

Advances in CRT

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Anthony S. Tang, MD, University of British Columbia, Victoria, British Columbia, Canada, reported that the future of cardiac resynchronization therapy (CRT) will be based on indications for treatment, patient selection, imaging guidance to enhance efficacy, and the advantages and disadvantages of various lead and implant placement methods. Dr. Tang discussed key findings from recent clinical trials with CRT and summarized critical issues for its future.

In a registry study on bundle branch block morphology and other predictors of outcome after CRT in Medicare patients, Bilchick et al. [*Circulation* 2010] found that right bundle branch block (RBBB), ischemic cardiomyopathy, New York Heart Association (NYHA) Class IV status, and advanced age were powerful adjusted predictors of poor outcome after cardiac resynchronization defibrillator therapy (CRT-D).

The Resynchronization/Defibrillation for Ambulatory Heart Failure Trial [RAFT; Tang AS et al. *N Engl J Med* 2010] examined CRT by QRS morphology. In this study, 1798 patients with NYHA Class II or III heart failure (HF), left ventricular ejection fraction (LVEF) $\leq 30\%$, and intrinsic QRS duration ≥ 120 ms or paced QRS duration ≥ 200 ms were randomly assigned to receive either an implantable cardioverter defibrillator (ICD) alone or an ICD plus CRT. The primary outcome was death from any cause or hospitalization for HF.

Patients were followed for a mean of 40 months. The primary outcome occurred in 297 of 894 patients (33.2%) in the ICD-CRT group and 364 of 904 patients (40.3%) in the ICD group (HR in the ICD-CRT group, 0.75; 95% CI, 0.64 to 0.87; $p < 0.001$). In the ICD-CRT group, 186 patients died versus 236 in the ICD group (HR, 0.75; 95% CI, 0.62 to 0.91; $p = 0.003$), and 174 patients were hospitalized for HF versus 236 in the ICD group (HR, 0.68; 95% CI, 0.56 to 0.83; $p < 0.001$).

The effectiveness of CRT by QRS morphology in the Multicenter Automatic Defibrillator Implantation with Cardiac Resynchronization Therapy trial [MADIT-CRT; Zareba W et al. *Circulation* 2011] aimed to determine whether QRS morphology identifies patients who benefit

from CRT-D and whether it influences the risk of primary and secondary endpoints in patients who were enrolled in the MADIT-CRT trial. HF event or death was the primary endpoint of the trial.

Hazard ratios for the primary endpoint for comparisons of CRT-D patients versus those who only received an ICD were significantly ($p < 0.001$) lower in left bundle branch block (LBBB) patients (0.47; $p < 0.001$) than in those patients without LBBB patients (1.24; $p = 0.257$). The risk of ventricular tachycardia, ventricular fibrillation, or death was decreased significantly in CRT-D patients with LBBB but not in non-LBBB patients.

Ongoing trials are focused on patients with heart block other than LBBB. The Pacing Affects Cardiovascular Endpoints in Patients with Right Bundle-Branch Block trial [PACE-RBBB; NCT01169493] is testing the hypothesis that right ventricular pacing that is delivered with an AV interval that maximizes ventricular synchrony is equivalent to biventricular (biV) pacing for improvement in cardiac performance, HF symptoms, and positive ventricular remodeling in patients with HF and RBBB. The study will have 2 experimental arms (RV DDD-40 [fusion pacing]) and biV DDD40) and a control. The primary outcome measure is LV remodeling (defined as a decrease in LV end-systolic diameter of > 5 mm).

The Biventricular Versus Right Ventricular Pacing in Heart Failure Patients with Atrioventricular Block study [BLOCK HF; NCT00267098] is addressing questions regarding CRT treatment for patients with atrioventricular (AV) block. Researchers are testing if biV pacing, compared with right ventricular pacing, decreases hospitalizations and clinic visits that are precipitated by HF symptoms, extends life, and delays HF symptoms.

The primary outcome measures of this randomized, double-blind trial are time to a composite of all-cause mortality, HF, related urgent care, or a significant increase in LV end-systolic volume index. This study began in 2003. With an estimated enrollment of 1636 subjects, its expected completion date is November 2013.

Dr. Tang concluded that the future of CRT will rest on clarified indications for patients with AV block, RBBB only, permanent AF, relatively preserved LV, and narrow QRS. It will also be determined by the utility of endocardial LV pacing and of imaging to guide lead implantation.