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DRUG THERAPY AND PACEMAKER AN EFFECTIVE COMBINATION FOR EVEN MILD HEART FAILURE PATIENTS

Chicago, Il -- For patients diagnosed with severe heart failure, where the heart cannot pump a sufficient amount of blood through the body because of structural or functional problems, the usual and optimal course of action in some patients is to implant a cardiac resynchronization therapy (CRT) device or artificial pacemaker, which stimulates both ventricles.

A study presented today at the American College of Cardiology's 57th Annual Scientific Session, suggested that the use of CRT, already proven effective treatment in patients with severe heart failure, might provide similar benefits on patients with a more mild disease when combined with drug therapy. ACC.08 is the premiere cardiovascular medical meeting, bringing together cardiologists and cardiovascular specialists to further breakthroughs in cardiovascular medicine.

A biventricular pacemaker, or CRT, can pace both sides of the heart and resynchronize a heart that does not beat in synchrony - common in patients with heart failure. CRT has been shown to reduce the size of the heart, inducing reverse left ventricular (LV) remodeling in NYHA III-IV patients. The REVERSE study, (REsynchronization reVERses Remodeling in Systolic left vEntricular dysfunction study) is a year-long, multi-center, randomized, double-blind controlled trial to assess whether CRT plus optimal medical therapy (CRT ON) can manage the progression of heart failure compared to optimal medical therapy alone (CRT OFF).

The primary endpoint of the study was the HF clinical composite response, which was analyzed comparing percent change in CRT ON versus CRT OFF and comparing the distribution of patients who had improved. The finding was that they were unchanged or

worsened on the therapies. The secondary endpoint, left ventricle end-systolic volume index (LVESVi), was also evaluated after 12 months. A total of 610 pts were randomized in 73 centers in the US, Canada and Europe. Eligible patients had NYHA Class II heart failure or I with previous symptoms, QRS-duration \geq 120 ms and LV ejection fraction \leq 40 percent. Patients had to be on optimal drug therapy, e.g., ACE inhibitors or angiotensin receptor blockers, on stable dose for at least one month and on beta-blockers for three months and on stable dose for at least one month prior to enrollment in REVERSE.

Changes in heart failure medications were not allowed over the course of the REVERSE study unless by clinical necessity. Optimizing medication before randomizing patients into the study ensured that any reverse remodeling that occurred in patients throughout the study were indeed induced by CRT and not by medical therapy.

Combined therapy proved effective in this study population. While large differences were not seen between the two groups in the percent worsened in the HF clinical composite response, 54% of patients improved with CRT ON, compared to 40% improvement with CRT OFF. When distributed between improved, unchanged and worsened outcomes, the CRT ON group fared better overall compared to the CRT OFF group. Patients assigned to CRT ON experienced improvement in reverse remodeling and CRT decreased the risk of heart failure hospitalization.

This indicates that CRT in mildly symptomatic heart failure patients not only reverses LV modeling, but also influences morbidity. Since heart failure-related hospitalizations are an indicator of mortality, it is possible that CRT over a longer period of observation might lower mortality in patients with mild heart failure, and in spite of optimal medical therapy, these patients should be considered for CRT to modify or reverse disease progression.

Not surprisingly, the study found that quality of life and six minute hall walk distance did not improve significantly in this patient population, suggesting that while specific factors may have improved, the overall patient experience may not have changed dramatically.

“REVERSE demonstrates that CRT, in combination with optimal medical therapy reverses left ventricular remodeling in asymptomatic and mildly symptomatic heart failure patients,” said Cecilia Linde, MD, PhD, Karolinska University Hospital, Stockholm Sweden, and lead study author. “Extended study will further determine the significance of the study’s finding and what long-term benefits may exist with this combination therapy.”

Dr. Linde will present “The REVERSE study, (REsynchronization reVERses Remodeling in Systolic left vEntricular dysfunction study) in the Late-Breaking Clinical Trials II session on Tuesday, April 01, 2008, 10:00 a.m. - 11:30 a.m., McCormick Place, North Hall B1.

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The American College of Cardiology (www.acc.org) represents the majority of board certified cardiovascular physicians in the United States. Its mission is to advocate for quality cardiovascular care through education, research, promotion, development and application of standards and guidelines – and to influence health care policy. ACC.08 is the largest cardiovascular meeting, bringing together cardiologists and cardiovascular specialists to share the newest discoveries in the treatment and prevention, while helping the ACC achieve its mission to address and improve issues in cardiovascular medicine.