Title

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Re: "The Complexity of Diagnosing High-Altitude Pulmonary Edema: A Case Report and Review of the Differential Diagnosis of Greater Than Expected Hypoxemia at Altitude" by Reno et al. (High Alt Med Biol 2019;20:181–186)

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Dear Editor,

The case report by Reno et al. (2019) describes a 58-year-old woman who experienced symptomatic hypoxemia and high-altitude pulmonary edema (HAPE) as she attempted to ascend Mount Kilimanjaro. The authors concluded that the cause of the low oxygen saturations was due to a combination of undiagnosed mild pulmonary hypertension and intrapulmonary shunting. We are concerned that the etiology was misdiagnosed, highlighting a common problem with accurately diagnosing a patent foramen ovale (PFO).

In brief, the patient underwent evaluation for a right-to-left shunt with a transthoracic echocardiography (TTE) with bubble study and a PFO was ruled out because the agitated saline bubbles observed in the left side of the heart were delayed in appearance by five beats. There are two problems with this conclusion.

First, conventional TTE with bubble study has a sensitivity of 46% for detecting an intracardiac shunt, with improvement in sensitivity when performed with harmonic imaging, making it a poor screening examination (Mojadidi et al., 2014a, 2014b). This suboptimal sensitivity explains in part why there is a high likelihood that a PFO was missed in a patient with a high pretest probability for having a PFO. Given that the sensitivity of transcranial Doppler (TCD) for detecting a right-to-left shunt is 97%, it is our preferred initial screening method (Mojadidi et al., 2014c). An alternative method for diagnosing a PFO would be a transesophageal echocardiogram (TEE), which has a lower sensitivity (89%) (Mojadidi et al., 2014d) compared with TCD but yields additional information about the anatomy of the atrial septum.

Second, when performing a bubble study, one should not rely solely on the number of cardiac cycles before appearance of microbubbles in the left atrium to distinguish between cardiac and pulmonary right-to-left shunting. A number of factors play a role in when the PFO opens, including, but not limited to, the phase of respiration and the relative pressure in the right atrium compared with the left atrium (Velthuis et al., 2015). This is a common misconception that is propagated in the medical literature based on echocardiograms as distinguished from the true gold standard, which is a right heart catheterization with passage of a guidewire across the atrial septum (Chen et al., 1992). Operators who perform PFO closure and agitated saline bubble studies in the catheterization laboratory are familiar with the notion that a saline bubble bolus may pass immediately or be delayed by several heart beats in patients with a PFO proven by guidewire passage into the left atrium. The authors concluded that, based on the TTE bubble study finding of >5 seconds before appearance of bubbles, the hypoxemia with altitude was due to the presence of intrapulmonary shunting. We believe that this is an inaccurate conclusion and it is more likely that the patient had a PFO, which is well described in cases of HAPE (Allemann et al., 2006).

Although percutaneous PFO closure is approved by the Food and Drug Administration in instances of cryptogenic stroke only, we believe that, based on observational data (Godart et al., 2000) and the chronic need for the patient to take medications whenever she ascends to high altitudes, she will benefit from repeat testing for a PFO with a TCD. If a PFO were found to be present, the risks and benefits of PFO closure should be considered.

We urge future investigators to use a methodology that is more sensitive than TTE for PFO screening, such as TCD or TEE, which in turn will allow for conclusions based on more accurate data and for full exploitation of simple and effective therapeutic measures.

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Author Disclosure Statement

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