



FIGURE 280-1 Pathophysiologic correlations, general therapeutic principles, and results of specific “directed” therapy in heart failure (HF) with preserved ejection fraction. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.

parameters associated with worse outcomes: a blood urea nitrogen level greater than 43 mg/dL (to convert to mmol/L, multiply by 0.357), systolic blood pressure less than 115 mmHg, a serum creatinine level greater than 2.75 mg/dL (to convert to $\mu\text{mol/L}$, multiply by 88.4), and an elevated troponin I level. A useful clinical schema to identify treatment targets for the various phenotypic presentations and management goals in ADHF is depicted in Fig. 280-2.

VOLUME MANAGEMENT

Intravenous Diuretic Agents Intravenous diuretic agents rapidly and effectively relieve symptoms of congestion and are essential when oral drug absorption is impaired. When high doses of diuretic agents are required or when the effect is suboptimal, a continuous infusion may be needed to reduce toxicity and maintain stable serum drug levels. Randomized clinical trials of high-versus low-dose or bolus versus continuous infusion diuresis have not provided clear justification for the best diuretic strategy in ADHF, and as such, the use of diuretic regimens remains an art rather than science. Addition of a thiazide diuretic agent such as metolazone in combination provides a synergistic effect and is often required in patients receiving long-term therapy with loop diuretic agents. Change in weight is often used as a surrogate for adequate diuresis, but this objective measure of volume status may be surprisingly difficult to interpret, and weight loss during hospitalization does not necessarily correlate closely with outcomes. It is generally advisable to continue diuresis until euvolemia has been achieved. Physical examination findings, specifically the jugular venous pressure coupled with biomarker trends, are useful in timing discharge planning.

The Cardiorenal Syndrome The cardiorenal syndrome is being recognized increasingly as a complication of ADHF. Multiple definitions have been proposed for the cardiorenal syndrome, but at its simplest, it can be thought to reflect the interplay between abnormalities of heart and kidney function, with deteriorating function of one organ

while therapy is administered to preserve the other. Approximately 30% of patients hospitalized with ADHF exhibit abnormal renal function at baseline, and this is associated with longer hospitalizations and increased mortality. However, mechanistic studies have been largely unable to find correlation between deterioration in renal function, cardiac output, left-sided filling pressures, and reduced renal perfusion; most patients with cardiorenal syndrome demonstrate a preserved cardiac output. It is hypothesized that in patients with established heart failure, this syndrome represents a complex interplay of neurohormonal factors, potentially exacerbated by “backward failure” resulting from increased intra-abdominal pressure and impairment in return of renal venous blood flow. Continued use of diuretic therapy may be associated with a reduction in glomerular filtration rate and a worsening of the cardiorenal syndrome when right-sided filling pressures remain elevated. In patients in the late stages of disease characterized by profound low cardiac output state, inotropic therapy or mechanical circulatory support has been shown to preserve or improve renal function in selected individuals in the short term until more definitive therapy such as assisted circulation or cardiac transplantation is implemented.

Ultrafiltration Ultrafiltration (UF) is an invasive fluid removal technique that may supplement the need for diuretic therapy. Proposed benefits of UF include controlled rates of fluid removal, neutral effects on serum electrolytes, and decreased neurohormonal activity. This technique has also been referred to as aquapheresis in recognition of its electrolyte depletion-sparing effects. Current UF systems function with two large-bore, peripherally inserted venous lines. In a pivotal study evaluating UF versus conventional therapy, fluid removal was improved and subsequent heart failure hospitalizations and urgent clinic visits were reduced with UF; however, no improvement in renal function and no subjective differences in dyspnea scores or adverse outcomes were noted. More recently, in the Cardiorenal Rescue Study in Acute Decompensated Heart Failure (CARRESS-HF) trial,