

have added to the area under the receiver-operator characteristic curve for the standard risk factors' ability to prognosticate. We think that there has not been and will not be a major breakthrough in prevention, akin to what has dramatically occurred in diagnostic testing and intervention, until risk factors are used not for risk assessment, but to identify treatable causal factors after risk has more accurately been established by the level of subclinical atherosclerosis (5).

5. To those who raise cost effectiveness concerns related to widespread screening for subclinical atherosclerosis, reduction in the cost of calcium scanning to the level of mammography will make it the most cost-effective modality.
6. Finally, in both secondary and primary prevention, there has been a misplaced focus on simple changes in the treated risk factors, for example, low-density lipoprotein, rather than on measures of subclinical atherosclerosis and disease activity and endothelial function to evaluate the response of the disease, rather than the risk factors, to treatment.

**\*Harvey S. Hecht, MD**  
**Marc Colmer, MD**

\*Lenox Hill Heart and Vascular Institute  
130 East 77th Street  
New York, New York 10021  
E-mail: [hhecht@aol.com](mailto:hhecht@aol.com)

doi:10.1016/j.jacc.2009.02.043

#### REFERENCES

1. Hecht HS, Colmer M. Fantastic voyage: a patient's journey through cardiology from 1969–2008. *J Am Coll Cardiol* 2008;52:1366–9.
2. Becker A, Leber A, Becker C, Knez A. Predictive value of coronary calcifications for future cardiac events in asymptomatic individuals. *Am Heart J* 2008;155:154–60.
3. Detrano RC, Guerci AD, Carr JJ, et al. Coronary calcium as a predictor of near-term coronary heart disease events in major American ethnic groups: the Multi-Ethnic Study of Atherosclerosis (MESA). *N Engl J Med* 2008;358:1136–45.
4. Hecht HS. The deadly double standard: the saga of screening for subclinical atherosclerosis. *Am J Cardiol* 2008;101:1805–7.
5. Hecht HS. Atherosclerotic risk factors revisited. *Am J Cardiol* 2004;93:73–5. correspondence Letter to the editor

## No Benefit From Cardiac Resynchronization Therapy in Asymptomatic Patients

We congratulate Linde et al. (1) on the meticulously carried out REVERSE (REsynchronization reVERses Remodeling in Systolic left vEntricular dysfunction) trial that addressed the question of the clinical benefit of cardiac resynchronization therapy (CRT) in patients with New York Heart Association (NYHA) functional class II and I heart failure (1). Unfortunately, the composite primary end point as defined per the study protocol was negative. Still, the authors conclude that CRT, in combination with optimal medical treatment ( $\pm$  defibrillator), reduces the risk for heart failure hospitalizations and improves ventricular structure and function in NYHA functional class II and I. In our opinion, the

later statement is not supported by the presented data, which shows no benefit for NYHA functional class I patients (odds ratio: 0.87; 95% confidence interval: 0.37 to 2.03) in their subgroup analysis (Fig. 4 of Linde et al. [1]).

This disagreement raises the more philosophical question: whether these subgroup analyses make sense if the primary end point is negative—maybe due to a lack of statistical power? It seems that the well-known players such as wide QRS and low left ventricular ejection fraction are positive predictors for CRT success but not NYHA functional class I. Another intriguing finding of this subgroup analysis is that patients on diuretics did improve, whereas those not on diuretics did not. However, the use of diuretics reduced mortality and prevented hospital admissions in this patient population, which raises the question of whether the use of diuretics by themselves may have accounted for the documented beneficial effect (clinical composite end point, hospitalizations) in the CRT ON group and whether this confounding variable was corrected for in the main analysis (2).

**\*Stefan Osswald, MD**  
**Beat Schaer, MD**  
**Michael Kuhne, MD**  
**Christian Sticherling, MD**

\*Head Cardiac Arrhythmia Service  
University Hospital Basel  
CH-4031 Basel  
Switzerland  
E-mail: [sosswald@uhbs.ch](mailto:sosswald@uhbs.ch)

doi:10.1016/j.jacc.2008.12.078

#### REFERENCES

1. Linde C, Abraham WT, Gold MR, St John Sutton M, Ghio S, Daubert C, on behalf of the REVERSE (REsynchronization reVERses Remodeling in Systolic left vEntricular dysfunction) Study Group. Randomized trial of cardiac resynchronization in mildly symptomatic heart failure patients and in asymptomatic patients with left ventricular dysfunction and previous heart failure symptoms. *J Am Coll Cardiol* 2008;52:1834–43.
2. Faris R, Flather MD, Purcell H, Poole-Wilson PA, Coats AJ. Diuretics for heart failure. *Cochrane Database Syst Rev* 2006:CD003838.

#### Reply

We thank Dr. Osswald and colleagues for their interest in our paper (1). The REVERSE (REsynchronization reVERses Remodeling in Systolic left vEntricular dysfunction) study was designed as one population of New York Heart Association (NYHA) functional class I to II heart failure (HF) patients. We agree that the primary end point did not reach statistical significance (2), with 16% of patients worsened in the cardiac resynchronization therapy (CRT) ON group and 21% in the CRT OFF group ( $p = 0.10$ ). The clinical composite response was designed for severe HF patients and, to our knowledge, has not previously been used in mildly symptomatic or asymptomatic HF patients (3).

The fact that the primary end point did not reach statistical significance despite substantial improvement in left ventricular (LV) dimensions accompanied by a significantly reduced time to first HF related hospitalization might be due to the difference in utility of this end point or that the observation period was not long enough to demonstrate effects in NYHA functional class I to II patients. Dr. Osswald and colleagues are concerned about the