Dear Prof. Van de Werf

Williams et al. raise interesting questions on our study design.1 In general, a parallel group study with a significant difference in survival — all other comparisons must be interpreted with caution, partly because the original balanced groups may be distorted and partly because patients completing and providing data may be selected, but the result is still relevant from a clinical perspective. It is indeed true that exercise capacity was identical in patients who survived and completed the study. Therefore, in clinical practice, we cannot expect to obtain improved exercise capacity in the average patient receiving an ACE inhibitor.

Williams et al. imply that a crossover study would have been preferable. In such a study design patients who die only complete part of the study, and the comparison is made only on patients who survive, but this change in design removes only some of the bias of a parallel group study. The baseline characteristic balance is strictly maintained with patients being their own control, but the bias introduced by selected patients surviving is important in this type of study design. The crossover study with only selected patients completing the study is difficult to extrapolate to clinical practice. A crossover study introduces further hazards of carryover and time-dependent effects. Therefore, it is fair to say that there is no ideal way of studying exercise tolerance and other non-fatal phenomena whenever the intervention has a substantial effect on survival.

Finally, we have to correct a misunderstanding of the numbers of dropouts. As it is shown in Table 2 and Fig. 1, out of 254 patients who participated in the first exercise test, 196 patients ended 1-year follow-up. Thus, only 58 (23%) patients were withdrawn or died — a difference that was not statistically significant in a comparison of the two treatment arms.

References
1. Abdulla J, Burchardt H, Abildstrøm SZ et al. The angiotensin enzyme inhibitor trandolapril has neutral effect on exercise tolerance or functional class in patients with myocardial infarction and reduced ventricular systolic function.
2. Blocking only one pathway does not necessarily predict stent restenosis (and/or in-stent thrombosis) and/or a worse clinical outcome.7 The medical community urgently needs a large, well-designed prospective trial, using the three tests — all together — as surrogate end-point for platelet function in order to conclude this dilemma and better guide our daily practice. Until then, physicians are urged to continue implement the guidelines and prescribe statins to CAD patients with or without clopidogrel coadministration.