The study results were presented by Bruce L. Rollman, MD, University of Pittsburgh, Pittsburgh, PA, the primary investigator of the study.

Additional reading:

- Rollman BL et al. Telephone-Delivered Collaborative Care for Treating Post-CABG Depression: A Randomized Controlled Trial. *JAMA* 2009;302:2095-2103.
- Rollman BL et al. The Bypassing the Blues Treatment Protocol: Stepped Collaborative Care for Treating Post-CABG Depression. *Psychosomatic Medicine* 2009;71:217-230.
- www.bypassingtheblues.pitt.edu

Results from the J-CHF Study

Results from the Japanese Chronic Heart Failure (J-CHF) study indicate that carvedilol, in doses as low as 2.5 mg/day, can produce long-term beneficial effects in Japanese patients with mild to moderate chronic heart failure (CHF) and reduced left ventricular ejection fraction (LVEF). The results were presented at the American Heart Association 2009 Scientific Sessions in Orlando, FL, by Masatsugu Hori, MD, Osaka University, Osaka, Japan, the principal investigator of the study.

J-CHF was a prospective, randomized, open-label, blinded endpoint study. The objectives were to determine the optimal minimal dose of the beta-blocker carvedilol for Japanese patients with CHF and to determine predictors of response to beta-blocker therapy. A total of 364 subjects aged 20 to 80 years (74% men; mean age ~60 years) with mild to moderate heart failure (New York Association [NYHA] class II or III) and an LVEF ≤40% were randomly assigned to receive carvedilol 2.5 mg/day (n=118), 5 mg/day (n=116), or 20 mg/day (n=118). Subjects were stratified according to underlying disease, severity, age, gender, and hospital admission status.

The primary study endpoint was a composite of all-cause death and hospitalization for cardiovascular diseases and heart failure. Secondary endpoints included all-cause death, death from heart failure, and sudden death; hospitalization for cardiovascular diseases or heart failure; the need to modify treatment due to worsening of heart failure; aggravation of NYHA class; and changes in LVEF and plasma B type natriuretic peptide (BNP).

There were no significant differences as to the primary endpoint between 2.5 mg/day versus 5.0 mg/day (HR, 0.862; 95% CI, 0.491 to 1.514; p=0.606) and 2.5 mg/day versus 20 mg/day (HR, 1.004; 95% CI, 0.583 to 1.731; p=0.99). Differences in the secondary endpoints were also not significant. Adverse events were dose-dependent and increased with higher doses of carvedilol. Increases in discontinuation rates were also dose-dependent (1.7%, 2.6%, and 3.4% in the 2.5-mg, 5-mg, and 20-mg dose groups, respectively). Significantly ($p<0.05$) fewer patients in the 2.5-mg dose group had a change in treatment dose relative to the 20-mg dose group.

LVEF significantly ($p<0.05$) improved in all dose groups but was not dose-dependent (30.4±7.9 vs 42.6±14.5, 29.8±6.5 vs 42.6±13.6, and 30.4±7.0 vs 43.2±12.8 for the 2.5-mg, 5.0-mg, and 20-mg/day groups, observation period, and Week 48, respectively). Heart rate (HR) and BNP log significantly ($p<0.05$) decreased in a dose-dependent manner. Multivariate analysis revealed that decreases in HR and BNP during the observation period were predictive of treatment response.

"Our results indicate that therapeutic response to carvedilol shows a high amount of variability between individuals, and we had better select the dose that can achieve reductions in heart rate and/or plasma BNP beyond dosage," Dr. Hori concluded. He recommended initiating carvedilol at the lowest dose in Japanese patients and increasing the dose incrementally until the desired reductions in HR and/or BNP are achieved and suggested that further study is warranted to understand optimal dosing in different ethnic populations with different genetic backgrounds.

Prof. Marco Metra, MD, University of Brescia, Brescia, Italy, the discussant for the J-CHF study, noted that the results are not in agreement with previous studies, including one by Dr. Hori that used carvedilol in Japanese patients [Hori M et al. *Am Heart J* 2004], which showed a dose-dependent relationship between beta-blocker agents and improved LVEF, as well as improvement of CHF, based on a global assessment by the attending physician. He listed several limitations of the J-CHF study, including not having a placebo group and being underpowered for detecting a dose effect.

Results of the FRANCE Registry

Results from the FRANCE (French Aortic National CoreValve and Edwards) Registry, presented by Helene Eltchaninoff, MD, University of Rouen, Rouen, France, demonstrated high implantation success with excellent and sustained hemodynamic and clinical improvement in high-risk patients with severe aortic stenosis

who were treated with transcatheter aortic valve (TAVI) replacement.

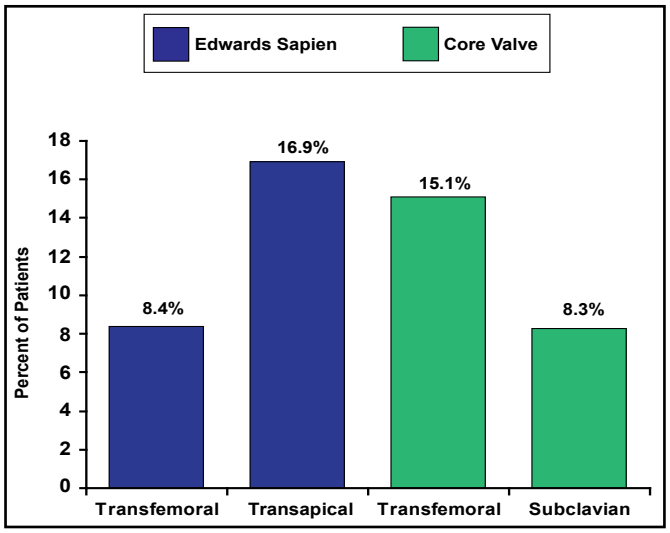
TAVI is an emerging treatment for patients with aortic stenosis who are at too high a risk to undergo conventional surgical replacement of the aortic valve. The FRANCE Registry is a multicenter prospective clinical registry that was developed to evaluate the safety and efficacy of the two aortic valve replacement devices that are currently available in France. The two valves that were used in the registry were the Edwards Sapien balloon-expandable valve (68% of patients), using either a transfemoral (39%) or transapical (29%) approach, and the CoreValve self-expandable valve (32% of patients), using a transfemoral (27%) or subclavian approach (5%).

Study patients were required to have severe aortic stenosis (effective orifice area [EOA] <1 cm^2/m^2) and severe symptoms (New York Heart Association [NYHA] Class ≥2) and be at high surgical risk (Logistics EuroScore >20%, Society of Thoracic Surgeons [STS] mortality risk score >10%), or have a contraindication to surgery). The primary endpoint of the study was 30-day mortality. Secondary endpoints (up to 3 years) included mortality, major adverse cardiac events, hemodynamics, and quality of life.

A total of 244 patients (mean age 82 years; 56% men) were recruited between February and September 2009. Diabetes was present in 27% patients; 23% had a previous myocardial infarction; 10% had a previous stroke; and ~42% had coronary artery disease. The only significant (p=0.02) difference between the four subgroups was the presence of peripheral artery disease and abdominal aortic aneurysm, which were more common in patients who were treated with a transapical or subclavian approach. The mean baseline EuroScore was 25.6%; mean STS score was 16%. The mean aortic annulus (21.9±1.8 mm) was slightly smaller in patients who received the Edwards due to the availability of the 23-mm stent and larger in the CoreValve group due to the availability of a 29-mm stent. The mean EOA was 0.68±0.16 cm^2. Mean left ventricular ejection fraction was 51% (47% [p=0.02] in patients who received the Edwards valve via the transfemoral approach). Two-thirds of the procedures were done in the cardiac catherization lab.

The devices were successfully implanted (defined as successful delivery and deployment of the valve without death on the table) in 97% of patients. Failure occurred in 7 patients; there were 4 procedural deaths. There was no difference between the groups in 30-day mortality (mean 12.7%; p=0.32; Figure 1). Hemodynamic results immediately after implantation were significant (mean increase in EOA from 0.68±0.16 cm^2 to 1.74±0.47 cm^2; p<0.001). The rate of new pacemaker implantation (overall mean 11.8%) was significantly (p<0.001) higher in the CoreValve group (25% to 27%) compared with 4% to 5% in the Edwards valve group. The transfusion rate (mean 21.3%) was higher when a transapical (27.4%) or subclavian (83.3%) approach was used.

Figure 1. 30-Day Mortality.



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Vascular complications (mean 6.5% of patients) were comparable between the four groups. Postimplantation aortic regurgitation occurred in <10% of patients. Factors that were predictive of 30-day mortality (by univariate and multivariate analysis) were prior CABG and Euroscore ≥25%.

A total of 111 patients have reached the 6-month follow-up. Survival at 6 months is 76.5%. Hemodynamic and clinical results are persistent.

RecordAF Trial Confirms No Advantage for Rate Versus Rhythm Control Strategy for in Patients with AF

The clinical outcomes that are associated with rate control versus the restoration and maintenance of normal sinus rhythm in the treatment of atrial fibrillation (AF) have been explored in a number of large-scale clinical trials [Wyse DG et al. *N Engl J Med* 2002; Van Gelder et al. *N Engl J Med* 2002]. No advantages for either treatment strategy with respect to major cardiovascular (CV) outcomes have