

Underuse of β -Blockers in Heart Failure: How to Improve Outcomes

Examining the role of β -blockers in the treatment of heart failure was the focus of the meeting "Heart Failure Management: Are We Really Succeeding?" held in Atlanta, Georgia, on November 6, 1999. The meeting was supported by an educational grant from Astra-Zeneca. This Special Report supplement features highlights of the proceedings of that meeting.

The meeting was chaired by Milton Packer, MD, of the Columbia University of Physicians and Surgeons and the Columbia-Presbyterian Medical Center in New York City. The meeting featured presentations by Dr. Packer as well as Stephen S. Gottlieb, MD, of the University of Maryland School of Medicine in Baltimore, Maryland; Barry H. Greenberg, MD, of the University of California at San Diego Medical Center; and Sidney Goldstein, MD, of Case Western Reserve University School of Medicine in Cleveland, Ohio and the Henry Ford Hospital in Detroit, Michigan.

Once strictly contraindicated in the treatment of heart failure, β -blockers have traveled 180° in clinical philosophy to attain the status of a component of optimal clinical management for most heart failure patients.

Compelling evidence from a variety of clinical trials has demonstrated that treatment with a β -blocker can reduce the risk of death and hospitalization in stable patients who have New York Heart Association (NYHA) class II or class III heart failure. β -blockers have not been evaluated in a

sufficient number of patients with class IV heart failure to warrant an indication for that patient population.

Placebo-controlled clinical trials involving more than 10,000 patients have shown a 30% to 35% reduction in mortality risk among heart failure patients treated with β -blockers. The magnitude of the benefit is at least 35% to 40% for worsening heart failure resulting in hospitalization or death. The data have been corroborated and extended by several thousand additional patients involved in trials that were not placebo controlled. Consideration of data from clinical studies of β -blocker use in post-myocardial infarction patients pushes the overall clinical experience beyond 100,000 patients.

Despite the clear beneficial effect of β -blockade, the agents have remained underused in cardiovascular medicine. The extent of underuse was demonstrated recently in an analysis of data from the Cooperative Cardiovascular Project (CCP), an investigation of the care provided to Medicare patients with myocardial infarctions. A review of more than 200,000 cases showed that about a third of the patients had been prescribed a β -blocker at the time of hospital discharge. The CCP review showed that the beneficial effects of β -blocker therapy spanned a wide spectrum of patient subgroups, which is consistent with previous data from a variety of sources. Notably, patients at highest risk derived the greatest benefit from β -blocker therapy.

The amount of consistent, positive data for β -blocker use in heart failure led to the organization of the largest clinical trial, the Metoprolol Controlled Release/Extended Release (CR/XL) Randomized Intervention Trial in Congestive Heart Failure (MERIT-HF). In this study of almost 4000 randomized patients, those treated with a β -blocker had a 34% reduction in mortality risk, a 45% reduction in the risk of sudden death, and a 50% reduction in the risk of death due to worsening heart failure. The MERIT-HF study also demonstrated the safety and tolerability of β -blockade: the rate of permanent discontinuation was higher in the placebo group. As with most of the major β -blocker clinical trials that preceded it, MERIT-HF was terminated prematurely because of the emergence of large, highly significant differences between the treatment groups.

The mechanisms by which β -blockers have such a profound impact on the clinical course of heart failure remain unclear. A variety of possibilities has been suggested. Evidence from clinical studies has demonstrated that β -blockers, like angiotensin-converting enzyme (ACE) inhibitors, can prevent and possibly even reverse deleterious cardiac remodeling. Virtually all long-term, placebo-controlled studies have demonstrated improvement in ejection fraction in heart failure patients treated with β -blockers. Some evidence has indicated improved cardiac performance observed with β -blockers might be related to changes in the natural history of heart failure.

β -blockers favorably alter electrophysiologic properties of heart cells to reduce the risk of arrhythmias. The benefits of β -blockade in ischemic heart disease have suggested that the agent's anti-ischemic effect contributes to improved outcome. Recent evidence indicates that β -blockers may reduce the generation of harmful oxygen-free radicals. In all likelihood, these and other potential mechanisms

of action have a collaborative effect, and no single mechanism can account for all of the benefits observed with β -blocker therapy.

The weight of the data favoring β -blocker use to treat heart failure persuaded a panel of more than 150 heart failure experts to specify β -blockade as a component of optimal heart failure therapy, as delineated in recently published guidelines. After an extensive review and discussion of the data, the panel concluded, "All patients with stable NYHA class II or class III heart failure due to left ventricular systolic dysfunction should receive a β -blocker unless they have a contraindication to its use or have been shown to be unable to tolerate treatment with the drug." The panel

ACRONYM LIST

The following acronyms appear within the pages of this Special Report supplement:

ACE	Angiotensin-converting enzyme
APACHE II	Acute Physiology and Chronic Health Evaluation
ATLAS	Assessment of Lisinopril and Survival
CAD	Coronary artery disease
CCP	Cooperative Cardiovascular Project
CIBIS	Cardiac Insufficiency Bisoprolol Study
COPD	Chronic obstructive pulmonary disease
LVEDP	Left ventricular end-diastolic pressure
MDC	Metoprolol in Dilated Cardiomyopathy
MERIT-HF	Metoprolol Controlled Release/Extended Release (CR/XL) Randomized Intervention Trial in Congestive Heart Failure
MI	Myocardial infarction
NYHA	New York Heart Association

went on to state, “ β -blockers are indicated for the long-term management of chronic heart failure.”

To put the contributions of β -blockers in proper perspective, one must realize that the beneficial effects noted in multiple clinical trials of heart failure patients have come in addition to the benefits of ACE inhibitors, which have a demonstrated ability to reduce heart failure mortality in their own

right. The cumulative effect of the data has been to create a mandate for the use of ACE inhibitors and β -blockers to treat most heart failure patients. Neither agent should be considered optional. Only when the lessons learned from clinical trials have been applied in clinical practice on a routine basis will heart failure patients gain the full benefit that has been unequivocally demonstrated for β -blockers.