Medical Therapy Urged in Advanced Heart Failure

Available drug treatments can save the life of one in four patients receiving them, one expert says.

BY DOUG BRUNK
San Diego Bureau

SAN DIEGO — With no medical therapy, patients with stage C and D heart failure face a 2-year mortality risk of 35%, Lee Goldberg, M.D., said at the 100th International Conference of the American Thoracic Society.

But clinicians can reduce the 2-year mortality in this population of patients by 12%-24% if they treat patients with the available medical therapies.

"The number needed to treat to save one life is four patients," said Dr. Goldberg of the heart failure/transplant program at the University of Pennsylvania Health System, Philadelphia.

"So it's extremely cost effective to treat heart failure patients. Many of the medical therapies we have are underutilized—especially in patients who are less symptomatic," Dr. Goldberg said.

He reviewed the following treatments, commonly used in patients with stage C and D heart failure:

► **Diuretics.** Although there are no clinical trial data proving their efficacy in this patient population, diuretics are the most commonly prescribed drugs for patients with advanced heart failure.

"But we know from epidemiologic data that diuretics don't change the natural history of heart failure," Dr. Goldberg said. "Morbidity and mortality after taking them doesn't change very much."

Loop diuretics are the most commonly used type, although many centers use thiazide diuretics in combination to augment the effects of loop diuretics.

"I would titrate to signs and symptoms of volume overload," he advised. "Many disease management programs have action plans of sliding-scale diuretics to help patients control their volume status. It keeps them out of the hospital and keeps them safe, but it doesn't prolong their life, and it doesn't change the [heart] remodeling process."

The symptomatic benefits of diuretics occur more rapidly than those of other drugs, and diuretics are the only class of drugs that adequately control chronic fluid retention. Adverse effects may include volume depletion and renal insufficiency. Metabolic effects may include electrolyte imbalance, hyperuricemia, and hyperglycemia.

There are lingering questions about this approach, however: Will newer agents replace the loop diuretics? Which are the best combinations? "These questions still need to be studied," he said.

► **ACE inhibitors.** There are "buckets of data" on the use of these agents in advanced heart failure. ACE inhibitors interfere with the renin-angiotensin system and enhance the action of kinins. "They alleviate symptoms, reduce death, and reduce hospitalizations," Dr. Goldberg said. "So they hit all three of our goals [in treating these patients]: heart remodeling, symptoms, and mortality."

These drugs are typically given to all patients with systolic dysfunction. "A lot of people believe they should also be used in diastolic dysfunction, but we don't have good data for that yet," he said.

Adverse effects may include hypotension, azotemia, hyperkalemia, cough, and angioedema. Unanswered questions include whether there is a class effect. "The answer is probably yes," he said. Also, it is not known whether there is a significant interaction with aspirin. "Most of us are comfortable using both aspirin and ACE inhibitors," said Dr. Goldberg, also of the University of Pennsylvania.

► **β-Blockers.** These drugs inhibit the adverse effects of the sympathetic system, and they delay and reverse heart remodeling. "The No. 1 way to increase the ejection fraction in patients with heart failure is to actually put them on a β-blocker," Dr. Goldberg said.

β-Blockers are currently given to all patients with systolic heart failure in the absence of fluid overload. Adverse effects may include hypotension, bradycardia, and worsening heart failure.

ACE inhibitors 'hit all three of our goals: heart remodeling, symptoms, and mortality.'

DR. GOLDBERG

The ideal target dose for β-blockers has not been determined. This is one remaining question about this class of drugs. "There is probably not a class effect," he said. "It appears that the long-acting β-blockers and nonselective β-blockers may have an advantage over the shorter-acting and selective ones."

► **Angiotensin II receptor blockers.** These drugs block the effect of angiotensin II at the receptor site. They delay heart remodeling and reduce symptoms, and they have been shown to reduce hospitalizations and deaths.

ARBs are currently given to patients who can't tolerate ACE inhibitors—specifically, the side effects of angioedema and cough.

The Valsartan Heart Failure Trial (Val-HeFT) and the Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity (CHARM) trial showed some improvement in the efficacy of ARBs when used with ACE inhibitors. However, patients in the Val-HeFT trial who took ARBs with an ACE inhibitor and a β-blocker had worse outcomes. This association was not found in the CHARM trial.

Adverse effects may include hypotension, azotemia, hyperkalemia, and cough.

Will ARBs ever replace ACE inhibitors? That's a key question about this class of drugs, Dr. Goldberg said.

► **Digoxin.** This drug has no impact on mortality, but it does appear to improve symptoms. Dr. Goldberg cautioned that digoxin carries a high risk of renal insufficiency and an increased risk of drug interactions. "Therefore, we limit the use of digoxin only to patients with symptomatic heart failure," he said.

He recommends using the lowest possible dose of the drug and maintaining drug levels below 1.0 ng/mL.

A recent study of heart failure patients found that digoxin had no effect on quality of life, compared with placebo, in terms of perceived health, physical functioning, depression, anxiety, anger, and the 6-minute walk test (J. Card. Fail. 2003;9:4-12).

► **Aldosterone antagonists.** Trials of these agents show improved mortality for class IIIB or class IV patients, but not in heart failure patients with less severe disease, Dr. Goldberg said.

The role of these drugs with β-blockers is not well defined, and they are contraindicated if patients are on both an ACE inhibitor and an ARB due to a risk of hyperkalemia.

► **Nitrates.** The Vasodilator-Heart Failure Trial (V-HeFT) demonstrated that nitrates in combination with hydralazine are not as effective as ACE inhibitors, yet they are better than placebo.

The African-American Heart Failure Trial (A-HeFT) showed that nitrates and hydralazine improved mortality when used with ACE inhibitors and β-blockers, but their value when added to traditional therapy is unknown in other racial groups. ■

LVAD Users Can Have Unrelated Surgery Without Complications

WASHINGTON — Patients with left ventricular assist devices who undergo surgery that is unrelated to their device can safely manage the operation without device complications, according to results achieved at a single center.

The likelihood that a patient with a left ventricular assist device (LVAD) will require surgery unrelated to the LVAD is increasing as a result of growing clinical experience with such devices, the development of longer-lasting LVADs, and growth in indications for permanent devices, Devin M. Nelson said during a moderated poster session at the annual conference of the American Society for Artificial Internal Organs.

A total of 16 patients underwent 24 surgical procedures during 1998-2005 at LDS Hospital, Salt Lake City, without any deaths or complications related to the LVAD. Five patients underwent more than one surgery on separate occasions, and two of the patients had two procedures performed during the same surgical session, Mr. Nelson reported.

Most (86%) of the surgical sessions occurred after the patient's hospital discharge for LVAD implantation. LVADs supported the patients for a range of 9-1,511 days before surgery and continued to do so for range of 21-991 days after surgery, said Mr. Nelson, a bioengineering research assistant with the Utah Artificial Heart Program at the hospital.

The most common surgical procedures included hernia repair (five), excision of melanoma (three), cholecystectomy (three), and lower limb amputation (three).

A trained mechanical circulatory support member attended each surgery to monitor the function of the LVAD. All surgeries also involved a cardiac anesthesiologist.

—Jeff Evans

Low Body Temperature Linked to Increased Mortality in Heart Failure

WASHINGTON — Body temperature below 36° C at hospital admission was independently associated with a lower survival rate in a study of 56,659 patients with advanced heart failure.

Disordered thermoregulation is common in patients with advanced heart failure, and body temperature measurements may improve risk assessment in these patients, Brahmajee K. Nallamothu, M.D., wrote in a poster presented at the Clinical Research 2005 meeting sponsored by the American Federation for Medical Research.

Dr. Nallamothu, a cardiologist at the University of Michigan, Ann Arbor, and his associates reviewed data on patients aged 65 years and older who were participating in the National Heart Care Project.

The mean body temperature upon hospital admission was 36.5° C, and most of the patients' admission temperatures were between 36 and 38° C. However, 10,754 (18.5%) of the patients had body temperatures below 36° C and 1,145 (1.9%) had body temperatures above 38° C.

After multivariate analysis, patients with body temperatures below 36° had significantly higher mortality, both in hospital (adjusted risk ratio, 1.28) and at 1 year after their hospitalizations (adjusted risk ratio, 1.14). Body temperatures above 38° were not significantly associated with in-hospital mortality, but they were significantly associated with lower mortality after 1 year (adjusted risk ratio, 0.80).

—Heidi Splete