6. Segal N, Davis MD, Mikesky AE. Efficacy of blood flow-restricted low-load resistance training for quadriceps strengthening in men at risk of symptomatic knee osteoarthritis. *Geriatr Orthop Surg Rehabil*. 2015;6(3):160–167.
7. Centner C, Wiegel P, Gollhofer A, König D. Effects of blood flow restriction training on muscular strength and hypertrophy in older individuals: A systematic review and meta-analysis. *Sports Med*. 2019;49(1):95–108.
8. Hughes L, Paton B, Rosenblatt B, Gissane C, Patterson SD. Blood flow restriction training in clinical musculoskeletal rehabilitation: A systematic review and meta-analysis. *BrJ Sports Med*. 2017;51(13):1003–1011.
9. Cerqueira MS, de Brito Vieira WH. Effects of blood flow restriction exercise with very low load and low volume in patients with knee osteoarthritis: Protocol for a randomized trial. *Trials*. 2019;20(1):135.
10. Hughes L, Rosenblatt B, Haddad F, et al. Comparing the effectiveness of blood flow restriction and traditional heavy load resistance training in the post-surgery rehabilitation of anterior cruciate ligament reconstruction patients: A UK national health service randomised controlled trial. *Sports Med*. 2019;49(11):1787–1805.

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Reply to letter to the Editor about the article ''The addition of blood flow restriction to resistance exercise in individuals with knee pain: a systematic review and meta-analysis''

Dear Editor

We appreciate the comments on our article ''The addition of blood flow restriction to resistance exercise in individuals with knee pain: a systematic review and meta-analysis'' (Cuyul-Vásquez et al.[1]). We would like to take the opportunity to address several points raised in these comments.

First, it is important to consider that performing subgroup analyses for meta-analysis with less than 10 studies and with high heterogeneity among the included studies, is not recommended.[2,3] In our meta-analysis for pain intensity, the small number of included clinical trials (n = 5), the considerable heterogeneity (i^2 = 76%) of these trials, and the lack of plausible interaction, justify our decision not to report a subgroup analysis. We understand how the contrast between the results of previous investigations and the findings of our study could be questioned. For this reason, in response to your letter, we performed a subgroup analysis for pain intensity, independently combining studies that used high intensity versus low intensity resistance exercises in the control group.

The comparison between low intensity resistance exercise (30%-1RM) combined with blood flow restriction (BFR) versus high intensity resistance exercise (70% -1RM),[4–6] showed no benefits of BFR for pain relief (pooled SMD = -0.08, 95% CI = -0.41, 0.26, p = 0.66, I^2: 0%). For the comparison between low intensity resistance exercise (30%-1RM) with or without BFR,[4,7,8] the pooled SMD also showed no added effectiveness of BFR on pain relief (SMD= -0.51, 95% CI = -1.57, 0.55, p = 0.34, I^2: 87%). Therefore, both comparisons are not statistically and clinically significant.[9] While this subgroup analysis is affected by the limitations described in the first point of this letter, these findings support the conclusions of our systematic review with meta-analysis, that adding BFR to resistance exercise does not provide additional benefits to decrease knee pain.[1]

Conflicts of interest

The authors declare no conflicts of interest.

References

1. Cuyul-Vásquez I, Leiva-Sepúlveda A, Catalán-Medalla O, Araya-Quintanilla F, Gutiérrez-Espinoza H. The addition of blood flow restriction to resistance exercise in individuals with knee pain: A systematic review and meta-analysis. *Braz J Phys Ther*. 2020;24(6):465–478.
2. Richardson M, Garner P, Donegan S. Interpretation of subgroup analyses in systematic reviews: A tutorial. *Clin Epidemiol Glob Heal*. 2019;7(2):192–198.
3. Higgins JPT, Thomas J, Chandler J., Cumpston M., Li T., Page M.J., Welch VA. Cochrane Handbook for Systematic Reviews of Interventions version 6.0 (updated July 2019). Cochrane, 2019. Available from www.training.cochrane.org/handbook.
4. Ferraz RB, Gualano B, Rodrigues R, et al. Benefits of resistance training with blood flow restriction in knee osteoarthritis. *Med Sci Sports Exerc*. 2018;50(5):897–905.
5. Bryk FF, dos Reis AC, Fingerhut D, et al. Exercises with partial vascular occlusion in patients with knee osteoarthritis: A randomized clinical trial. *Knee Surg Sports Traumatol Arthrosc*. 2016;24(5):1580–1586.
6. Giles L, Webster KE, Mcclelland J, Cook JL. Quadriceps strengthening with and without blood flow restriction in the treatment of patellofemoral pain: A double-blind randomised trial. *Br J Sports Med*. 2017;51(23):1688–1694.
7. Segal N, Davis MD, Mikesky AE. Efficacy of blood flow-restricted low-load resistance training for quadriceps strengthening in men at risk of symptomatic knee osteoarthritis. *Geriatr Orthop Surg Rehabil*. 2015;6(3):160–167.
8. Segal NA, Williams GN, Davis MC, Wallace RB, Mikesky AE. Efficacy of blood flow-restricted, low-load resistance training in women with risk factors for symptomatic knee osteoarthritis. *PM R*. 2015;7(4):376–384.

9. Lee AC, Driban JB, Price LL, Harvey WF, Rodday AM, Wang C. Responsiveness and minimally important differences for 4 patient-reported outcomes measurement information system short forms: Physical function, pain interference, depression, and anxiety in knee osteoarthritis. *J Pain*. 2017;18(9):1096–1110.

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Second letter to the Editor about the article ''The addition of blood flow restriction to resistance exercise in individuals with knee pain: a systematic review and meta-analysis''

We read with interest the recent systematic review entitled ''The addition of blood flow restriction to resistance exercise in individuals with knee pain: a systematic review and meta-analysis'' by Cuyul-Vásquez et al.[1]

The use of blood flow restriction (BFR) by musculoskeletal rehabilitation and sports medicine professionals is increasingly popular which makes this systematic review an important addition. Although the authors reported that they conducted the review following recommendations in the Cochrane Handbook,[2] there are some important departures, which have likely introduced biases and inconsistencies we would like to draw attention to.

Our first concern is how the data for pain reduction (Fig. 3A in Cuyul-Vásquez et al.[1]) were extracted and pooled. Their results suggest no difference between interventions (SMD = −0.37, 95% CI: −0.93, 0.19) at short-term follow-up.

On close inspection of the raw data used to generate the described effect sizes, we suspect a few critical errors may have inadvertently crept into the final analyses which have influenced the ultimate outcomes as calculated and reported. Firstly, the authors appear to have not imported and pooled homogenous outcome measures, but instead different methods of calculating these measures. Specifically, it is hard to justify pooling ''mean ± standard deviation (SD)'' values for Numerical Pain Rating Scale (NPRS), Visual Analogue Scale (VAS), and Western Ontario and McMaster Universities Osteoarthritis Index pain subscale ($WOMAC_{pain}$),[3–5] along with ''mean difference ± SD'' values for Knee injury and Osteoarthritis Outcome Score pain subscale ($KOOS_{pain}$),[6] and ''percentage (%) mean difference ± SD'' values for $KOOS_{pain}$,[7] notwithstanding the use of standardized mean differences (SMD). Furthermore, it would appear that the direction of the effect estimate has been reversed in one study.[7] The net effect of this is that the effect estimate in the study of Segal et al.[7] is overestimated 4.5 times, and the overall effect size has been extremely (37 times) overestimated based on our calculations (SMD = −0.010, 95% CI: −0.267, 0.247) as depicted in Fig. 1A. In addition, they excluded from the meta-analyses a study[8] that reported pain outcomes ($KOOS_{pain}$) that appears to meet their inclusion criteria for quantitative synthesis (SMD = −0.058, 95% CI: −0.311, 0.236 — Fig. 1B) given the clinical heterogeneity of the studies pooled in this review.[9]

Another concern is how the authors' reported and selected data throughout the review. Specifically: (a) the corresponding sample sizes for the included studies deviate from the numbers reported in original publications, for example in Giles et al.,[5] the sample of the strengthening group was n = 39 and not 30; (b) the inclusion of a single-session study by Korakakis et al.,[10] that does not meet the inclusion criteria (i.e. treatment duration between two weeks to three months); (c) the exclusion from the knee function meta-analysis of studies reporting relevant outcome measures, such as the Kujala patellofemoral score[5] and KOOS.[8]

The pooling of heterogeneous outcome measures, the discrepancies in eligible studies, and the overestimation of the pooled effect estimate suggest that these recommendations on the effectiveness of BFR should be interpreted with some caution until the authors provide clarification. Anecdotally, BFR training is very common,[11,12] however is also associated with potentially serious side effects[13,14] and decisions on its use need to be based upon unbiased summaries of the available evidence.