine (\( \mathrm{N} \)-NMMA). Boyer et al. (2) conclude that P vs. N exhibit appropriate basal and stimulated BA nitric oxide (NO) release.

We propose the following considerations to further interpret the above findings. 1) The blood pool of NO goes beyond the “instantaneous” endothelial capacity of NO synthesis (indirectly assessed by \( \mathrm{L} \)-NMMA inhibition of NO synthase) and comprises nitrosyl-/nitroso-proteins, including intracellular Hb (5). 2) Lower NO bioavailability in blood has been reported among stable anemic vs. matched nonanemic patients (1). 3) The direct relation reported by Boyer et al. (2) between [Hb] and FMD conflicts with an inverse relation consistently described by others in hypertensive, diabetic, anemic, and healthy subjects (3, 6). 4) Deoxyhemoglobin (deoxyHb) [but not oxyhemoglobin (oxyHb)] releases bioactive NO and is a recognized crucial mediator of physiological hypoxic dilatation of the systemic microcirculation (5) and, consequently, of upstream arteries (4). 5) The physiological deoxyHb-NO reactions may explain several findings by Boyer et al. (2) in P vs. N, e.g., the larger baseline BA diameter and the reduced BA response to acetylcholine. These (as well as the well-established reduced FMD with increasing [Hb]) (3, 6) may simply reflect a reduced dilator potential of basally dilated systemic arteries and arterioles in P vs. N. Bradykinin and substance P, more than acetylcholine, can act independently of NO (4), and this might explain the similar vessel response to these agents in P vs. N.

While agreeing with the overall conclusions of Boyer et al. (2), we believe Hb’s carriage of NO in red blood cells and deoxyHb’s release of NO in the systemic microcirculation need to be considered when comparing systemic vascular function of P vs. N individuals.

DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the author(s).

REFERENCES