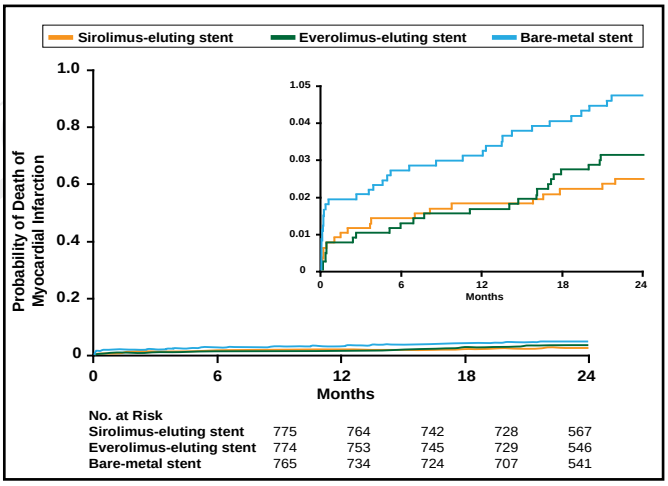
significant difference in non-MI-related TVR between the DES patients and those who received the BMS (SES, p=0.007; EES, p=0.002), although there was no statistically significant difference between the two DES groups. This resulted in a significant difference in the composite of cardiac death, nonfatal MI, and TVR (MACE), which was significantly reduced by both of the DES (SES, p=0.009; EES, p=0.005) . Limitations of the study include low overall number of events, resulting in reduced power to detect differences between groups (the 2.2% absolute difference in the primary endpoint between SES and BMS was not statistically different despite representing an ~85% relative increase), and unblinded adjudication of approximately one-third of reported events.

Figure 1. Kaplan-Meier Estimates of Composite Primary Endpoint at 24 Months.



"In contemporaneous stenting of large coronary arteries, late safety problems with drug-eluting stents could not be confirmed, and there was even a trend in the opposite direction," said Dr. Kaiser. The findings, he noted, should influence medical practice.

Results of this study were published simultaneously in *The New England Journal of Medicine*. Kaiser C et al. *N Eng J Med* 2010.

ACT Trial Results Should Change Clinical Practice

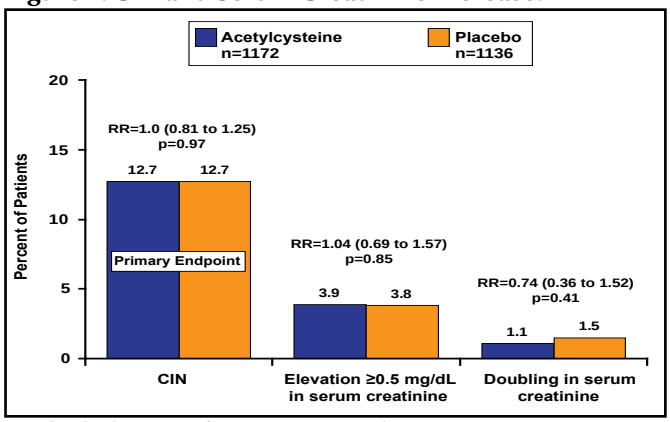
Based on the results of the Acetylcysteine for the prevention of Contrast-Induced nephropathy (ACT; NCT00736866) trial, there is no evidence that the antioxidant N-acetylcysteine (NAC) reduces the risk of contrast-induced nephropathy (CIN) in patients who are undergoing coronary and vascular angiography. That was the message from Otavio Berwanger, MD, PhD, Hospital do Coração, São Paulo, Brazil, after he presented the main results of the ACT trial.

The study was designed to test the hypothesis that using NAC could reduce the risk of CIN (defined as a ≥25% elevation in serum creatinine above baseline 48 to 96 hours postangiography) in patients who were undergoing coronary and vascular angiography. Secondary outcomes included mortality, the need for dialysis, cardiovascular mortality, side effects, and doubling of serum creatinine. CIN occurs in between 9% and 38% of patients with risk factors, such as renal failure, diabetes, and age >70 years [McCullough PA et al. *Am J Card* 2006]. Although there have been no large, randomized, placebo-controlled trials that have been designed to test the benefit of NAC on CIN risk, its use has become widespread.

ACT enrolled 2308 patients with at least one risk factor for CIN (ie, age >70 years, chronic renal failure, diabetes, heart failure or left ventricular ejection fraction <45, shock). The patients were randomized to receive NAC 1200 mg twice daily (2 doses pre- and 2 doses postprocedure) or placebo and underwent intravascular angiography at 46 centers in Brazil. The mean patient age was 68 years, 61% were diabetic, and the mean volume of contrast that was delivered was 100 cc.

The incidence of CIN was 12.7% in both the NAC and placebo groups (RR, 1.00; 0.81 to 1.25; p=0.97; Figure 1), with nearly identical rates of mortality or the need for dialysis (2.2% vs 2.3%; p=0.91), total mortality (2% vs 2.1%; p=0.80), need for dialysis (0.3% for both; p=0.97), and cardiovascular mortality (1.5% vs 1.6%; p=0.93). The findings were consistent regardless of the type of contrast that was used for the procedure or the procedure itself (67% coronary diagnostic angiographies, 29% percutaneous interventions, 4% vascular procedures).

Figure 1. CIN and Serum Creatinine Increase.



Reproduced with permission from O. Berwanger, MD, PhD.

The ACT II trial, currently in the planning stages, is designed to compare saline with bicarbonate and to investigate different types of contrast dye in the search to find one that is less toxic to the kidneys or to find another compound that offers a protective effect.

SMART-AV: No Benefit to Customized AV Delay in CRT

For heart failure patients who are undergoing cardiac resynchronization therapy (CRT), echocardiographic- or ECG-based optimized AV delay does not improve upon standard programming approaches, according to new findings from the SmartDelay Determined AV Optimization: A Comparison to Other AV Delay Methods Used in Cardiac Resynchronization Therapy (SMART-AV) trial.

When added to optimal medical therapy, CRT has the potential to reduce heart failure hospitalizations, improve quality of life, and prolong survival in patients with heart failure and prolonged QRS duration. Achieving the full benefits of CRT, however, may depend on programming the optimal AV delay. To date, techniques for AV optimization have varied across major CRT trials, including Cardiac Resynchronization-Heart Failure (CARE-HF) and Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION). No consensus approach has emerged to date.

The SMART-AV trial was designed to compare current options for AV optimization, including the investigational ECG-based SmartDelay device algorithm, which calculates AV delay based on left ventricular (LV) lead location, intraventricular timing, and sensed and paced AV intervals. The trial included 980 patients with New York Heart Association (NYHA) class III or IV heart failure, reduced ejection fraction (EF ≤35%), and prolonged QRS duration (≥120 ms) who were indicated for a CRT device. All patients were also receiving optimal pharmacological therapy. Those with complete heart block, a history of CRT use, or an inability to tolerate pacing at VVI-40-RV for up to 14 days were excluded from the study.

Patients were randomly assigned to AV delay that was optimized with SmartDelay (n=332), echocardiography-optimized AV delay (n=323), or a fixed empirical AV delay of 120 ms (n=326). The primary endpoint was LV end-systolic volume (LVESV) at 6 months. Secondary endpoints included structural outcomes, such as EF and LV end-diastolic volume, as well as functional outcomes, including 6-minute-walk distance, NYHA class, and quality of life.

Kenneth A. Ellenbogen, MD, Virginia Commonwealth University School of Medicine and Medical College of Virginia Hospitals, Richmond, Virginia, USA, presented the results of SMART-AV.

At 6 months, the SmartDelay algorithm provided a median LVESV reduction of 21 mL, which was comparable with the median reductions of 19 mL in the echocardiography group (p=0.52) and 15 mL in the fixed-delay group (p=0.66). Secondary structural and functional endpoints were also similar across the three study groups.

In a post hoc subgroup analysis, the primary efficacy findings were consistent across several subgroups, defined by heart failure etiology (ischemic vs nonischemic), percentage of atrial pacing (≥30% vs <30%), QRS width (≥150 ms vs <150 ms), and left bundle branch block (present or absent). When evaluated by gender, however, women responded better to the SmartDelay algorithm than to fixed AV delay (interaction p=0.02). By comparison, no differences were seen between the SmartDelay and echocardiography groups in women or across any study groups in men.

Given the SMART-AV findings, AV optimization is not warranted for routine use in heart failure patients who receive CRT, Dr. Ellenbogen said. However, AV optimization may have a future role in the treatment of selected heart failure patients, such as the 30% of patients who do not respond initially to standard CRT.

The SMART-AV findings were also published simultaneously online in *Circulation*. Ellenbogen KA et al. *Circulation* 2010.

Results From EMPHASIS-HF

The addition of eplerenone to optimal medical therapy has been shown to reduce morbidity and mortality among patients with acute myocardial infarction that is complicated by left ventricular dysfunction and NYHA Classs II heart failure (HF) [Pitt B et al. *N Engl J Med* 2003; Pitt B et al. *N Engl J Med* 1999]. In a late-breaking clinical trial that was presented by Faiez Zannad, MD, PhD, University of Nancy, Nancy, France, the addition of eplerenone to evidence-based therapy improved survival rates for patients with mildly symptomatic systolic HF.

The Eplerenone in Mild Patients Hospitalization and Survival Study in Heart Failure (EMPHASIS-HF; NCT00232180) was designed to evaluate the effect of eplerenone, a selective aldosterone antagonist, on mortality and morbidity in patients with NYHA class II