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EDITORIAL COMMENT

Multi-Imaging Modality Facilitates Screening of Pulmonary Hypertension at High Altitude*

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Pulmonary hypertension (PH) is a severe hemodynamic condition in natives and long-term residents at or higher than 2,500 m above sea level, which contributes to pulmonary embolism, polyrhythmia, and high-altitude pulmonary hypertension (HAPH).[1] HAPH, first reported by Rotta et al,[2] is characterized by living at an altitude above 2,500 m, mean pulmonary artery pressure (mPAP) >30 mm Hg (or systolic pulmonary artery pressure (SPAP) >50 mm Hg), and no other identified causes of PH (eg, excessive polycythemia, chronic obstructive or interstitial lung diseases, neurologic dysfunctions) according to the Qinghai criteria in 2005.[1,3] The prevalence of HAPH varies among different altitudes, ethnics, and ancestral history of colonization to high altitude. Millions of people permanently live in the Qinghai-Tibet Plateau, and hundreds of thousands of tourists visit western China annually, so early identification of PH at high altitude has great significance.[3] However, the invasive nature and limited availability of right heart catheterization (RHC) hampers early identification of PH at high altitude. Therefore, noninvasive examinations would be heavily leaned on during the screening and diagnosis of PH at high altitude.

Based on reports by Kojonazarov et al,[4] echocardiography achieved 70% sensitivity and 88% specificity in identifying PH in highlanders, compared with electrocardiography (ECG) (59% sensitivity and 81% specificity). The correlation coefficient between the results of echocardiography and those of catheterization was 0.78. Thus, a combination of ECG with echocardiography may be useful for screening HAPH. Moreover, the diameter of the main pulmonary artery (MPA) and the ratio of MPA diameter to that of ascending aorta (AA) are common metrics to predict and screen PH and were reported to be significantly different ($P < 0.0001$) between control subjects and PH patients.[5] However, Terpenning et al[6] suggested that the previously proposed threshold of MPA diameter (3.15 cm) is not specific for identifying the patients with PH. It has also been reported that the mPAP predicted by MPA volume and echocardiographic SPAP showed excellent correlation with the mPAP measured by RHC ($r = 0.89$; $P < 0.001$). The areas under the receiver operating characteristic curves for predicting PH were 0.94 for the predicted mPAP, 0.90 for the MPA volume, and 0.92 for the echocardiographic PASP.[7] Furthermore, the automated right ventricle/left ventricle ratio correlated more strongly with RHC metrics than MPA diameter and MPA-to-AA diameter ratio measured manually.[8]

In this issue of *JACC: Asia*, Zeng et al[9] retrospectively analyze the features of computed tomography, computed tomographic angiography, echocardiography, and pulmonary angiography in 25 patients with suspected PH who lived in Tibet at an average altitude of 4,000 m. Furthermore, Zeng et al[9] developed a model which may provide a useful method for predicting and screening patients with PH for further invasive measurements. In this model, the authors demonstrated that the left lower pulmonary artery-bronchus ratio (ABR) (OR: 1.13; $r = 0.821$) and the ratio of right to left atrial diameter (rRLA) (OR: 1.09;

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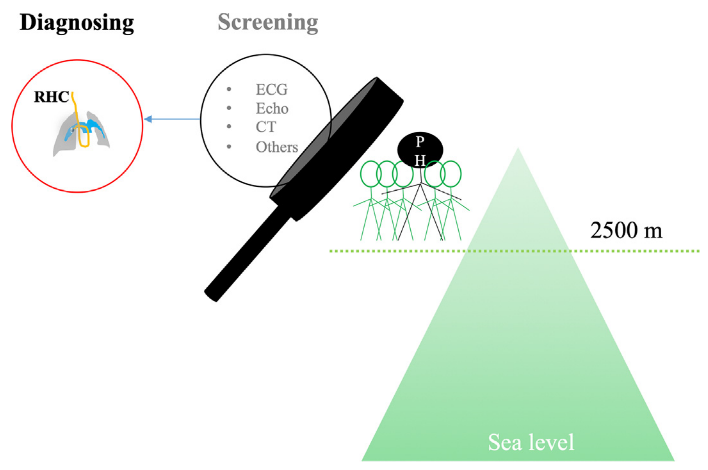
$r = 0.649$) were significantly associated with PH in high altitude (all $P < 0.0001$). The mPAP predicted by left lower ABR and rRLA as covariates showed high correlation with the mPAP measured by RHC ($r = 0.907$; $P < 0.0001$). The authors also showed the typical pathologic changes, such as media thickening and smooth muscle cell proliferation in pulmonary arteries, of the patients with PH at high altitude. Moreover, they proposed that SPAP by echocardiography, MPA diameter, and the ratio of MPA to AA diameter might not be accurate for predicting PH at high altitude. In our opinion, however, it is still early to draw such a conclusion, because multiple factors, including interoperator bias and limited sample size, might affect the performance of the predicting model. In addition, Zeng et al[9] performed pulmonary angiography and described "coral sign" in the PH of highlanders, particularly at the lower pulmonary artery, which might be educational for teaching. Intriguingly, ABR, a previously overlooked metric in chest computed tomography measured in this study, showed good prediction value for screening PH at high altitude. A study by Choe et al[10] had demonstrated that ABR was significantly associated with pulmonary hemodynamics in patients with congenital heart defects. Therefore, ABR might be more useful for predicting PH, although further investigations are necessary to confirm this.

There were some limitations in this study. The sample size is small, and the prediction model needs validation. Hemodynamic data such as pulmonary vascular resistance, cardiac output index, and mixed venous oxygen saturation, were not provided; echocardiographic metrics, such as right atrial area, right ventricular area, and tricuspid annular plane systolic excursion, were not measured. These parameters may also play important roles in screening, diagnosing, and evaluating PH at high altitude. The result of ECG, the examination with easy accessibility and great importance in screening PH, should be included.

Taken together, using multiple imaging modalities could facilitate development of predicting models for PH in highlanders (Figure 1). Discrepancy among the reported studies could be attributed to the differences in population cohorts, sample size, and the metrics examined. Large-sample, well designed, and externally validated cohort studies are warranted.

FIGURE 1 **Schematic Diagram of Multiple Noninvasive Modalities for PH at High Altitude**



With the use of a combination of electrocardiography (ECG), echocardiography (Echo), and computed tomography (CT), a suspected PH patient at high altitude is screened and referred to a pulmonary hypertension (PH) center for right heart catheterization (RHC) to confirm the diagnosis.

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