Heart Failure’s Dark Secret
Does Anyone Really Care About Optimal Medical Therapy?

Today, most heart failure physicians focus on devices and transplantation; hospital-based management teams devoted only to achieving optimal medical therapy are scarce. The financial demands on heart failure specialists are enormous. A viable business plan can no longer be based on the misguided hope that payers will reimburse generously for prescriptions of digitalis and diuretics; in contrast, cardiac procedures generate meaningful revenues. A growing advocacy now encourages the use of ventricular assist devices in ambulatory patients on the basis of the dual misconceptions that the hazards are readily managed and that the clinical responses to medical therapy are poor. The biases in favor of performing procedures are so great that a National Institutes of Health–sponsored randomized trial comparing left ventricular assistance and optimal medical therapy in ambulatory patients was closed because of slow recruitment.

In its place, a nonrandomized study of 200 patients (ROADMAP [Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management]) was carried out and reported major advantages in patients who chose to receive a left ventricular assist device compared with those who chose to receive optimal medical management. The numerous limitations of the study are beyond the scope of this article, but it is intriguing that the authors failed to identify optimal medical therapy. Patients not electing a device were prescribed guideline-based treatments, but strangely, the authors do not tell us about the doses of renin-angiotensin inhibitors or β-blockers, the use (if any) of aldosterone antagonists or digoxin, or efforts to titrate diuretics to achieve euvolemia. We are not informed of the patients’ systolic blood pressures, but we are told that their cardiac filling pressures and natriuretic peptide levels were increased. However, larger doses of diuretics were not used, although the patients had preserved renal function. We know that the patients who received a left ventricular assist device were treated by heart failure specialists, but we do not know who directed medical therapy in the patients who did not undergo a procedure.

What is optimal medical therapy for heart failure in 2016? Some think that the answer lies in guidelines documents, but guidelines do not define to what degree a patient’s medical therapy can vary from the target doses used in clinical trials and still be considered adequate. How should we view the use of low doses ofvalsartan or carvedilol once daily if a physician fears (but has not demonstrated) that the patient might not tolerate more intense regimens? What asymptomatic level of systolic blood pressure or azotemia should lead a physician to stop uptitration of a diuretic or an inhibitor of the renin-angiotensin system? What are the valid reasons for not prescribing a β-blocker at the target doses shown to be effective in clinical trials? Why do physicians avoid the use of digoxin, although this inexpensive drug safely reduces the risk of hospitalizations? Perhaps the patients in the ROADMAP study received optimal medical therapy, but how would we know? We do know that a large number received implantable defibrillators and cardiac resynchronization devices.

The Table provides my personal view of pharmacological therapy for heart failure in 2016. I define inadequate as commonly prescribed but without supporting evidence.
from clinical trials, and I consider adequate to be identical to optimal. After all, how can the use of an angiotensinconverting enzyme inhibitor (even at target doses) be considered adequate if we know that patients live longer on an angiotensin receptor neprilysin inhibitor? Many readers might challenge specific suggestions, but doing so would miss my point entirely. If people want to test or propose a new treatment or device as superior to optimal medical therapy, we should expect them to document how assiduous the attempts were to achieve the targets described in the Table (or some alternative targets).

Thirty years ago, cardiologists were expected to be experts in the use of antianginal drugs. Patients who had exertional angina were treated with maximally tolerated combinations of nitrates, β-blockers, and calcium channel blockers. Interventional coronary revascularization procedures were offered primarily to those who remained disabled on optimal medical therapy. The battle between the use of drugs and procedures raged for years because we had no reliable data that either intervention did anything except relieve symptoms. However, in 2016, everyone with obstructive coronary artery disease is considered for an interventional procedure, whether he or she has angina or not. This enthusiasm has been prompted by outcomes data and potentially by revenue considerations. Today, there seems to be little interest in prescribing adequate antianginal drug therapy; new antianginal agents (eg, ranolazine) wither from lack of use. However, in 2016, everyone with obstructive coronary artery disease is considered for an interventional procedure, whether he or she has angina or not. This enthusiasm has been prompted by outcomes data and potentially by revenue considerations. Today, there seems to be little interest in prescribing adequate antianginal drug therapy; new antianginal agents (eg, ranolazine) wither from lack of use. Similarly, procedures are routinely preferred to drugs in the management of patients with serious cardiac arrhythmias because pharmacological approaches have so often failed to provide meaningful clinical benefits.

Table. Different Approaches to Defining Pharmacologic Therapy for Ambulatory Patients With Chronic Heart Failure and Reduced Ejection Fraction

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Commonly Prescribed But Inadequate Regimen</th>
<th>Adequate Regimen Based on Target Interventions in Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diuretic</td>
<td>Furosemide 40 mg orally once daily in a patient with fluid retention and without azotemia</td>
<td>Diuretic (≥1) titrated to achieve euvolemia, defined at the bedside or with the use of a pulmonary artery sensor in appropriate patients</td>
</tr>
<tr>
<td>Inhibitor of the renin-angiotensin system</td>
<td>Once daily dosing with low doses of a twice-daily angiotensin receptor blocker</td>
<td>Target doses of an angiotensin receptor neprilysin inhibitor shown to be effective in clinical trials</td>
</tr>
<tr>
<td>Inhibitor of the sympathetic nervous system</td>
<td>Metoprolol tartrate 25 mg twice daily</td>
<td>Carvedilol 25 mg twice daily</td>
</tr>
<tr>
<td>Mineralocorticoid receptor antagonist</td>
<td>No use</td>
<td>Spironolactone 25 mg or eplerenone 50 mg daily</td>
</tr>
<tr>
<td>Direct-acting vasodilator</td>
<td>Intermittent use of low doses of nitrates</td>
<td>No use or target doses of isosorbide dinitrate and hydralazine in appropriate patients</td>
</tr>
<tr>
<td>Additional neurohormonal or heart rate modulation</td>
<td>None</td>
<td>Low doses of digoxin, target doses of ivabradine in patients with a heart rate &gt;70 bpm who are demonstrably intolerant of more intensive β-blockade</td>
</tr>
</tbody>
</table>

for heart failure that reduce morbidity and mortality seem little deterred by the incalculable expense of death and the unreasonable financial and medical costs of ventricular assist devices. This seems inexplicable because, in striking contrast to our history with antianginal and antiarrhythmic drugs, optimal medical therapy in patients with heart failure actually modifies the clinical course of the disease. Annual mortality rates in patients with mild to moderate symptoms and normal renal function have now dipped to <5%.

We say we care about the pathophysiological mechanisms of heart failure, and we claim to value the work of our basic science colleagues who are seeking to understand the molecular basis of disease progression. However, will their discoveries ever amount to anything? We now live in a world in which, when something is broken, we prefer to replace or circumvent it rather than to understand what went wrong and to direct therapies to the underlying pathophysiological processes. That is what has happened to our patients with coronary artery disease and serious cardiac arrhythmias. Is that what will happen to our patients with heart failure, although we can save their lives with drugs?

DISCLOSURES

Dr Packer has consulted for Admittance, Amgen, AstraZeneca, Bayer, BioControl, Boehringer Ingelheim, Boston Scientific, Celldyn, Cardiorentis, Daiichi Sankyo, GlaxoSmithKline, Novartis, NovoNordisk, Takeda, and ZS Pharma.

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FOOTNOTES

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REFERENCES


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