Among systolic HF patients, low SDC was associated with a 3% absolute reduction (compared to 34% mortality in the placebo group, 31% of patients with low SDC died during the study) and a 22% relative reduction (adjusted hazard ratio 0.78, 95% CI, 0.68–0.87; P < 0.0001) in all-cause mortality. Similarly, among diastolic HF patients, low SDC was associated with a 4% absolute reduction (compared to 23% mortality in the placebo group, 19% of patients with low SDC died during the study) and a 25% relative reduction (adjusted hazard ratio 0.75, 95% CI, 0.43–1.31; P = 0.313) in all-cause mortality. Thus, although Dr Rahimtoola is correct that the mortality difference in the diastolic HF group did not achieve conventional statistical significance, we believe that the overall study findings are most consistent with the view that digoxin at low SDC reduces mortality by about 20–25%, independent of ejection fraction.

To further clarify this issue, a more detailed analysis of the DIG ancillary trial, including Kaplan–Meier curves, will be the subject of a future report.3

References


An open label, single-centre, randomized trial of spinal cord stimulation vs. percutaneous myocardial laser revascularization in patients with refractory angina pectoris: the SPIRiT trial

McNab et al.1 are to be congratulated to have performed the first randomized controlled trial (RCT) to compare percutaneous myocardial laser revascularization (PMR) with spinal cord stimulation (SCS). The results are encouraging and confirm previous results on both therapy modalities.

In the introduction, they have mentioned the many techniques for patients with refractory angina. They have stated that there is little evidence directly comparing these multiple therapeutic modalities, not mentioning the RCT performed by Tio et al.2 to compare PMR with vascular endothelial growth factor.

We would like to draw the attention to the introduction, where they have stated that SCS is supported by one RCT, however, at the end of the next paragraph they refer to another RCT of SCS, which is one of several RCT’s to support SCS.3

This study’s primary objective was to compare the effect of SCS vs. PMR on treadmill exercise time (ETT) over a periods of 12 months. They report that the difference in total exercise time at 12 months, adjusted for baseline, was 0.59 min between both groups (P = 0.466).

In the methods, they describe that they additionally assessed the change in ETT within each group using a paired Student’s t-test. However, these findings are not mentioned in the results. These findings seem important as the ETT within the SCS group increased from 6.38 ± 3.45 to 7.08 ± 0.67, and in the PMR group the ETT decreased from 7.41 ± 3.68 to 7.12 ± 0.71, which in itself is already noteworthy.

Moreover, we do not understand why (only) the ETT duration is not presented consistently [at baseline as mean (SD) and at follow-up as mean (SEM)]. As the SEM gives an idea of the accuracy of the mean and the SD gives an idea of the variability of single observations, it is more appropriate to present data as mean (SEM).

Finally, possible interesting information on the ischaemic burden during ETT is not mentioned in this study. We wonder if this is due to ECG disturbances by active SCS during ETT, and whether they tried to filter these electrical disturbances, as described before by an ambulatory electrocardiographic study.3

It is a well-developed study, giving SpiRiT for future investigations, although it is not quite clear where SPIRiT stands for.

References


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Online publish-ahead-of-print 2 June 2006
Letters to the Editor

Online publish-ahead-of-print 2 June 2006

An open label, single-centre, randomized trial of spinal cord stimulation vs. percutaneous myocardial laser revascularization in patients with refractory angina pectoris: the SPIRiT trial: reply

We thank Dr de Vries and colleagues for their comments. In response, we would like to make the following points.

First, with regards to the study by Tio et al.,1 in our introduction, we did not intend to present a comprehensive review of all treatments for refractory angina, only to highlight the paucity of randomized trial data. Dr de Vries and colleagues correctly state that there are other randomized studies of spinal cord stimulation (SCS), apart from the ESBY study that we cited in our introduction, that fulfil accepted criteria to be deemed ‘trials.’ However, these other studies suffer from methodological issues that we felt were sufficiently important that their results should best be considered as hypothesis generating rather than supporting. Typically, these studies had small sample sizes (10–12 per group) and no sample size calculation, yet reported multiple outcomes (the study cited, for example, enrolled 12 patients in the SCS group and 13 controls). We should have been more explicit in our reasoning for proposing that the ESBY study was the only randomized trial to support SCS.

Secondly, this study was not powered for within group analyses and there are justifiable concerns that such findings may represent regression to the mean. These data were contained in original submissions but removed as a result of criticism from multiple reviewers.

Thirdly, baseline data were summarized as mean (SD) to enable the population from which these subjects were drawn to be characterized. As some patients did not experience angina during the exercise test, time to angina was estimated from Kaplan–Meier survival curves, and summarised as mean (SEM). All follow-up data were reported as mean (SEM) as we are interested in the precision of the mean estimates.

Next, with regards to the ischaemic burden during exercise tolerance test, this was not an a priori endpoint. As a generalization, one of our concerns regarding the literature in this field is the tendency of studies to report positive secondary outcomes when the primary outcome is negative. This is particularly the case when studies have not been adequately powered for such secondary endpoints. Nevertheless, following the comments of Dr de Vries and colleagues we have analysed these data and can report there is no significant difference between the two groups.

Finally, the SPIRiT acronym was the source of some mirth during the study as participants and workers alike struggled to find the meaning in its form. The origin may be found (with some imagination to be fair) in the Spinal cord stimulation vs. Percutaneous myocardial laser revascularization Randomised Trial.

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doi:10.1093/eurheartj/ehl050

Online publish-ahead-of-print 2 May 2006

Obstructive sleep apnoea: hypoapnoea syndrome reversibly depresses cardiac response to exercise

As a research team interested in both obstructive sleep apnoea syndrome (OSAS) and exercise physiology, we read with great interest the recent publication of Alonso-Fernandez et al.1 regarding the cardiac response of OSAS patients during exercise and its modification by continuous positive airway pressure (CPAP). We greatly appreciate the design of this study dealing with such a relevant subject. Indeed, metabolic and cardiovascular abnormalities encountered in OSAS may account for exercise intolerance and fatigability reported in these patients.2 Hence, physiological adaptations in OSAS patients at exercise deserve attention. However, we are greatly concerned with the stroke volume (SV) and cardiac output (Qc) values reported in this study. According to Figure 2, at 60% maximal workload, SV reached 200 mL and Qc reached 30 L min⁻¹ in the control group. Such values are surprising and in the same range as that measured in high-level endurance cyclists.3 Taking into account a Qc of 30 L min⁻¹ and assuming a mean oxygen extraction of 0.12 L min⁻¹ at 60% VO₂peak (direct Fick method) in healthy subjects, oxygen consumption recalculation leads to 41 mL min⁻¹ kg⁻¹ (3.6 L min⁻¹, average body weight of 88 kg), a value greater than VO₂peak measured in the control group i.e. an average of 25 mL min⁻¹ kg⁻¹. An extrapolation to maximal exercise intensity would lead to a VO₂peak of 60 mL min⁻¹ kg⁻¹. A part of the Qc and SV values determined in this study is not valid and may weaken the conclusions of this well-designed paper. At first, owing to the apparent overestimation of Qc in controls [but normal in OSAS as Qc = VO₂/(0.0572 + (0.0011%VO₂max))], the first conclusion stating OSAS is associated with a lower Qc and SV response during exercise may be disputed. Secondly, although the reproducibility of cardiac indexes between baseline and sham-CPAP is very reassuring, the Qc of at least nine subjects treated with CPAP seemed to be greatly overestimated (Figure 3). We cannot assert these overestimations would challenge the positive effect of CPAP on cardiac indexes. However, abnormally high Qc values obtained with CO₂ re-breathing method should be taken as indicative rather than definitive evidence that CPAP improved Qc in OSAS patients.