Reviewer's report

Title: Eccentric Exercise versus Usual-Care with Older Cancer Survivors: The Impact on Muscle and Mobility-A Randomized Clinical Trial

Version: 1 Date: 24 September 2010

Reviewer: Lee Jones

Reviewer's report:

Major Compulsory Revisions

This paper describes the efficacy of a supervised exercise intervention (eccentric resistance training), relative to usual care control, on muscle strength, size, power, and functional capacity in a heterogeneous sample of 40 older cancer survivors. The exercise intervention was conducted three times/week for 12 weeks. Authors reported significant improvements in several study endpoints following exercise training. It was concluded that eccentric resistance training was feasible, safe, and efficacious for older cancer survivors.

The efficacy of resistance training in older cancer survivors who may be at higher risk of cachexia and frailty addresses an important question, however, this study has several major methodological limitations that considerably dampen my enthusiasm for this paper. Of these, the most important is subject recruitment and randomization. The authors state that this is a randomized controlled trial (RCT) but this is not correct. In the results section, the authors state that a total of 49 patients were ‘randomized’ to study groups (n=28 exercise group, n=21 control group) but this imbalance resulted from 8 patients dropping out during the intervention period, however the imbalance appears to have occurred prior to patient drop-out. Furthermore, it is then stated that ‘because of the exploratory nature of the study, after a drop-out, the next group assignment was to the group that experienced the drop-out to ensure equal numbers in the groups. As described, this no longer appears to be randomization but rather forced allocation into experimental groups. As such, the trial can not be described as ‘randomized’ which raises concerns about study validity. Finally, the patients that were lost-to-follow-up were excluded from final analyses so the results do not follow the fundamental intention-to-treat principle for randomized controlled trials.

Another major issue is the statistical analysis. For example, it is stated in the statistical analysis section that the primary analysis focused on the group x time interaction effect, suggesting that authors examined between group differences in study outcomes over the course of the intervention (baseline to 12 weeks), which would be appropriate for an apparent RCT design. However, it is not clear if this approach was followed. For example, when describing the muscle size results, the authors describe that ‘post-intervention’ cross sectional area was a statistically significant group x time interaction (p=0.001). However, a close inspection of the presented data indicates virtually no within group changes in
this endpoint over the course of the intervention. Thus, it is not clear how the significant group x time interaction effect was achieved. Furthermore, there was a statistically significant difference between groups on this endpoint at baseline (prior to randomization) that favored the control group but it is not explained how differences in endpoints at baseline were handled in the change score analysis. This pattern of analysis and results is repeated for virtually all study endpoints. The entire statistical analysis section needs to be clarified and repeated with inclusion of data from subjects that were lost-to-follow-up.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

'I declare that I have no competing interests'