

subgroup analysis in a neutral study and more specifically by the “lack of benefit” in NYHA functional class I patients and in those not on diuretics (1). We understand their concern but want to point out that subgroup analyses are performed in larger studies to clarify whether a presumed treatment effect can be generalized over many clinically relevant conditions.

The main finding was an overall positive effect over nearly all subgroups, with an odds ratio of 0.70 in favor of CRT. The study was not powered to show a benefit in NYHA functional class I patients alone and, therefore, statistical significance for this small group of patients should not be expected. Nonetheless, the results indeed favor CRT ON in NYHA functional class I patients with an odds ratio of 0.87. Improvements in left ventricular end-systolic volume index between NYHA functional class I and II patients were substantial in both NYHA functional class I and II groups as well as for patients with and without diuretics. Diuretics were not randomized in any way. The on-diuretics group included both CRT ON and CRT OFF patients, so if “diuretics by themselves may have accounted for the documented beneficial effect,” then both CRT ON and CRT OFF patients would have shown the same improvement. Therefore, this is not a confounding variable.

We thus believe that our conclusion, that CRT reduces the risk for HF hospitalization and reverses LV remodeling over the course of 12 months in patients with American College of Cardiology/American Heart Association stage C, NYHA functional class I and II HF, raising the possibility that CRT might delay disease progression in HF patients with mild HF through LV reverse remodeling, is valid. Because the REVERSE study was not dimensioned as a morbidity/mortality trial we will have to wait for the ongoing MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy) and RAFT (Resynchronization/defibrillation for Ambulatory heart Failure Trial) studies and the 24-month REVERSE study results to obtain the final answer as to whether CRT may modify disease progression in mildly symptomatic HF patients (4,5).

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Early Repolarization in the Athlete

An “abnormal” resting electrocardiogram is common in top-ranking, endurance-trained athletes (1). These abnormalities belong to physiological changes induced by training, as sinus bradycardia, high QRS and T-wave voltages, and early repolarization (ER), consisting of an elevation of QRS–ST junction, or a QRS notching/slurring. Until now, ER has been considered benign (2).

In a previous article (3), we underlined differences between ventricular repolarization anomalies in top-level athletes and those present in patients with Brugada syndrome. ER was observed in 89% of athletes, a value largely different from what was recently observed by Rosso et al. (4) in a young athletic group (22%).

The difference in ER prevalence between our athletes and those studied by Rosso et al. (4) could be that the former were competitive athletes and the Rosso et al. (4) subjects were noncompetitive. Moreover, in this study, different from the control group, the athletic patients were not age-matched with patients with idiopathic ventricular fibrillation (IVF) and were younger (range 17 to 19 years vs. 24 to 70 years). So, the difference in the prevalence of J-point elevation in IVF subjects (42%) may be due more to the younger age than to athletic conditioning. We observed a similar ER prevalence (36%) in our young nonathletic controls (mean age, 25 years) (3).

Recently, it was suggested that, in some cases, ER may not be benign (4,5). We would like to stress that top-level endurance-trained athletes represent a peculiar group of subjects in whom ER and some other electrocardiogram anomalies are almost the rule. None of our athletes has suffered from major ventricular arrhythmias from the time of the study onward (3). In this way, the meaning of ER, in particular, in left pre-cordial leads, especially when associated with high QRS and T-wave voltages, must be considered a complete benign phenomenon, reversible after a few months of detraining.

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Reply

Drs. Bianco and Zeppilli point out that the prevalence of the “early repolarization” pattern among athletes included as controls in our study (1) is lower than the prevalence observed in their own series of athletes (2) (22% vs. 89%). In fact, the prevalence of this electrocardiographic phenomenon among athletes varies in different series from 7% to 100% (3,4). These large discrepancies are likely due to different definitions of “early repolarization.”

It is not easy to explain the high prevalence of “early repolarization” among athletes. Increased vagal tone may play a role. However, early repolarization is not abolished by autonomic blockade (5). Also, young males have more early repolarization (6). Therefore, differences in ion-current density at different myocardial layers (6), mediated by myocardial androgen receptors (7), may underlie the changes in action-potential contour that create the early repolarization pattern (6). Yet, the effects of sports on androgen levels are not trivial. Exercising raises testosterone transiently (8). On the other hand, long-term endurance exercise decreases total- and free-testosterone levels (9).

Three controlled studies showed that J-waves are more prevalent among patients with idiopathic ventricular fibrillation (VF) than among sex- and age-matched controls (10–12). The high prevalence of early repolarization reported in the athletes-series (2–4) should not be extrapolated to the idiopathic-VF series because of the different definitions used. Specifically, idiopathic-VF studies emphasize the presence of J-point elevation; the main finding in athletes was ST-segment elevation (2–4).

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