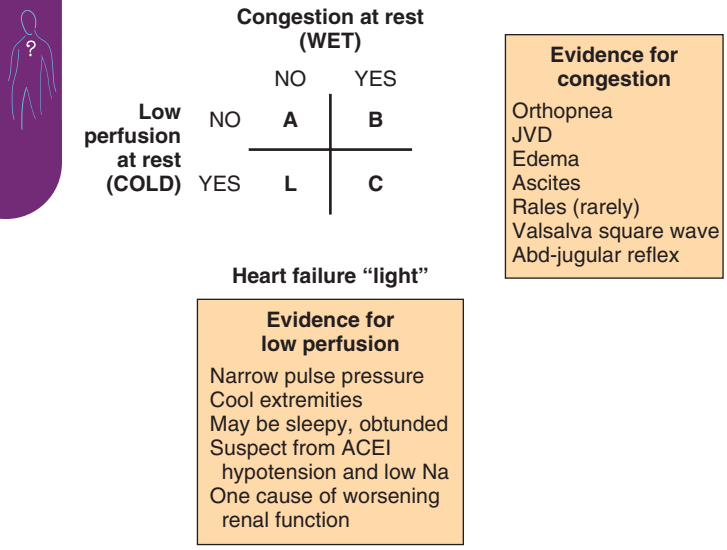

FIGURE 5-7 Diagram of a 2×2 table of hemodynamic profiles for patients with heart failure. Most patients can be classified in a 2-minute bedside assessment according to the signs and symptoms shown, although in practice, some patients may be on the border between the warm-and-wet and cold-and-wet profiles. The classification helps guide initial therapy and prognosis for patients with advanced heart failure. Most patients with hypoperfusion also have elevated filling pressures (i.e., cold and wet profile). Patients with symptoms of heart failure at rest or minimal exertion without clinical evidence of elevated filling pressures or hypoperfusion (i.e., warm and dry profile) should be carefully evaluated to determine whether their symptoms result from heart failure. A, Warm and dry profile; Abd, abdominal; ACEI, angiotensin-converting enzyme inhibitor; B, warm and wet profile; C, cold and wet profile; JVD, jugular venous distention; L, cold and dry profile; Na, serum sodium. (Modified from Nohria A, Lewis E, Stevenson LW: Medical management of advanced heart failure, JAMA 287:628–640, 2002.)

TABLE 5-3 PRECIPITANTS OF HEART FAILURE

Dietary (sodium and fluid) indiscretion
Noncompliance with medications
Development of cardiac arrhythmia
Anemia
Uncontrolled hypertension
Superimposed medical illness (pneumonia, renal dysfunction)
New cardiac abnormality (acute ischemia, acute valvular insufficiency)

patient symptom reports, and there was no significant change in renal function.

If a patient remains volume overloaded and does not adequately respond to loop diuretic monotherapy, adding additional agents (i.e., metolazone, thiazide diuretics, carbonic anhydrase inhibitors, aldosterone receptor blocker, and arginine vasopressin blockers) that block reabsorption at other locations in the nephron may provide adequate diuresis, an approach called *sequential nephron blockade*. This strategy is particularly useful for patients with intrinsic renal dysfunction or significant hyponatremia due to volume overload.

Angiotensin-Converting Enzyme Inhibitors and Angiotensin Receptor Blockers

ACE inhibitors and angiotensin receptor blockers (ARBs) inhibit the RAAS and reduce afterload primarily by vasodilation. Both drug classes have an excellent safety profile and significant morbidity and mortality benefits for symptomatic and asymptomatic LV dysfunction with or without coronary artery disease. On a cellular level, ACE inhibitors slow the progression of cardiovascular disease by multiple pleiotropic effects, including improved endothelial function; antiproliferative effects on smooth muscle cells, neutrophils, and monocytes; and antithrombotic effects. Meta-analyses suggest a 23% reduction in mortality and a 35% reduction in the combination end point of mortality and hospitalizations for HF among patients treated with ACEI inhibitors.

ACE inhibitors should be avoided in pregnant patients, patients considering pregnancy, and patients with a history of angioedema. The major side effect of ACE inhibitors is a persistent dry cough, which occurs in up to 20% of patients and is related to increased bradykinin levels associated with ACE inhibitor use. Other possible side effects include hypotension, hyperkalemia, and azotemia. Renal function and potassium levels should be checked 1 week after initiation and after dose titration.

ARBs prevent the binding of angiotensin II to its receptor, which decreases the release of bradykinin. ARBs should be reserved for patients who proved to be ACE inhibitor intolerant, primarily because of cough. Angioedema occurs in less than 1%.

β-Blockers

Historically, β-blockers were considered contraindicated in HF for many years due to the reliance on sympathetic tone to maintain adequate cardiac output and end-organ perfusion. Because unopposed adrenergic stimulation was ultimately found to be deleterious to the myocardium, β-blockers were introduced into clinical practice. The beneficial effects were thought to result from decreasing heart rate, β-receptor upregulation, altered myocardial metabolism, improved calcium transport, inhibition of the RAAS, improvement in endothelial dysfunction, and decreased levels of circulating cytokines.

The three approved β-blockers used in HF are metoprolol succinate, carvedilol, and bisoprolol. The estimated reduction in all-cause mortality in the Metoprolol CR/XL Randomised Intervention Trial in Congestive Heart Failure (MERIT-HF), Carvedilol Post-Infarct Survival Control in Left Ventricular Dysfunction Study (CAPRICORN), Carvedilol Prospective Randomized Cumulative Survival (COPERNICUS), and Cardiac Insufficiency Bisoprolol Study II (CIBIS-II) trials was approximately 35%. These effects largely result from prevention of sudden cardiac death through mechanisms inhibiting the adrenergic pathway and its deleterious effects.

Long-term treatment with β-blockers can lessen the symptoms of HF, improve the patient's clinical status, and improve the overall sense of well-being. β-Blockers should be withheld from patients with markedly decompensated acute HF until they are clinically stable, because the drugs are negatively chronotropic and acutely result in diminished cardiac output. β-Blockers should be titrated to the maximum doses achieved in clinical trials because they have been proved to improve LVEF and reduce or reverse the degree of negative LV remodeling.