

Heart Failure Society News

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In This Edition

Society News

- HFSA's Third Annual Scientific Meeting
- HFSA's Nursing Committee

ACC Highlights

- MERIT-HF Trial
- REACH Trial
- Predictors of Mortality
- Pharmacologic Therapy Roundup

HFSA's Third Annual Scientific Meeting Set for San Francisco

The HFSA's Third Annual Scientific Meeting promises 4 days packed with more than 40 sessions reviewing the latest basic science, clinical trial results, controversies, how-to sessions, and 13 satellite programs.

"It will be a very intense meeting, with a well-balanced program, with something of interest to everyone: the clinician, the nurse, and the basic science investigator," said Dr. Michael Bristow, scientific program co-chairman for the meeting, which takes place Wednesday, September 22, through Saturday, September 25, at the Hyatt Regency (Embarcadero), San Francisco.



President Arthur Feldman (left) and Michael Bristow at the 1998 HFSA Scientific Meeting

heart failure that have been investigated over a long period of time, have been confirmed, and have gone on to affect our knowledge of the treatment and natural history of the clinical syndrome," said Dr. Bristow, head of cardiology at the University of Colorado Health Sciences Center, Denver. In four State of the Science sessions, speakers will visit the cutting edge of heart failure research.

Trial Results and Debate Sessions

The meeting will also feature late-breaking results from clinical trials.

Controversial issues – such as the role of anticoagulants in patients with moderate or severe left ventricular dysfunction and the use of implantable defibrillators in high-risk patients – will

(continued on page 2)

Landmarks of Heart Failure and State of the Science

One highlight of the meeting will be its Landmarks of Heart Failure sessions. "These are concepts in

Heart Failure Society News

Editors

Arthur M. Feldman, MD, PhD
President,
Heart Failure Society of America
Director, The Cardiovascular Institute
of the UPMC Health Systems
Pittsburgh, Pennsylvania

Gary S. Francis, MD
Director, Coronary Intensive Care
Cleveland Clinic Foundation
Cleveland, Ohio

Marvin A. Konstam, MD
Chief, Division of Cardiology
New England Medical Center
Boston, Massachusetts

Marc A. Silver, MD
Professor of Medicine
Director, Heart Failure Institute
Director, Cardiovascular Disease
Fellowship Christ Hospital and
Medical Center
Oak Lawn, Illinois



Debra K. Moser

HFSA Forms Nursing Committee

Recognizing the essential role of nurses in heart failure treatment and research, the HFSA announced the formation of a nursing committee. Debra K. Moser, DNSc, RN, Associate Professor at Ohio State University and Coeditor of the *Journal of Cardiovascular Nursing*, will chair the committee.

The preliminary goals include:

- furthering the role and increasing the visibility of nursing in heart failure
- increasing funding for nurse-initiated research and nursing studies in the context of major clinical trials
- developing new initiatives in nursing research.

The selection process for members is underway. Invited members will serve for 3-year terms. The first meeting of the nursing committee will be held

at the annual HFSA meeting in San Francisco in September.

In discussing its mission, Dr. Moser said, "Nurses bring a unique perspective to the treatment of patients that complements the pharmacologic and therapeutic focus – we have a well-rounded view of the person that includes psychosocial and other aspects essential to optimizing care." ■

Society Membership Tops 1,000

Commenting on HFSA's membership recruitment drive, Dr. Marc Silver noted, "We are pleasantly surprised by the numbers. The Society now has over 1,000 members, and about 25% of those are nurses. We are especially pleased that so many nurses have joined, as they play an increasingly important role in heart failure management."

(continued on page 2)

MERIT-HF: Metoprolol Cuts Mortality 34% in Heart Failure Patients

The beta blocker metoprolol reduced annual mortality by 34% in heart failure patients followed for a mean of 2.4 years, according to Dr. Ake Hjalmarson, who presented the results of the Metoprolol CR/XL Randomized Intervention Trial in Congestive Heart Failure (MERIT-HF).

The magnitude of benefit was similar among virtually all patient subgroups, added Dr. Hjalmarson, Goteborg University, Goteborg, Sweden. Preliminary results from the double-blind placebo-controlled trial were announced last year when the trial ended early due to the highly significant reduction in mortality observed among patients receiving metoprolol.

Patient Profile

The MERIT-HF trial included 3,991 heart failure patients in Europe and the United States who were randomly assigned to either metoprolol (n=1990) or placebo (n=2001).

Patient Profile

- Average age: 64
- 77% male, 23% female
- New York Heart Association (NYHA) heart failure class:
 - Class II: 41%
 - Class III: 55%
 - Class IV: 4%
- Average ejection fraction for all patients: 28%
- Ischemia present: 65%

Dose Titration

A starting dose of 12.5 mg or 25 mg of metoprolol, determined by the treating physician, was doubled weekly as tolerated. The target dose of 200 mg once daily was achieved in 64% of patients; 87% received 100 mg a day or more. The average daily dose was 159 mg.

MERIT-HF Annual Mortality Rate (mean follow-up 2.4 years)

	Metoprolol (n=1990)	Placebo (n=2001)
Deaths	145	217
Annual Mortality Rate	7.2%	11%

All patients were also on standard heart failure therapy; 95% received an angiotensin converting enzyme (ACE) inhibitor or an angiotensin II receptor antagonist, and 90 percent were on diuretics.

There were 217 deaths among the placebo patients, for an annual mortality rate of 11%. In contrast, there were just 145 deaths among the metoprolol patients, for an annual mortality rate of 7.2%. In addition to the highly significant 34% reduction in overall mortality (p=0.0062), treatment with metoprolol led to a 38% decrease in cardiovascular mortality, a 41% decrease in sudden death, and a 49% reduction in death by progressive heart failure.

Use of Beta Blockers

Following his presentation, Dr. Hjalmarson was asked whether he thought all patients with heart failure or a low ejection fraction

should be on a beta blocker, and if so, which one? He responded that with the relatively low numbers of NYHA class IV patients in both the MERIT-HF and the CIBIS II (Cardiac Insufficiency Bisoprolol Study II), "We have wide confidence intervals and some uncertainty."

"I would say one has to be careful in that group, and we need very experienced doctors to start [beta blocker] treatment in Class IV patients," he said. "But all other patients we see as outpatients, which could be from Class I patients with left ventricular dysfunction and no symptoms up to Class III, should be given ACE inhibitors, other standard therapy, and a beta blocker."

As to the choice of beta blocker, Dr. Hjalmarson urged physicians to "focus on those drugs with proven effectiveness and that have been accepted by the authorities" and not to assume that the reductions in mortality are based on "a class effect." In a press conference he said the beta blockers metoprolol and bisoprolol, which are lipophilic, have been shown to reduce mortality, but hydrophilic beta blockers, such as atenolol, have not. Dr. Hjalmarson said there are less data on carvedilol, but with its lipophilic properties, it probably "fits in" with metoprolol and bisoprolol. ■

(continued from page 1)

HFSA's Third Annual Scientific Meeting

be addressed in two organized debates.

Return to Hyde Park

Perhaps one of the more unusual sessions will feature "Hyde Park Hypotheses" – provocative talks on a variety of issues in heart failure. The session takes its name from the Speakers' Corner tradition in Hyde Park, London, where "people get up on the soap box and expound on whatever they wish," Dr. Bristow explained.

"Heart failure has become a major disease syndrome from the standpoint of economic cost, the scientific effort directed toward solving the problems associated with it, and the critical mass of people working in this area," Dr. Bristow said. "This is a multidisciplinary meeting centered around one topic – one disease syndrome – which is somewhat unique. It really appeals

to a multilevel constituency: clinicians, nurses, and basic scientists – all of those who are interested in heart failure," he concluded.

Registration materials and the full meeting program are available by calling the HFSA at (612) 626-3864 or by visiting the Society's web site at (www.hfsa.org). ■

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(continued from page 1)

Membership

As chairman of the membership committee, Dr. Silver spearheads efforts to increase awareness about the HFSA and to boost its ranks. He said the Society has booths at the 1999 meetings of the American College of Cardiology and the American Heart Association, and it welcomes members from the Americas as well as abroad.

For an annual fee of \$95, members receive subscriptions to two society journals (plus the *Heart Failure Society News*) and discounted registrations at scientific meetings. "We also offer discounted membership and meeting registration for trainees," Dr. Silver added.

Membership applications may be downloaded from the Society's web site at www.hfsa.org. ■

Heart Failure Rising; More Cardiologists Involved in Management

The prevalence of congestive heart failure appears to be rising, as is the rate of involvement by cardiologists, according to results from the Resource Utilization Among Congestive Heart Failure Study (REACH) reported by Dr. Peter A. McCullough and colleagues at the Henry Ford Health System, Detroit, Michigan, at the March scientific session of the American College of Cardiology.

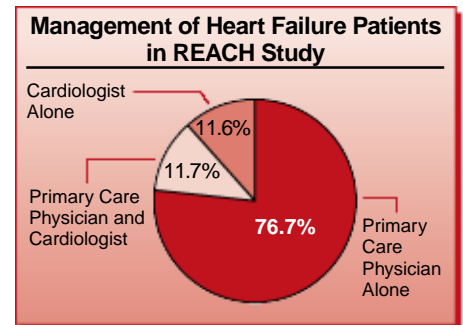
"We conclude there is an increase in the CHF prevalence pool that can be considered a chronic diseases epidemic experienced by large health systems across the U.S. today," Dr. McCullough and his colleagues said. "This calls for epidemic resource planning and management on the provider, health system, and national levels."

The investigators identified 26,442 patients with CHF from 1989-1997 from electronic medical records coded by physicians with one or more ICD-9 heart failure or related disease codes. The patients' mean age was 69.8 years; 52.3% were female and 47.7% were male.

Dr. McCullough and his colleagues found that the mean annual incidence of heart failure was 5/1000 health system patients. During the study period, however, the prevalence of heart failure rose from 9/1000 patients to 20/1000 patients ($p < 0.0000001$).

The REACH study revealed that 76.7% of heart failure patients received their treatment from primary care physicians alone. Cardiologists co-managed care in

11.7% of cases and managed care alone in 11.6% of cases. However, the investigators found a clear trend toward greater involvement by cardiologists over time ($p < 0.0001$), with increasing involvement of cardiologists in primary and consultative care "early in the individual course" of the disease. ■



Routine Clinical Parameters Predict Heart Failure Mortality

High heart rates, worsening symptoms, and poor renal function were among the clinical factors that most reliably predicted mortality in a 5-year study of 575 congestive heart failure patients, Dr. Prakash C. Deedwania and colleagues reported.

"These data indicate that routine clinical parameters provide reliable prognostic information," concluded Dr. Deedwania and colleagues of the Veterans Affairs Medical Center and University of California, San Francisco School of Medicine. "Data from additional expensive diagnostic tests add little to improve their predictive value."

The investigators examined 71 variables derived from clinical symptoms, vital signs, and biochemical tests in the 575 consecutively admitted heart failure patients

Of these patients, 174 (30%) suffered cardiac death over the study period. High heart rate emerged as the most significant predictor of death (85 ± 1 vs. 78 ± 1 bpm). Other significant predictors included worsening paroxysmal nocturnal dyspnea, worsening of symptoms, number of blocks

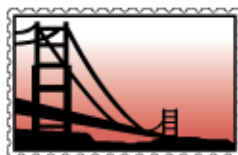
at dyspnea, and higher blood urea nitrogen (BUN), creatinine, and potassium. Left or right ventricular ejection fraction, exercise capacity, and data from Holter monitor or echocardiogram were not significant predictors of mortality. ■

Predictors of Mortality in 575 Heart Failure Patients

High Heart Rate	$p < 0.0001$
Worsening Paroxysmal Nocturnal Dyspnea	$p < 0.001$
Progression of Symptoms	$p < 0.001$
Number of Blocks at Dyspnea	$p < 0.001$
High Blood Urea Nitrogen	$p < 0.001$
High Creatinine	$p < 0.001$
High Potassium	$p < 0.001$

The Third Annual Scientific Meeting of the *Heart Failure Society of America* will be held Wednesday, September 22, through Saturday, September 25, at the Hyatt Regency (Embarcadero), San Francisco. Program and registration information may be obtained by calling the HFSA corporate office at (612) 626-3864, or the information can be downloaded from the Society's web site at www.hfsa.org.

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Heart Failure Awareness Campaign

The HFSA is developing a national program to increase public awareness of heart failure. "Despite the fact that heart failure is a disease of epidemic proportions in the United States, the lay public cannot separate heart failure from a heart attack. Most people think that patients with heart failure cannot maintain a quality of life," stated HFSA President Arthur Feldman. He announced that "In collaboration with corporate sponsors, Bozell/Kamstra advertising, and a subcommittee of the HFSA Executive Council, the Society is formulating a campaign that will increase public awareness, improve patient care, and enhance funding for research. We hope to provide additional information about this exciting new venture in forthcoming issues of *Heart Failure Society News*."

Pharmacologic Therapy Roundup

A number of promising developments in drug therapy were reported at the March meeting of the American College of Cardiology.

TNF Receptor Fusion Protein, Etanercept

Douglas L. Mann, M.D., and Guillermo Torre, M.D., Baylor College of Medicine, Houston, Texas, and Arthur Feldman, M.D., Ph.D., director of UPMC Health System Cardiovascular Institute, reported the results of a phase I trial of etanercept, a genetically engineered tumor necrosis factor (TNF) receptor fusion protein, in 47 patients with NYHA class III-IV heart failure.

Patients received 5 mg/m² (n=16) or 12 mg/m² (n=15) injections of etanercept or placebo (n=15) twice weekly for 3 months. Etanercept was well tolerated, the investigators reported, with a similar incidence of adverse events and infections in all treatment groups. Etanercept patients showed an improvement in NYHA class and quality of life over the 3-month study, with more consistent improvement at the higher dose. Sixty-seven percent of the higher-dose patients improved in NYHA class, compared to 56% of the lower-dose patients and 43% of placebo patients. The median improvement on quality-of-life scores for the higher-dose etanercept patients was 25%, compared to 19% for the lower dose patients and 10% for placebo patients. Dr. Feldman said, "We are encouraged by the initial study. [This] represents the first time that genetic engineering has been brought to bear on the problem of congestive heart failure."

Based on the positive results of this study, a large multicenter phase II/III trial of etanercept is underway. RENAISSANCE (Randomized Enbrel North American Strategy to Study Antagonism of Cytokines) will enroll more than 900 NYHA class II-IV patients throughout the United States and Canada. Patients who may qualify should contact Dr. Feldman or Virginia Schneider, R.N., nurse coordinator for the study, at (412) 647-1666 or (412) 647-6882.

Improvements in Left Ventricular Ejection Fraction in Etanercept Phase I Trial

	Improvement ≥ 5%	Improvement ≥ 10%
Placebo (n=16)	19% of patients	0% of patients
Etanercept 5 mg/m ² (n=16)	23% of patients	8% of patients
Etanercept 12 mg/m ² (n=15)	33% of patients	13% of patients

Dofetilide in Heart Failure and Post-MI

Dr. Lars Kober, Gentofte University Hospital, Hellerup, Denmark, examined the efficacy and safety of dofetilide in 506 patients with heart failure or recent myocardial infarction with impaired left ventricular function and accompanying atrial fibrillation. Patients were among a larger group of 3028 who were randomly assigned to receive dofetilide in two Danish Investigations of Arrhythmia and Mortality ON Dofetilide (DIAMOND CHF and DIAMOND MI).

Among 249 patients who received dofetilide, 73 (29.3%) were hospitalized for worsening heart failure over a median follow-up

period of 17 months. In contrast, 102 (39.6%) of 257 placebo patients were hospitalized for worsening heart failure. The risk reduction of 0.67 was significant (p<0.009). Mortality among the two groups of patients was similar (44.5% among dofetilide patients vs. 45.1% among placebo patients).

Nesiritide Provides Symptomatic and Hemodynamic Benefit

Dr. William T. Abraham, of the University of Colorado Health Sciences Center, Denver, and colleagues explored the use of nesiritide (human b-type natriuretic peptide) in a randomized double-blind placebo-controlled trial of 124 decompensated heart failure patients with a history of NYHA class III or class IV disease. The investigators infused patients with placebo, 0.015 *g/kg/min or 0.03 *g/kg/min of nesiritide and evaluated their global symptoms, dyspnea, and hemodynamics 6 hours later.

Among the 57 class IV patients, 59% of higher-dose nesiritide patients experienced improvement in global symptoms, compared to 50% of lower-dose patients and 7% of placebo patients. Pulmonary capillary wedge pressure (PCWP) decreased by 36% in class IV patients who received the higher dose of nesiritide and decreased by 15% in lower-dose patients, but it increased by 20% in placebo patients.

Findings were similar among the 67 class III patients: 54% of higher-dose nesiritide patients experienced improvement in symptoms, compared with 68% of lower-dose patients and 20% of placebo patients, while PCWP decreased by 33% in higher-dose class III patients and 25% in lower-dose patients, but increased by 2% in placebo patients.

"Nesiritide produces rapid symptom improvement and dose-related improvement in hemodynamics in patients with acutely decompensated heart failure, regardless of baseline disease severity," the investigators said.

Eplerenone Dose Evaluation

Dr. Bertram Pitt and colleagues at the University of Michigan School of Medicine, Ann Arbor, treated 321 patients with NYHA class II-IV heart failure in a study of eplerenone, a selective aldosterone receptor antagonist. Patients were randomized to receive eplerenone 25, 50, or 100 mg daily, 25 mg twice daily, spironolactone 25 mg daily as a positive control, or placebo.

After 12 weeks, patients who received spironolactone or 50 mg or more of eplerenone showed significant decreases in b-type natriuretic peptide and increases in urinary aldosterone and renin compared with placebo (p ≤ 0.05). A clinically significant increase in the incidence of hyperkalemia appeared on eplerenone 100 mg daily; 12% compared to 8.7% for spironolactone. Male patients experienced a significant increase in total testosterone on spironolactone compared with placebo (p ≤ 0.05).

"[Eplerenone] appears pharmacologically similar to [spironolactone] with the exception of a lack of an effect on serum testosterone," Dr. Pitt said. "A dosing strategy of 50 mg daily appears pharmacologically effective and safe in patients with [heart failure] maintained on standard therapy, including an ACE-I." ■