Altitude exposure has long been recognized as a cardiac stress. Early accounts of alpine climbs mention a diagnosis of “cardiac fatigue” based on tachycardia, palpitations, shortness of breath, and chest percussion (fonendoscopy) of enlarged hearts (1). Heart failure syndromes have been reported at high altitudes under various names including brisket disease in cattle brought to high-altitude pastures in Utah and Colorado (2), chronic mountain sickness (CMS) or Monge’s disease in the inhabitants of the South American altiplano (3), less frequently in Han Chinese immigrants to Tibet (4), subacute mountain sickness corresponding to a form of rapidly evolving right ventricular failure observed in Indian soldiers posted at the high-altitude borders in China (5), in Han Chinese infants brought to reside in Tibet (6), and occasional echocardiographic high-altitude right heart failure in previously healthy travelers (7). When diagnosed at high altitudes, heart failure is almost always predominantly right sided. This is explained by hypoxic pulmonary vasoconstriction and remodeling as a cause of increased right ventricular (RV) afterload and possibly a contribution of negative inotropic effects of ambient hypobaric hypoxia (8).

In this context, the report by Pratali et al. (9) in this issue of JACC, of normal cardiac adaptation to exercise in high-altitude dwellers with CMS may appear provocative, but what is the exact meaning of CMS? A recent expert consensus conference defined CMS as a syndrome of chronic maladaptation to altitude characterized by symptomatic polycythemia (with hemoglobin >21 g/l in men and >19 g/l in women), severe hypoxemia, and relative hyperventilation with or without pulmonary hypertension and eventual right ventricular failure (10). Thus, although (right) heart failure is generally thought to be an inescapable consequence of CMS, it is not necessarily present at diagnosis, and it is unclear as to how often heart failure complicates CMS. As for pulmonary hypertension in CMS, it is variable, more often mild to moderate than severe, in proportion to decreased arterial oxygenation (11) and increased viscosity of the blood (12). Pulmonary hypertension in CMS is exacerbated by exercise, with steep pressure-flow relationships and pulmonary artery pressures reaching systemic levels in a proportion of patients (11–13). Nonetheless, this is still not heart failure. There is thus a confusion of terms in the literature about the cardiac complications of high-altitude exposure that should be better clarified with help of more data at a next expert consensus meeting.

Pratali et al. (9) measured pulmonary vascular pressures, cardiac output, and indexes of RV and left ventricular (LV) function and dimensions using Doppler echocardiography and tissue Doppler imaging at rest and at exercise. Their study included 46 patients with CMS and 41 healthy controls all living permanently at the altitude of 3,600 to 4,000 m in La Paz, Bolivia. Pulmonary artery pressures at rest were on average at the upper limit of normal (at sea level) in both groups, but increased markedly at exercise, as expected. Pulmonary vascular resistance (PVR) increased in the CMS patients and remained unchanged in the control subjects, in contrast to the decrease in PVR due to the distensibility of resistive vessels normally seen in healthy subjects at sea level (14).

Indexes of resting RV or LV function measured by Pratali et al. (9) did not differ between CMS patients and control subjects, with the exception of...
some increase in RV dimensions and decreased fractional area change (estimating ejection fraction) in the CMS patients. In agreement with previous studies, both healthy control subjects and CMS patients had a few slight alterations in indexes of LV and RV diastolic and systolic function, including the Tei index, compared with reported measurements in healthy sea level volunteers (15–18). However, RV contractility (assessed by end-systolic [actually peak systolic] pressure vs. area) increased during exercise in adaptation to increased loading conditions, indicating preserved contractile reserve. Similar results with validation of the end-systolic to area ratio against magnetic resonance imaging have been recently reported in healthy subjects at sea level (19). It is of interest that increased during exercise in adaptation to increased loading conditions, indicating preserved contractile reserve. However, as always in previously healthy individuals with pulmonary vascular hyper-reactivity to hypoxia and subsequent severe hypoxic pulmonary hypertension (8,12). Even so, high-altitude dwellers have been reported to lead normal active lives despite very high pulmonary artery pressures (21). This is also seen in patients with severe pulmonary arterial hypertension (idiopathic or associated to congenital heart diseases) in whom the right ventricle sometimes remains adequately coupled to a hypertensive pulmonary circulation for extensive periods of time. The understanding of the pathobiology of RV function adaptation and eventual failure in severe pulmonary hypertension remains a challenge (22). Extramyocardial factors may also have to be taken into consideration. Fluid retention may be aggravated by relatively higher arterial PCO2 in CMS patients as a cause of increased renal reabsorption of sodium and bicarbonate (12). Whether preconditioning of the right ventricle occurs in physically active mountaineers as in highly trained endurance athletes (19) would be interesting to investigate.

Pratali et al. (9) are to be commended for their elegant noninvasive study showing that the (right) heart at high altitudes is most often well adapted with preserved contractile reserve. However, as always in medicine, exceptions occur that may be of even greater pathophysiological interest than the rules. More research with clearer definitions and concepts is needed in this fascinating area. In the meantime, the risk of high-altitude-induced right heart failure should not be neglected by cautious clinicians advising high-altitude dwellers and travelers.

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