Moreover, our selection criteria with respect to intraventricular asynchrony were highly restrictive and may have led to selection of patients with a very unfavorable prognosis.

Fourth, we agree with Dr. Gasparini and colleagues that the screening of patients suitable for CRT based on merely clinical criteria may be sufficient in specific settings. However, we are of the opinion that this simplification could increase the number of non-responders to CRT: this issue is critical, and current research for the identification of responders is in active development. There is evidence that left intraventricular asynchrony detected at echocardiography may represent the best parameter for the identification of responders to CRT (3,4). Therefore, we are convinced that the selection of patients for CRT should necessarily include the evaluation of mechanical asynchrony, the latter representing the pathophysiologic substrate for resynchronization pacing in heart failure patients.

**REFERENCES**


**Cerebroprotection Mediated by Angiotensin II**

I read with great interest the provocative study by Fournier et al. (1) on cerebroprotection mediated by angiotensin II. The investigators state that beta-blockers are remarkably ineffective in reducing the risk of stroke; however, they cite three studies all performed with one beta-blocker, atenolol, which has never been proven to reduce sudden death.

In general, the results of multiple studies with one drug cannot be interpreted as representing the class of that drug. In the case of beta-blockers in particular, publication of the Beta-blocker Evaluation of Survival Trial (BEST) (2), which failed to replicate the mortality reduction demonstrated by bisoprolol, metoprolol extended release, and carvedilol in systolic heart failure, clearly established the fallacy of assuming a class effect for the benefit of beta-blockers for that particular indication. Furthermore, in the recently published Carvedilol Or Metoprolol European Trial (COMET) (3), the stroke rate was reduced significantly (67%) with carvedilol compared with the short-acting metoprolol tartrate (4). Thus, the investigators need to limit their conclusion of the ineffectiveness of beta-blockers to atenolol and avoid invoking beta-blockers as a class in this argument.

**REFERENCES**


**REPLY**

Dr. Ghali raises an interesting point about our study (1) that deserves to be scrutinized. In hypertension, beta-blockers as a class have never been shown to reduce heart attacks or strokes (2,3). This is true for atenolol in several prospective placebo-controlled randomized trials, but also for propranolol in the Medical Research Council (MRC) study (4) and for oxprenolol in the International Prospective Primary Prevention Study in Hypertension (IPPPSH) (5). In Cardiac Insufficiency Bisoprolol Study (CIBIS-II), the rate of hospitalization for a stroke was almost twice as high in the bisoprolol arm as in the placebo arm (6). Thus, there are several prospective randomized studies with atenolol, propranolol, oxprenolol, or bisoprolol documenting that beta-blockers are not efficacious in reducing strokes.

A notable exception that Dr. Ghali mentioned is the Carvedilol Or Metoprolol European Trial (COMET) in congestive heart failure patients (7). However, carvedilol is a drug that is distinctly different from traditional beta-blockers in that it does have some alpha-blocking properties and other features that exert a more favorable effect on systemic hemodynamic, metabolic endocrine findings, and target organ disease than do traditional beta-blockers (8). We also should emphasize that a stroke reduction in congestive heart failure without hypertension cannot necessarily be extrapolated to uncomplicated hypertension. Indeed, heart failure per se is a risk factor for stroke, but the pathogenesis is different from the one in hypertension and often involves emboli of cardiac origin. Because carvedilol was superior to metoprolol in preventing congestive heart failure and sudden death, it is likely that it...