Taking Heart Failure to New Heights: Its Pathophysiology at Simulated Altitude

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Exercise intolerance in patients with heart failure may be limited by the combined effects of limitations in central hemodynamic function and in skeletal muscle metabolism. Many of these patients travel to (or retire in) locations that are substantially above sea level. The usual medical advice for patients with heart failure, based primarily upon theoretical grounds and "clinical judgment," is to avoid high altitudes. This certainly seems reasonable in patients with poorly controlled heart failure. Little is known, however, about what sort of advice should be provided to stable patients who wish to travel to high altitudes.

In this issue of **The Green Journal**, Agostoni et al (1) provide some practical guidance about limitations in specific activities among patients with stable heart failure, based on their exercise tolerance at sea level and the altitude to which they will travel. Several changes occur with altitude that might make it difficult for patients with heart failure to travel to high elevations. In normal people who travel to elevations of greater than 3000 m, the differential between the lower partial pressure of the thinned air and the normal pressure within the capillary wall may cause the extrusion of fluid and acute pulmonary edema (2). In addition, there is an acute increase in circulating catecholamine levels (3). In normal people at altitude, however, exercise results in less lactate production at each level of exercise than occurs with exercise at sea level. This is the so-called "lactate paradox" (4). There is also more reliance on skeletal muscle metabolism for performance (5) and a higher extraction ratio of oxygen at each level of exercise (6).

There are several pathophysiological processes in patients with chronic heart failure that might be exacerbated at high altitude, making it hazardous to spend time in environments where the reduced partial pressure of oxygen may promote further deterioration in cardiac function. These included high circulating levels of catecholamines; increased trans-capillary permeability in the lung, often with subclinical edema; poor skeletal muscle metabolism; high oxygen extraction in the periphery; high resting serum lactate levels; poor pulmonary function; and, often, ischemic heart disease (7). Exacerbation of these conditions by travel to high altitude may worsen heart failure. During hypoxia at altitude, the work of breathing may increase substantially in patients with severe heart failure who have stiff lungs, thus becoming a major component of total body oxygen consumption. In addition, there is a potential for worsening of ischemic heart disease. Hence the hesitancy on the part of clinicians to advise patients on this issue.

In their study, Agostoni et al quantified the reduction in exercise tolerance with increasing levels of simulated altitude—as reproduced by reducing the level of inspired oxygen—experienced by patients with heart failure of varying degrees of severity (1). They compared their findings in these patients with a normal control group, and suggested a scientific rationale for their observations. They made several major observations. They confirmed that heart failure patients have altered pulmonary function compared with normal subjects. Patients with heart failure have decreasing maximum exercise tolerance with increasing simulated altitude, and the slope of the deterioration in maximal work and oxygen consumption with increasing altitude is greater in those with more severe heart failure. Their findings make it possible to estimate the percent reduction in exercise capacity with increases in altitude among normal subjects and among patients with heart failure. The investigators developed a regression equation for three degrees of heart failure that can estimate the expected functional limitation of patients with heart failure at various altitudes. They also provided a table of expected limiting activities for each functional class of heart failure at each altitude that corresponded with the observed limitation of work capacity that they observed.

Although this paper is an important contribution, it is only a start. More research should be done to define the limitations imposed on the physiologic responses to altitude in patients with heart failure. The investigators simulated altitude exposure by reducing the partial pressure of inspired oxygen at sea level. However, altitude exposure may be very different physiologically than hypoxia at sea level. Other components of altitude exposure, such as reduced pressure of the air at the level of the alveolus, and perhaps circulating catecholamine levels, are not reproduced in this model. In addition, the investigators studied the acute effects of lowered partial pressure of oxygen, whereas the acute and chronic responses to altitude may differ due to acclimatization to altitude (8). All of these issues need to be studied before we can confidently advise patients with heart failure whether it is safe to travel or live at elevations substantially above sea level.

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