

Correspondence

Commentary on aerobic versus isometric handgrip exercise in hypertension: a randomized controlled trial

Neil A. Smart^a, Debra J. Carlson^a, Ian Swaine^b, and Cheri McGowan^c

We, members of the International Working Group on Isometric Exercise, read with great interest the article by Pagonas *et al.* on the comparative effects of aerobic and isometric handgrip exercise (IRT). However, we believe the finding, that aerobic exercise induces reductions in blood pressure (BP), whereas isometric exercise training (handgrip) does not, to be compromised for several reasons:

First, the groups were not matched at baseline for resting SBP (office SBP – Table 2) differed by an egregious 8.8 mmHg between IRT and aerobic groups. Millar *et al.* [1] showed, some years ago, that account must be taken of baseline BP values, when analysing training-induced changes. The probability that a 9-mmHg differences in resting blood occurred by chance in a properly randomized study is very remote; moreover, the authors reported that this difference was not statistically significant ($P=0.36$). Because of these sizeable differences in baseline BP measures, the aerobic training group clearly had greater potential to regress to the mean.

The randomized allocation of patients into the three groups appears to have introduced selection bias. In the aerobic training group, 11 patients performed more than three exercise sessions weekly at baseline, compared with only six patients, doing a similar amount of aerobic exercise, in the handgrip training group. Moreover, the authors' stated there was no statistical significance of this, but the second paragraph of the results states that the significance level was less than 0.05. Surely, if the difference was NS, would it be more than 0.05? This also illustrates concerns about the 'parity' of the training stimulus provided to the patient groups. It is likely that about 40% of the aerobic training group were performing the precise training dose (of 2.5 h/week). When one considers that this aerobic exercise was neither structured nor supervised (unlike the isometric exercise – which is carefully controlled at a precise dose). We cannot ascertain the IRT as the maximum voluntary contraction (MVC) values are not reported by Pagonas *et al.* In order for the reader to determine whether the isometric training stimulus was adequate, MVC values before and after training should be shown. In most previous studies, an increase in MVC after training confirms the adequacy of the isometric training stimulus.

A suggestion of attrition bias could also be levelled Pagonas *et al.*'s study because of the 25% drop-out rate in the aerobic group. Although this is at the upper end of expectations, it is not atypical in aerobic studies. Nevertheless, an intention to

treat analysis showed significant antihypertensive effects disappear when the nonadherent patients are included in the aerobic group analysis. This indicates the primary analysis was flawed, as statistical significance would have emphasized the most dedicated 75% of the original aerobic group; the authors' conclusions about the relative superiority of aerobic exercise are incorrect. We do, however, acknowledge that aerobic exercise offers additional physiological adaptations that are unlikely with handgrip training, such as changes in lipoprotein subfractions and cardiorespiratory fitness improvements.

We are also concerned because Pagonas *et al.*'s study is clearly underpowered. The size of the baseline BP SDs, especially office BP – upon which the study seems to have been powered, were estimated at ± 10 mmHg when in fact most SD values for change in BPs are above ± 14 mmHg. This underestimation would have compromised the sample size calculation. In fact, one group mean office SBP SD was 22.7 mmHg, which would require a sample size of over 200 participants to show the desired 7 mmHg reduction in SBP!

Although numerous studies in hypertensive populations use bilateral handgrip training interventions, we do have additional concerns about its use in the current study based on recent meta-analysis findings. In brief, Inder *et al.* [2] showed that bilateral interventions appear to be suboptimal for isometric training-induced BP reduction. We suspect that IRT lowers BP through a local and not systemic effect, so, the study design, which alternates the hand grip exercise would have diluted the local muscle effects of IRT in that group. Furthermore, it is unclear if participants in all groups were asked to refrain from aerobic physical activity at least 24 h prior to their testing sessions. It is possible that participants from the aerobic training group had the benefit of postexercise hypotension at their posttesting session, and we are unsure this was not controlled. At the very least, these should be acknowledged as potential limitations of the study.

Finally, there are several incorrect statements or omissions that should be corrected via an erratum. First, in the Introduction, the authors state 'there is no data on the effects of isometric exercise on 24-h ambulatory BP...in patients with hypertension'. This is incorrect, as Stiller-Moldovan *et al.* [3] (no. 24 in the current reference list) observed clinically relevant reductions in mean 24-h ambulatory BP in a population of well controlled medicated hypertensive patients. This should also be reflected on Pg. 6 in the discussion of no. 24 findings. A second point for correction relates to the statement that the study of Pagonas *et al.* is NOT the first to utilize a sham low-intensity control group working at 5% MVC. Previous research has utilized low-intensity isometric training, the most recent was published in December 2016, Carlson *et al.* [4]. Third, the statement 'There are no homogenous results on hypertensive patients' on Pg. 6 is misleading. Pagonas *et al.* failed to cite the recent randomized controlled trial of isometric handgrip training in medicated hypertensive patients conducted by Badrov *et al.* [5] which supported handgrip-induced BP-lowering effects, and the supportive trial of Taylor *et al.* [6] (Pagonas *et al.* reference no. 26) was also

omitted. Fourth, the statement ‘Hence, handgrip exercise was not included in the current guidelines on treatment of hypertension’ on Pg. 6 is also misleading. Handgrip exercise is recommended as an adjunct to traditional aerobic exercise in both the 2013 American Heart Association Position Statement [7] entitled ‘Beyond Medications and Diet: Alternative Approaches to Lowering Blood Pressure A Scientific Statement From the American Heart Association’, the 2016 Canadian Hypertension Guidelines [8] as well as Australian guidelines [9].

We strongly urge more-carefully considered study designs and reporting in comparative studies like the one of Pagonas *et al.* Compromised randomization of patients, use of small sample sizes and use of bilateral limb prescriptions should all be avoided. Isometric training is a valuable adjunct therapy to manage hypertension, and compromised study designs and subsequent analyses such as this one erroneously prevent the transition of this valuable tool into clinical practice.

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Conflicts of interest

There are no conflicts of interest.

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^aSchool of Science and Technology, University of New England, Armidale, New South Wales, Australia, ^bCentre for Science and Medicine in Sport and Exercise, University of Greenwich, Chatham Maritime, Kent, UK and ^cDepartment of Kinesiology, University of Windsor, Windsor, Ontario, Canada

Correspondence to Neil A. Smart, PhD, School of Science and Technology, University of New England, Armidale, New South Wales, Australia. Tel: +61 416176288; fax: +61 267735011; e-mail: nsmart2@une.edu.au