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Original Study

Load-Specific Inflammation Mediating Effects of Resistance Training in Older Persons

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A B S T R A C T

Background: Little is known about the effects of resistance training (RT) on circulating cytokines in older adults. Also, dose-response relationships remain unclear. This study investigated the impact of RT at different external loads on circulating inflammatory mediators in older community-dwelling individuals.
Methods: Fifty-six community-dwelling older (68 ± 5 years) volunteers were randomized to 12 weeks of supervised RT (×3/week) at either high-resistance training [8 males, 10 females, 2 × 10−15 repetitions at 80% 1 repetition maximum (RM)], low-resistance training (9 males, 10 females, 1 × 80−100 repetitions at 20% 1 RM), or mixed low-resistance training (9 males, 10 females, 1 × 60 repetitions at 20% 1 RM followed by 1 × 10−20 repetitions at 40% 1 RM). Serum was available from 51 out of 56 participants at baseline and after 12 weeks for determination of interleukin (IL)-6, IL-8, IL-10, IL-1β, soluble tumor necrosis factor receptor (sTNFR)1, granulocyte macrophage colony-stimulating factor, and IL-1 receptor antagonist (ra).
Results: Twelve weeks of RT significantly increased sTNFR1 from 2.48 ± 0.57 ng/mL to 2.58 ± 0.59 ng/mL (overall time-effect $P = .033$) and Log IL-8 from 0.38 ± 0.18 pg/mL to 0.53 ± 0.32 pg/mL (overall time-effect $P = .007$). No time X group interaction ($P = .916$) was observed. In males of the high-resistance training group, there was an increase in Log IL-8 (from 0.45 ± 0.16 pg/mL to 0.68 ± 0.19 pg/mL; $P = .005$) and IL-1ra (from 68.60 ± 24.12 pg/mL to 79.56 ± 29.07 pg/mL; $P = .007$). No significant changes were found for the other markers.
Conclusions: Our results show that 12 weeks of supervised RT induced an overall significant increase of circulating IL-8 and sTNFR1, independently from the external load applied. We suggest that exercising until volitional fatigue is the main trigger for exercise-induced responses. However, training at high external load also increased anti-inflammatory IL-1ra in male participants, which might be beneficial in combating low-grade inflammation.

Regular physical exercise is suggested to be beneficial to the immune system as an efficient tool in fighting off chronic low-grade inflammatory profile (CLIP).[1] The beneficial effects of physical exercise on CLIP and age-related diseases are reported to be mediated by molecules produced by contracting skeletal muscles termed myokines.[2] In fact, exercise provokes an acute liberation of inflammatory cytokines, especially interleukin (IL)-6,[3] which is different from the acute phase response in pathologic conditions. The exercise-induced acute elevation in IL-6 is not preceded by increased tumor necrosis factor (TNF)-α levels,[4] but is immediately followed by elevations in IL-1 receptor antagonist (ra) and soluble tumor necrosis factor receptor (sTNFR)[4] (inhibiting IL-1β and TNF-α), and the anti-inflammatory cytokine IL-10. Here, IL-6 is believed to have inflammation-reducing effects, by stimulating immune cells to produce anti-inflammatory

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cytokines.[5,6] In the long term, these acute exercise-induced increases in IL-6 at each exercise session and its accompanying release of inflammation-reducing cytokines are believed to reduce CLIP.

The exercise-induced myokine production seems to be maintained at a higher age; there is a general consensus among exercise immunologists that intensive aerobic exercise training is effective in inducing a robust cytokine response.[7,8] However, given the significant age-related loss of muscle mass and muscle strength, resistance training at high external load [ie, 2–3 sets of 8–12 repetitions at 70%–85% of the 1 repetition maximum (RM)] is of major importance at higher age.[9] Studies on the impact of resistance training on cytokine response in older persons are scarce compared with the extensive literature on aerobic exercise training. In 2005, we demonstrated that a regular resistance training session is sufficient to obtain a significant acute increase in circulating IL-6 in older adults.[10] We[11] have also shown that 12 weeks of resistance exercise significantly reduced the basal levels of IL-6, thus, reflecting lower CLIP. This is consistent with the findings of Peake et al[12] who found a significant decrease in basal IL-6 levels following 12 months resistance training compared with control. In contrast, Bruunsgaard et al[13] reported no change in basal levels of IL-6, TNF-α, and sTNFR1 in frail nursing home residents following 12 weeks of resistance training. This might have been due to the participants' frail state, which could have had a negative impact on the exercise-induced myokine production. Kapasi et al[14] also found no immune-enhancing effects of a 32-week combined exercise training in frail older subjects.

Despite the benefits of resistance training at high external load on muscle mass and strength, many clinicians hesitate to prescribe resistance exercise with high external load in older persons.[15] As an alternative, resistance training at lower external load is often offered to older persons. Onambele-Pearson et al[16] reported a significant decrease in TNF-α levels with a low external (2–4 sets of 8–11 reps at 40% of 1 RM) compared with a high-external load (2–4 sets of 8–11 reps at 80% of 1 RM) protocol,[16] but studies investigating the dose-response relationship of resistance training on CLIP remain scarce. To the best of our knowledge, most studies using low-to-moderate-resistance exercise protocols only reduce the external load without substantially increasing the number of repetitions.[16–19] Taking into account the importance of training to volitional fatigue for optimizing muscular adaptations,[20] a training protocol with both a reduction in the external load as well as a substantial increase of the number of repetitions (until volitional fatigue) might be optimal. Previously, we[21] reported that 12 weeks of high-resistance training (HIGH, 2 × 10–15 repetitions at 80% of 1 RM) led to a higher increase in 1 RM than low-resistance training (LOW, 1 × 80–100 repetitions at 20% of 1 RM) in community-dwelling adults aged 60 and older. However, this difference disappeared when a mixed low-resistance (LOW+, 1 × 60 repetitions at 20% of 1 RM, followed by 1 × 10–20 repetitions at 40% of 1 RM) protocol was compared with HIGH group. In addition, the HIGH, LOW, and LOW+ exercise programs had a similar outcome on muscle hypertrophy.

In the present study we compared the effects of 12 weeks of supervised resistance training at these 3 different external loads (HIGH, LOW, and LOW+) on basal levels of inflammatory mediators in older adults. Therefore, the main objective of this study was to investigate the impact of supervised resistance training at different external loads on peripheral serum circulatory inflammatory mediators in older community-dwelling individuals.

Methods

Study Design and Participants

This was a randomized intervention study. The recruitment strategy and main study procedures have been previously reported in detail.[21] Participants were excluded if they were involved in any structured endurance exercise and/or participated in resistance exercise during the last 6 months before the study, were suffering from hip or knee problems, or showed unstable cardiovascular disease, neuromuscular disease or acute hernia. Briefly, 56 elderly volunteers were enrolled, and allocated to 1 of 3 training protocols: HIGH (n = 18), LOW (n = 19), and LOW+ (n = 19) (Figure 1). Randomization was stratified for sex, age, and baseline isometric knee extension strength. Five participants were excluded (1 from the HIGH, 3 from the LOW, and 1 from the LOW+ intervention group) from all statistical analyses because they lacked serum samples for cytokine analysis at either baseline or at 12 weeks (Figure 1). Each participant gave a written informed consent after reading and understanding the risks and benefits associated with the study. The study protocol was approved by the local ethics committee in accordance with the Declaration of Helsinki.

Resistance Training Protocol

The resistance training program took place at a local fitness and health center for a duration of 12 weeks. The training program has been previously reported.[21] Briefly, after an initial familiarization session in which training techniques were explained and demonstrated, participants exercised 3 times weekly on nonconsecutive days for 12 weeks (total of 36 sessions). The exercises (leg press, leg extension, and seated row) were performed on Technogym (Technogym, Gambettola, Italy) devices, designed for resistance training. Each exercise session started with a brief warm-up (10 minutes) on a cycle ergometer (Technogym Bike Excite, Gambettola, Italy) or on a treadmill (Technogym Run Excite, Gambettola, Italy). Exercises were performed at a moderate speed with rest periods of 2 minutes in between, and the training sessions were closely monitored by qualified fitness instructors. All participants were verbally encouraged to continue the exercises until failure (ie, inability to perform more repetitions because of local muscle fatigue). Immediately after each individual exercise, participants graded their level of perceived exertion on the OMNI-Resistance Exercise Scale of Perceived Exertion (scale from 0 to 10).[22] As described previously,[21] the 1 RM was evaluated every 4 weeks (at baseline, before the first training session in week 5 and week 9, and after 12 weeks of training), and training loads were adapted accordingly. The training volume on the test sessions in week 5 and week 9 was reduced to only the leg extension exercise.

The exercise protocols were designed to be approximately equal in volume (% 1 RM × number of repetitions). The HIGH resistance protocol (2 sets separated by 1-minute intervals of 10–15 repetitions at 80% of 1 RM) was based on ACSM's guidelines for resistance training.[23] These guidelines recommend performing at least 1 set to the point of failure for healthy individuals. In the HIGH group, the external resistance was initially set at 80% of 1 RM. To ensure that maximal effort would be reached at the end of each set, participants were instructed to perform at least 10 to 15 repetitions. Two sets were performed with 1 minute of rest between sets. In the LOW group, participants were instructed to complete 1 set of 80–100 repetitions at 20% of 1 RM. Participants in the LOW+ group were instructed to complete first 60 repetitions at 20% of 1 RM, and immediately afterwards (no rest), the external load was increased to 40% of 1 RM and participants were instructed to perform 10–20 additional repetitions. During every exercise session, participants were asked to perform a maximum number of repetitions. If they could perform more repetitions than the target range (ie, 80–100 or 10–15), the external load was increased. As previously described,[21] adherence (number of training sessions attended as a percentage of the total number of training sessions) to the program was 95.7% in the HIGH group, 95.8% in the LOW group, and 95.3% in the LOW+ group, with no significant differences between groups.