with possible adverse clinical consequences was neither robust nor well supported by external data. Several large ongoing randomized double-blinded clinical trials are evaluating the clinical benefit and safety of niacin and ezetimibe (although none of these trials is comparing the two directly). Such large-scale trials will serve as the foundation for shaping future guidelines and clinical practice with niacin and with ezetimibe.

Additional reading:

- Taylor AJ et al. Extended-Release Niacin or Ezetimibe and Carotid Intima-Media Thickness. *N Engl J Med*. Published online 16 November 2009.
- Kastelein JJP & Bots ML. Statin Therapy with Ezetimibe or Niacin in High-Risk Patients. *N Engl J Med*. Published online 16 November 2009.

Collaborative Care Improves HRQoL, Physical Functioning, and Mood Symptoms in Patients with Post-CABG Depression

Results from the Bypassing the Blues trial (NCT00091962) indicate that depression screening shortly after coronary artery bypass graft (CABG) surgery, telephone follow-up using evidence-based depression treatment protocols, and patient education that is supervised by primary care physicians (ie, collaborative care) can improve health-related quality of life (HRQoL), physical functioning, and mood symptoms and thereby speed patient recovery following CABG surgery.

Post-CABG depression is common (20% to 25% incidence) and has been associated with delayed recovery, increased hospital readmissions, cardiovascular events, and death. The Bypassing the Blues trial was designed to test the effectiveness of a telephone-delivered collaborative care strategy for treating post-CABG depression versus doctors' usual care. Post-CABG patients who expressed mood symptoms that were indicative of depression (Patient Health Questionnaire [PHQ-2] positive screen) preceding discharge, followed by a PHQ-9 score ≥10 at 2 weeks posthospitalization, were randomly assigned to an 8-month course of collaborative care (n=150) or their physicians' "usual care" (n=152). Results were also compared with a group of 151 randomly sampled nondepressed post-CABG patients (PHQ-2 negative and PHQ-9 <5).

The intervention consisted of telephone contact at regular intervals, during which the nurses provided basic psycho education, assessed treatment preferences (eg, self-management workbook, antidepressant pharmacotherapy, referral to a mental health specialist), monitored treatment response, and suggested changes to patients and their primary care physicans (PCP) following a discussion with a study psychiatrist and PCP. The study investigators did not prescribe or dispense any antidepressant medications, and patients who were interested in pharmacotherapy were required to obtain this treatment from their PCP and at cost. No pharmaceutical or industry support was involved in this trial.

The primary outcome measure was mental HRQoL, as measured by the Short Form-36 Mental Component Summary (SF-36 MCS) at 8 months. Secondary outcome measures included assessment of mood symptoms (Hamilton Rating Scale for Depression [HRS-D]), physical HRQoL (SF-36 PCS), and functional status (Duke Activity Status Index [DASI]); and rehospitalization rate.

The 302 depressed subjects were well matched by baseline randomization status; however, depressed subjects were slightly younger than those in the nondepressed comparison group (mean age 64 vs 66 years; p=0.03). Approximately 25% of depressed patients were already using an antidepressant medication at baseline.

Depressed subjects who were randomized to collaborative care experienced a significant improvement in HRQoL compared with subjects in the usual care group beginning at 2 month follow-up that was equivalent to a small to moderate effect size (ES) of 0.30 (95% CI, 0.17 to 0.52; p=0.01) and a number needed to treat (NNT) of 4.9 (3.2 to 10.4; p<0.001) to achieve a 50% or greater decline from baseline HRS-D score. The improvement in mood symptoms appeared to be more prominent in men (ES, 0.53; 95% CI, 0.23 to 0.84; p<0.001). Patients who received collaborative care also had improved scores on the HRS-D for mood symptoms (ES, 0.30; 95% CI, 0.08 to 0.53; p=0.009), the SF-36 PCS (ES, 0.26; 95% CI, 0.03 to 0.48; p=0.03) for physical status, and DASI (ES, 0.32; 95% CI, 0.09 to 0.54; p=0.006) for physical functioning. The mean HRQoL and physical functioning of patients who received intervention did not reach those of the nondepressed comparison group for any of the measures.

Overall, while there was no difference in the incidence of rehospitalization between study arms by randomization status, there was a trend toward fewer rehospitalizations for cardiovascular causes among depressed men who were randomized to their intervention (13%) versus men who were randomized to usual care (25%; p=0.07). However, the study was underpowered to detect a difference in cardiovascular events of mortality (1% overall mortality by 8-month follow-up). Cost data are not yet available.

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