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## You can do more to slow the progression of heart failure

Don't hesitate to urge patients to exercise—or to treat their hypertension with a streamlined 4-step approach.

### Practice recommendations

- Use B-type natriuretic peptide (BNP) levels as an aid not only in the diagnosis of heart failure (HF), but to track its progression as well (A).
- Prescribe exercise training for patients with stable heart failure; exercising at 40% to 70% of maximum capacity for 20 to 45 minutes several times a week offers benefits on par with pharmacotherapy (A).
- Consider using the Simplified Treatment Intervention to Control Hypertension (STITCH) algorithm for hypertensive patients or those who are at risk of developing HF; this step-care strategy is effective in treating hypertension, a leading cause of HF (C).
- Consult a specialist before prescribing both an angiotensin-converting enzyme (ACE) inhibitor and an angiotensin receptor blocker (ARB) for a patient with advanced HF; studies of combination therapy for this patient population have had mixed results (C).

#### Strength of recommendation (SOR)

A Good-quality patient-oriented evidence

B Inconsistent or limited-quality patient-oriented evidence

C Consensus, usual practice, opinion, disease-oriented evidence, case series

Family physicians are all too familiar with heart failure (HF). This debilitating condition accounts for approximately 3.4 million outpatient visits to US physicians annually,<sup>1</sup> and fully two-thirds of HF patients are cared for by primary care physicians.<sup>2</sup>

A host of comorbid conditions—coronary artery disease, valvular heart disease, diabetes, dyslipidemia, metabolic syndrome, obesity, chronic renal insufficiency, and hypertension chief among them—contribute to the development of HF.<sup>3</sup> Of these, hypertension is the most important factor. In more than 75% of cases, high blood pressure precedes HF,<sup>1</sup> and an individual's lifetime risk of developing HF is strongly associated with poor blood pressure control.<sup>4</sup> Hypertension is the most significant controllable factor in the management of HF as well. Because of the nexus between hypertension and HF, we encourage physicians to think of these 2 conditions as a single entity—and to recognize that a reduction of even a few millimeters of mercury can have huge clinical benefits.

This review, which highlights a recently tested hypertension algorithm along with other recent developments and long-established treatment strategies, will help you do everything possible to slow the progression of this debilitating and deadly disease.

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Author Randy Wexler describes STITCH in greater detail at [www.jfponline.com](http://www.jfponline.com)

## ■ BNP's increasing role in evaluating heart failure

A diagnosis of HF in patients with known heart disease is based on functionality and symptoms, assessed with the help of 2 classification schemes<sup>5,6</sup> (TABLE 1) and a variety of tests. (Patients who present with the signs and symptoms of HF but no evidence of the comorbid conditions typically associated with it should be screened for other, noncardiac causes—human immunodeficiency virus, hepatitis C, hemochromatosis, hypothyroidism, and substance abuse among them.<sup>6</sup>)

**Diagnostic testing.** Baseline serum chemistries include a complete blood count, urinalysis, electrolytes, magnesium, blood urea nitrogen, creatinine, and blood glucose levels, and liver and thyroid function tests.

**B-type natriuretic peptide (BNP)**, a homeostatic marker secreted by the heart in an attempt to maintain stable blood pressure and plasma volume and avoid fluid retention, is increasingly recognized as an important aid, not only in diagnosing HF but in gauging its severity, managing symptoms, and determining the prognosis.<sup>7,8</sup> BNP concentrations <80 pg/mL have been found to have a negative predictive value of 98%, and are also highly sensitive (98%) and specific (98%) for the diagnosis of HF.<sup>9,10</sup>

Testing may also include a 12-lead electrocardiogram as well as a posterior-anterior/lateral chest x-ray. Echocardiography is often used to evaluate left ventricular function and ejection fraction<sup>6</sup>—a key to establishing whether the patient has systolic (reduced ejection fraction) or diastolic (preserved ejection fraction) HF.

An ejection fraction ≤40% is characteristic of systolic HF, which affects approximately 60% of patients with heart failure<sup>11</sup> and is the focus of the following discussion of treatments.

## ■ Early interventions: Get patients moving

For all patients with stable HF—and those

TABLE 1

### Classifying heart failure: 2 systems

#### NEW YORK HEART ASSOCIATION

**Class I:** No limitation of physical activity; ordinary activity does not cause undue fatigue or dyspnea.

**Class II:** Slight limitation of activity; comfortable at rest, but ordinary physical activity results in fatigue or dyspnea.

**Class III:** Marked limitation in activity.

**Class IV:** Unable to carry on any physical activity without symptoms; symptoms present even at rest.

#### AMERICAN COLLEGE OF CARDIOLOGY/ AMERICAN HEART ASSOCIATION

**Stage A:** Conditions strongly associated with heart failure (HF); at high risk of HF.

No identified structural or functional abnormalities of the pericardium, myocardium, or cardiac valves; no signs or symptoms of HF.

**Stage B:** Structural heart disease strongly associated with HF, but no known signs or symptoms.

**Stage C:** Current or prior symptoms of HF associated with underlying structural heart disease.

**Stage D:** Advanced structural heart disease, with marked symptoms of HF at rest despite maximal medical therapy. Specialized interventions required.

**Sources:** Criteria Committee of the New York Heart Association. *Diseases of the Heart and Blood Vessels—Nomenclature and Criteria for Diagnosis*. 6th ed. 1964;<sup>5</sup> Hunt et al. *Circulation*. 2005.<sup>6</sup>

at high risk of developing it—behavioral modification is a key component of treatment. Lifestyle intervention should be directed at weight loss and diet, including control of salt intake; increased physical activity; and smoking cessation.

**Don't shy away from exercise.** Although many physicians hesitate to prescribe exercise to patients with HF, physical activity should be a routine recommendation for all but the most debilitated patients.<sup>6</sup> Regular exercise has been shown to decrease symptoms, increase functional capacity, and improve the quality of life, with benefits comparable to those of pharmacotherapy.<sup>6,12,13</sup>

Studies of the beneficial effects of

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**Hypertension precedes the development of HF more than 75% of the time.**

exercise were based on sustaining 40% to 70% of maximum capacity for 20 to 45 minutes, 3 to 5 days a week.<sup>6</sup> A good walking program—of at least 30 minutes 4 to 5 days each week—should not be difficult for patients to maintain.

### ■ **BP treatment guidelines: The old and the new**

As noted earlier, controlling hypertension is crucial, not only to prevent HF but to attenuate its progress. But blood pressure management is suboptimal in the United States, with many patients failing to achieve recommended levels of pressure reduction. It's been suggested that the complexity of standard treatment guidelines may be part of the problem.

**STITCH step care is a newer option.** Researchers designed the Simplified Treatment Intervention to Control Hypertension (STITCH) Trial, a cluster randomized study of patients at multiple family medicine clinics in Canada, to evaluate whether a simplified step-care algorithm would yield better results.

The STITCH algorithm has 4 treatment steps:

**Step 1:** Initiate therapy by pairing a diuretic with either an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin receptor blocker (ARB).

**Step 2:** Increase combination therapy to the highest dose tolerated.

**Step 3:** Add a calcium channel blocker and increase to the highest tolerated dose.

**Step 4:** Add a non-first-line antihypertensive agent (alpha-blocker, beta-blocker, or spironolactone).

Researchers found that after 6 months, 64.7% of patients on the STITCH protocol had achieved target blood pressure, compared with 52.7% of those whose treatment was based on the Canadian Hypertension Education Program (CHEP) guidelines ( $P=.03$ ).<sup>14</sup> The CHEP protocol is similar to that of the Seventh Report of the Joint National Committee on Prevention, Detection,

Evaluation, and Treatment of High Blood Pressure (JNC 7);<sup>15</sup> both offer numerous options for initial treatment.<sup>16</sup>

In presenting the STITCH results at the 2007 annual meeting of the American Heart Association, the lead author described the use of a simple step-care approach as “an important way forward in the treatment of hypertension [which] may be a paradigm for managing a range of chronic diseases.”<sup>16</sup> Yet the STITCH algorithm has yet to be widely embraced; outside of the research community, most US physicians are relying on the JNC 7 guidelines.

**ACC/AHA recommendations** indicate that for patients at stage A—that is, those with conditions strongly associated with, and at high risk for, HF—management of hypertension should conform to national standards such as JNC 7. The JNC 7 guidelines recommend the use of a thiazide diuretic as the initial drug of choice for patients with essential hypertension. For those with diabetes, ACE inhibitors and ARBs are the first-line antihypertensive agents of choice.

Glucose control is also essential for stage A patients with diabetes. Treatment of lipid disorders and pharmacotherapy for metabolic syndrome are also recommended for stage A patients, as needed.

### ■ **Treatment escalates as HF progresses**

ACE inhibitors, ARBs, and beta-blockers are the preferred pharmacologic interventions for patients at stage B—those who have structural heart disease strongly associated with HF but are not yet symptomatic. Anyone who has had a myocardial infarction (MI) should be started on a beta-blocker and an ACE inhibitor, ACC/AHA recommends, unless a contraindication exists.<sup>6</sup> Similarly, any patient with a reduced ejection fraction should be started on an ACE inhibitor regardless of symptoms.<sup>6</sup>

The Heart Outcomes Prevention



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**Diagnostic testing for HF may include a 12-lead electrocardiogram, echocardiography, and a posterior-anterior/lateral chest x-ray.**

**TABLE 2**

**Treating heart failure: How the different drugs and devices rate**

STAGE	PHARMACOTHERAPY	LOE	DEVICE/INTERVENTION	LOE
A	Treat BP per JNC 7 ACE inhibitor or ARB for patients with vascular disease or diabetes	A	None	N/A
B	ACE inhibitor or ARB BB	A	None	N/A
C	<i>Routine use:</i> Diuretics ACE inhibitor BB <i>Select use:</i> Aldosterone antagonist ARB Digitalis	A	<i>Consider:</i> Biventricular pacer or ICD or both	B
D	Same as C	B	<i>Consider:</i> Heart transplant or LVAD; experimental protocols	C

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BB, beta-blocker; BP, blood pressure; ICD, implantable cardioverter defibrillator; JNC 7, the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; LOE, level of evidence; LVAD, left ventricular assist device.

Adapted from: Hunt SA, et al. *Circulation*. 2005.<sup>6</sup>

Evaluation (HOPE) study demonstrated a 23% relative risk (RR) reduction with the use of an ACE inhibitor in patients with coronary artery disease, peripheral vascular disease, or diabetes, compared with patients receiving a placebo.<sup>17</sup> The importance of a beta-blocker was established in a subanalysis of the Survival and Ventricular Enlargement Trial (SAVE), which found that patients taking beta-blockers in addition to an ACE inhibitor had a 32% RR reduction in progression of HF, compared with patients on an ACE inhibitor alone.<sup>18</sup>

We recommend an ACE inhibitor or an ARB and a beta-blocker, when appropriate, to slow the progression of HF pathophysiology. It is important to be aware of the potential adverse effects of certain beta-blockers in patients with HF. Only 3 beta-blockers are approved for use in this patient population in the United States—bisoprolol, carvedilol, and metoprolol succinate, which have been found to provide benefits that other beta-blockers do not.<sup>6,15</sup>

**Stages C and D: Tx considerations and controversies**

Treatment for patients at stage C should include all components of therapy for patients at stages A and B, but with a more aggressive use of pharmacotherapy (TABLE 2). Patients with stage C HF, by definition, are symptomatic, and the ACC/AHA recommendations reflect concern about their increasingly compromised status. Thus, in addition to the use of ACE inhibitors or ARBs and beta-blockers, modest use of diuretics is recommended, as needed, for fluid volume control.<sup>6</sup> Diuretics should be used judiciously, though, with ongoing evaluation to avoid the excessive loss of potassium and magnesium, which can lead to volume depletion and lethal arrhythmias. Limiting sodium consumption is an important dietary restriction for stage C patients.

**Aldosterone antagonists may also be considered** on a case-by-case basis for patients with stage C HF. Due to their potassium-sparing effects, aldosterone

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**Only 3 beta-blockers are approved for use in patients with HF in the United States: bisoprolol, carvedilol, and metoprolol succinate.**

antagonists, used in conjunction with standard therapies, may have a positive effect on electrolyte balance. Potassium levels must be carefully monitored, however, and potassium supplementation reevaluated for patients who are put on an aldosterone antagonist.<sup>19</sup>

**Digitalis may also be helpful** in select patients who remain symptomatic despite maximal pharmacotherapy.<sup>20</sup> While it does not affect mortality, digitalis has been shown to reduce hospitalizations.<sup>21</sup>

**ACE inhibitor-ARB combination therapy**, another possible treatment for advanced HF, remains controversial. The Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial (ONTARGET), detailed in “ACE inhibitors and ARBs: One or the other—not both” in the January 2009 issue of *The Journal of Family Practice*, evaluated use of this dual therapy; the trial was also designed to determine whether telmisartan (an ARB) is inferior to ramipril (an ACE inhibitor) in patients at high risk for vascular events.<sup>22</sup> The researchers found that telmisartan is not, in fact, inferior to ramipril, and reported that for patients with HF, an ACE-ARB combination offers a potential benefit.

However, the clinical benefit of an ACE-ARB combination in this patient population was not clarified in this study, and may be potentially harmful. In the Valsartan Heart Failure Trial (ValHeFT), the combination of valsartan, an ARB, and an ACE inhibitor decreased hospitalizations but did not improve mortality.<sup>23</sup> Indeed, an increase in mortality was found when an ACE-ARB combination was used in conjunction with beta-blockers. Because beta-blockers are indicated for routine use in patients with HF, this finding was of particular concern.

In a meta-analysis of randomized trials using both an ACE inhibitor and an ARB in patients with left ventricular dysfunction, researchers found a “marked”

increase in adverse effects, including deteriorating renal function (RR=2.17), hyperkalemia (RR=4.87), and symptomatic hypotension (RR=1.05).<sup>24</sup> Although an ACE-ARB combination may benefit a subset of patients with HF, it is best to initiate such treatment only with the guidance of an HF specialist.

## ■ Beyond drug therapy: Assistive devices

Refractory end-stage HF requires a clear treatment plan, and should involve the recommendations of an HF specialist. Careful maintenance of fluid status is required, and an evaluation for cardiac transplantation may be considered.

**A left ventricular assist device (LVAD)** should also be considered for patients with an estimated 1-year mortality of >50%.<sup>6</sup> LVADs are mechanical heart pumps that were initially utilized as a “bridge” to transplant, but are increasingly being used as a palliative alternative for severely ill patients.<sup>25</sup>

Other devices—an **implantable cardioverter defibrillator (ICD)** or a **biventricular pacemaker**—should also be considered for patients at stage D, as well as stage C patients who are at increased risk of sudden death despite maximal drug therapy.<sup>6</sup> Patients who have had a previous MI or ventricular arrhythmia are at risk for a repeat episode.<sup>6</sup>

Use of an ICD can reduce mortality by 23% in selected patients.<sup>26</sup> Potential candidates for the device are patients who have an ejection fraction of <30%, mild to moderate symptoms, and a life expectancy of at least 1 year.<sup>6</sup>

Biventricular pacing, also known as **cardiac resynchronization therapy (CRT)**, has been found to improve the quality of life, functional status, and exercise capacity in some patients with advanced disease. CRT, which reduces symptoms of HF and improves cardiac function by reestablishing the mechanical sequence of ventricular activation and ventricular contraction, has also

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**Patients treated with the STITCH algorithm were significantly more likely to reach target blood pressure than patients whose treatment was based on national guidelines.**

been associated with reductions in hospitalization and death from progressive HF.<sup>27,28</sup>

The Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) trial demonstrated a 20% reduction in the 12-month risk of death or hospitalization from any cause with CRT, and the Cardiac Resynchronization-Heart Failure (CARE-HF) trial established that patients receiving CRT had a significantly lower risk of death than those receiving medical therapy alone (40% reduction).<sup>29,30</sup>

However, not all patients with HF have problems with conduction delay that result in a dyssynchronous heart beat. CRT is indicated only for patients who are in sinus rhythm and have:

- NYHA class III or IV HF
- an ejection fraction of <35%
- a prolonged QRS complex (>120 m/sec), and
- continued symptoms despite maximal medical therapy.<sup>6</sup>

Under these criteria, approximately 10% of patients with HF would qualify for CRT.<sup>31</sup> The restrictive criteria are due, in part, to the fact that this modality is relatively new and has been studied only in a small subset of patients.

## ■ Options for patients who are running out of them

For acutely decompensated hospitalized patients with volume overload, **ultrafiltration (UF)** is a useful alternative to diuretics. UF uses high pressure to “force” volume through the kidneys;<sup>32,33</sup> the technique maximizes diuresis, and is best suited for patients who have significant renal dysfunction or are not responding to standard diuretic therapy. UF makes it easier to remove the desired amount of fluid, and has a positive impact on pulmonary wedge pressure and cardiac output.<sup>34</sup> Its use in diuretic-resistant patients can decrease the length of stay and produce positive clinical benefits that may last up to 3 months.<sup>34</sup>

There are also a number of experimental strategies, surgical and otherwise. Among them are:

**Cardiac wrap surgery**, in which the heart is encased in a mesh bag attached with stitches, in an attempt to stop the progression of end-stage HF by preventing further dilation;<sup>25</sup>

**Ventricular restoration surgery**, a procedure in which scar tissue caused by MI is removed from the ventricular muscle and the left ventricle is reshaped and its size reduced in an attempt to restore some of the heart’s pumping ability;<sup>25</sup> and

**Enhanced external counterpulsation**, or EECp, a noninvasive technique in which pressure cuffs are placed on the calves, thighs, and buttocks and inflated and deflated in an attempt to increase blood flow back to the heart.<sup>25</sup> ■

### Disclosures

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**The use of ultrafiltration in diuretic-resistant patients can produce clinical benefits that may last up to 3 months.**