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Pathophysiology of Volume Overload in Acute Heart Failure Syndromes

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ABSTRACT

The inability to effectively regulate volume status is a major consequence of acute heart failure syndromes (AHFS). A variety of pathophysiologic processes contribute to this impairment, most notably neurohormonal activation of the renin-angiotensin-aldosterone system, arginine vasopressin, and the sympathetic nervous system. As a result, addressing volume overload is one of the most challenging aspects of AHFS management. Neurohormonal activation leads to substantial changes in hemodynamics and myocardial remodeling, which further contribute to the severity of heart failure (HF) disease and thereby cyclically increase the risk of further neurohormonal activation. Pulmonary capillary wedge pressure is a dependable reflection of volume status and has been used as a surrogate marker in recent studies to assess disease progression in response to innovative HF treatment strategies. Future approaches to HF treatment should focus on the more accurate assessment and management of volume status in an effort to improve patient care.

KEYWORDS: Atrial natriuretic peptide; B-type natriuretic peptide; Neurohormones; Pulmonary capillary wedge pressure; Renin-angiotensin-aldosterone system

Heart failure (HF) has an overwhelming impact on global health and healthcare costs. In the United States, approximately $4.0 billion in Medicare reimbursements related to HF were awarded in 2001.[1] This figure is unlikely to decrease in the near future because the disease has a disproportionate effect on the elderly, a growing segment of the US population. The most complex and potentially costly aspect of symptomatic HF care is acute heart failure syndromes (AHFS), which involve the management of altered volume status due to dysfunctional cardiorenal, hemodynamic, and neurohormonal processes.[2]

PATHOPHYSIOLOGY OF RENAL SODIUM AND WATER RETENTION IN ACUTE HEART FAILURE SYNDROMES

The renal sodium and water retention that leads to volume overload in patients with AHFS occurs in the presence of an increase in total blood volume. In normal subjects, an increase in total blood volume is associated with an increase in renal sodium and water excretion. The reverse occurs in patients with AHFS because the integrity of the arterial circulation, not total blood volume, is the primary determinant of renal sodium and water excretion.[3–5] Only an estimated 15% of total blood volume resides in the arterial circulation; thus, total blood volume can be increased primarily by expansion of the blood volume in the venous circulation, because underfilling of the arterial circulation occurs as a result of a decrease in cardiac output (**Figure 1**).[5]

The renal sodium and water retention that occurs in AHFS involves several mediators.[6] In contrast to normal subjects, patients with AHFS fail to escape from the renal sodium–retaining effect of aldosterone and also experience renal resistance to natriuretic peptides. Increased sodium reabsorption in the proximal tubule, and thus decreased sodium delivery to the collecting duct—sites of action of aldosterone and the natriuretic peptides—occurs in patients with AHFS secondary to renal consequences of arterial underfilling and neurohumoral activation. The decreased

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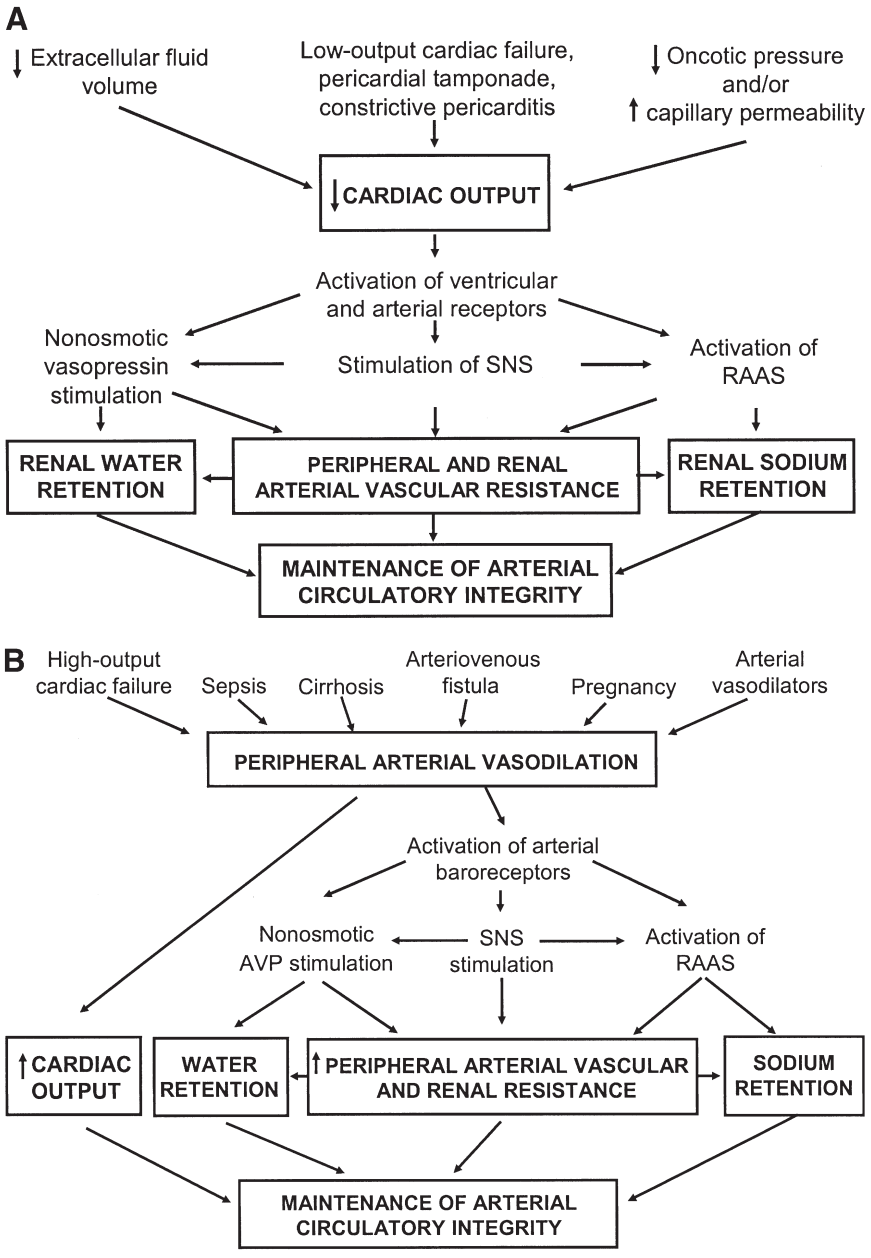

Figure 1 (*A*) Neurohumoral activation in response to arterial underfilling secondary to a decrease in cardiac output. (*B*) Neurohumoral activation in response to relative arterial underfilling secondary to peripheral arterial vasodilation. Cardiac output increases secondary to the diminished cardiac afterload. RAAS = renin-angiotensin-aldosterone system; SNS = sympathetic nervous system. (Adapted with permission from *Ann Intern Med.*[5])

distal sodium delivery in patients with AHFS no doubt contributes to the impaired escape from the sodium-retaining effect of aldosterone and the resistance to the natriuretic effect of atrial and ventricular peptides.

Decreased distention of arterial baroreceptors during arterial underfilling is associated with increased adrenergic discharge from the central nervous system, with resultant activation of the renin-angiotensin-aldosterone system (RAAS) (**Figure 2**).[6] Both adrenergic stimulation and increased angiotensin II activate receptors on the proximal tubular epithelium that enhance sodium reabsorption and diminish sodium delivery to the collecting duct. The increase in angiotensin II and aldosterone also increases cardiac remodeling and fibrosis.

Another outcome of the neurohumoral activation that occurs in cardiac failure is the baroreceptor-mediated nonosmotic release of arginine vasopressin (AVP).[7,8] This nonosmotic AVP stimulation overrides the osmotic regulation of AVP and is the major factor leading to the hyponatremia associated with AHFS.[9] In addition to activation of the V_2 vasopressin receptors on the collecting duct, which leads to aquaporin 2 water channel–mediated antidiuresis, the vascular V_{1a} receptors on vascular smooth muscle are activated by the nonosmotic release of AVP.[10] **Figure 3** illustrates