calculated number of patients necessary (n = 17) in this cross-over trial seems highly underestimated.

In a nearly threefold larger trial of 79 patients from Scandinavia, the same double-blind, cross-over design was used over two periods of three months on coenzyme Q10 100 mg/day or placebo. The beneficial results of this study were presented initially at The American College of Cardiology Meeting in 1992 (JACC 1992; 19:216A, abstract 774–6) and later published in the *Journal of Cardiac Failure* (3). Watson et al. (1) have not included this trial in their reference list.

In the Scandinavian Multicenter Study, a balanced randomization was used with respect to the diagnosis of ischemic versus nonischemic disease and the treatment with or without an angiotensin-converting enzyme inhibitor. There was a slight improvement on LV ejection fraction at volume load based on the results from the MUGA scans ($p = 0.025$). Maximal exercise capacity increased slightly but significantly ($p = 0.016$) and coenzyme Q10 mediated a significant decrease in the scoring for dyspnea ($p = 0.007$) and leg fatigue ($p = 0.04$) at end-exercise (using the Borg-scale). According to the scoring from the Quality of Life Questionnaire, the total score ($p = 0.016$), the physical activity level ($p = 0.048$) and the life satisfaction ($p = 0.016$) increased significantly during the coenzyme Q10 period.

During the last 15 years, only 2 of 12 double-blind heart-failure trials have been "neutral" (i.e., without positive effect or side effects), whereas the remaining 10 studies have been positive and statistically significant with respect to improvement in clinical and or hemodynamic parameters (4). In Watson and colleagues' "neutral study," adequate methods to assess myocardial function were used, but obviously the trial was insufficiently powerful to confirm or reject the hypothesized increase in LV function.

Svend Aage Mortensen, MD, DSc, FESC
Heart Center
Rigshopitalet
University Hospital of Copenhagen
Copenhagen, Denmark

PII S0735-1097(00)00668-9

REFERENCES

1. Watson PS, Scalia GM, Galbraith A, Burstow DJ, Bett N, Aroney CN. Lack of effect of coenzyme Q on left ventricular function in patients with congestive heart failure. J Am Coll Cardiol 1999;33:1549–52.
2. Waston PS, Scalia GM, Galbraith A, Burstow DJ, Bett N, Aroney CN. Lack of effect of coenzyme Q10 on left ventricular function in patients with congestive heart failure. Proceedings from an International Symposium: Oxidative Pathways in Health and Disease, University of Sydney, Australia, December 1–4, 1999.
3. Hofman-Bang C, Rehnquist N, Swedberg K, Wiklund I, Åström H, for the Q10 Study Group. Coenzyme Q10 as an adjunctive in the treatment of chronic congestive heart failure. J Card Fail 1995;1:101–7.
4. Overvad K, Diamant B, Holm L, Hølmer G, Mortensen SA, Stender S. Coenzyme Q10 in health and disease. Eur J Clin Nutr 1999;53:764–70.

REPLY

We thank Dr. Mortensen for his interest in our study (1). We assure him that the data we reported on patient demographics are correct—that over three-quarters of our patients suffered from dilated cardiomyopathy while the remainder had coronary heart disease. When we stated that we would require 17 patients in order to demonstrate an increase in left ventricular ejection fraction from 25% to 30% with a standard deviation (SD) of 5% using 95% confidence intervals (CI) with a power of 80% (1), we did no more than calculate the probability that our failure to show such as change (a negative study) would reflect a true lack of effort.

The design of the Scandinavian study to which Dr. Mortensen refers (2) was very similar to that of our trial. Despite having nearly three times as many patients, it also failed to show any significant difference ($p < 0.05$) in this primary end point. The study reported by Permanetter et al. (3) also failed to show any therapeutic effect of coenzyme Q_{10}. Meta-analysis of clinical trials of coenzyme Q_{10} treatment of congestive heart failure might be seen as encouraging but cannot be taken as any more than an argument for more blinded control studies (4,5).

We agree with Dr. Mortensen that if agents such as coenzyme Q_{10} are to be helpful, this would more likely be demonstrable early in the course of heart failure. Unfortunately, success in treating chronic failure with angiotensin-converting enzyme inhibitors (6), beta-adrenergic blockers (7), and spironolactone (8) means that it has become increasingly difficult to recruit patients for trials of unproven agents until they have been stabilized on what must now be regarded as standard therapy.

Paul S. Watson, MB, BS, FRACP
Gregory M. Scalia, MB, BS, FRACP
Andrew Galbraith, MB, BS, FRACP
Darryl J. Burstow, MB, BS, FRACP
Nicholas Bett, MB, BS, FRACP
Constantine N. Aroney, MD, BS, FRACP
Department of Cardiology and Heart Failure and Transplant Unit
The Prince Charles Hospital
Brisbane, Australia

PII S0735-1097(00)00667-7

REFERENCES

1. Watson PS, Scalia GM, Galbraith A, Burstow DJ, Bett N, Aroney CN. Lack of effect of coenzyme Q on left ventricular function in patients with congestive heart failure. J Am Coll Cardiol 1999;33:1549–52.
2. Hofman-Bang C, Rehnqvist N, Swedberg K, Wiklund I, Åström H. Coenzyme Q_{10} as an adjunctive in the treatment of chronic congestive heart failure. The Q10 Study Group. J Card Fail 1995;1:101–7.
3. Permanetter B, Rossy W, Klein G, Weingartner F, Seidl KF, Blomer H. Ubiquinone (coenzyme Q_{10}) in the long-term treatment of idiopathic dilated cardiomyopathy. Eur Heart J 1992;13:1527–33.
4. Soja AM, Mortensen SA. Treatment of chronic cardiac insufficiency with coenzyme Q_{10}: results of meta-analysis in controlled clinical trials. Ugeskr Laeger 1997;159:7302–8.
5. Overvad K, Diamant B, Holm L, Holmer G, Mortensen SA, Stender S. Coenzyme Q_{10} in health and disease. Eur J Clin Nutr 1999;53:764–70.
6. Yusuf S, Garg R, McConachie D. Effect of angiotensin-converting enzyme inhibitors in left ventricular dysfunction: results of the studies of left ventricular dysfunction in the context of other similar trials. J Cardiovasc Pharmacol 1993;22:S28–35.
7. Heidenreich PA, Lee TT, Massie BM. Effect of beta-blockade on mortality in patients with heart failure: a meta-analysis of randomized clinical trials. J Am Coll Cardiol 1997;30:27–34.
8. Pitt B, Zannad F, Remme WJ, et al. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. Randomized Aldactone Evaluation Study Investigators. N Engl J Med 1999; 341:709–17.