Benefits of Resistance Training with Blood Flow Restriction in Knee Osteoarthritis

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1Applied Physiology and Nutrition Research Group - School of Physical Education and Sport, University of São Paulo, SP, BRAZIL; and 2Rheumatology Division; Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Sao Paulo, SP, BR, University of São Paulo, SP, BRAZIL

ABSTRACT

FERRAZ, R. B., B. GUALANO, R. RODRIGUES, C. O. KURIMORI, R. FULLER, F. R. LIMA, A. L. DE SÁ-PINTO, and H. ROSCHEL. Benefits of Resistance Training with Blood Flow Restriction in Knee Osteoarthritis. Med. Sci. Sports Exerc., Vol. 50, No. 5, pp. 897–905, 2018. Purpose: Evaluate the effects of a low-intensity resistance training (LI-RT) program associated with partial blood flow restriction on selected clinical outcomes in patients with knee osteoarthritis (OA). Methods: Forty-eight women with knee OA were randomized into one of the three groups: LI-RT (30% one repetition maximum [1-RM]) associated (blood flow restriction training [BFRT]) or not (LI-RT) with partial blood flow restriction, and high-intensity resistance training (HI-RT, 80% 1-RM). Patients underwent a 12-wk supervised training program and were assessed for lower-limb 1-RM, quadriceps cross-sectional area, functionality (timed-stands test and timed-up-and-go test), and disease-specific inventory (Western Ontario and McMaster Universities Osteoarthritis Index [WOMAC]) before (PRE) and after (POST) the protocol. Results: Similar within-group increases were observed in leg press (26% and 33%, all \( p < 0.0001 \)), knee extension 1-RM (23% and 22%; all \( p < 0.0001 \)) and cross-sectional area (7% and 8%; all \( p < 0.0001 \)) in BFRT and HI-RT, respectively, and these were significantly greater (all \( p < 0.05 \)) than those of LI-RT. The BFRT and HI-RT showed comparable improvements in timed-stands test (7% and 14%, respectively), with the latter showing greater increases than LI-RT. Timed-up-and-go test scores were not significantly changed within or between groups. WOMAC physical function was improved in BFRT and HI-RT (−49% and −42%, respectively; all \( p < 0.05 \)), and WOMAC pain was improved in BFRT and LI-RT (−45% and −39%, respectively; all \( p < 0.05 \)). Four patients (of 16) were excluded due to exercise-induced knee pain in HI-RT. Conclusions: Blood flow restriction training and HI-RT were similarly effective in increasing muscle strength, quadriceps muscle mass, and functionality in knee OA patients. Importantly, BFRT was also able to improve pain while inducing less joint stress, emerging as a feasible and effective therapeutic adjuvant in OA management. Key Words: ARTHRITIS, CARTILAGE, REHABILITATION, WOMAC, HYPOXIA, KAATSU

Osteoarthritis (OA) is the most common form of arthritis and is considered a major cause of musculoskeletal pain, functional impairment, and reduced independence in older adults worldwide (1). For instance, OA-related knee and hip pain are considered direct causes of impaired walking and stairs climbing in the elderly in Europe and United States, being present in nearly 40% of individuals older than 60 yr (2,3). Osteoarthritis is a heterogeneous chronic disease traditionally characterized by cartilage involvement; currently, however, it is considered to involve the whole joint, including cartilage, subchondral bone, ligament, muscle, and periarticular soft tissues, such as synovial membrane and menisci. The disease encompasses changes in cartilage metabolism and synovial inflammation such as cartilage deterioration, joint space narrowing, osteophytes formation, and sclerosis of the subchondral bone (4).

Quadriceps muscle weakness is considered not only as an important risk factor for OA (5) but also as a main determinant of physical functioning in women with knee OA (6), with repercussions on proprioception (7) and tendency to falls (8). Additionally, a greater loss in lower extremity lean mass has been observed in women with knee OA when compared with healthy controls (9). This reduction in muscle mass is also associated with disease progression (10), pain (11) and with both presence and severity of age-related OA (12,13). Therefore, quadriceps strengthening and hypertrophy is thought as a first-line therapy (14), making resistance training (RT) a common practice within OA management (15,16).

In this respect, it has been postulated that the mechanical overload imposed on the muscle should be between > 65% of the one repetition maximum (1-RM) to improve muscle mass and strength (17). Importantly, patients with OA are often unable to exercise at such high-intensities, limiting the application of conventional high-intensity RT (HI-RT) in OA not only due to pain but also to the pathophysiology of
Recently, a great deal of attention has been drawn to blood flow restriction training (BFRT). It generally combines low-intensity (−20%–40% 1-RM) RT with partial blood flow restriction to the working muscles via inflatable air cuffs fixed in the proximal region of the limbs exercised (20–22). Interestingly, despite the very low intensities adapted in BFRT, it has been shown to promote increases in muscle size and strength comparable to those observed after conventional HI-RT (21,22), constituting a promising strategy for non-pharmacological intervention in OA. In fact, previous work has demonstrated BFRT to be effective in increasing muscle strength in both women at risk for knee OA (23); however, evidence of BFRT efficacy on OA is still scarce. Bryk et al. (24) have provided initial insight into the matter, with data showing BFRT to significantly improve muscle strength. It is worth noting that the authors did not include a control group (i.e., an intensity-matched −30% 1-RM nonocclusion group), limiting the conclusion regarding possible differential effects of BFRT to those of training intensity per se. More importantly, its effects on muscle mass are currently unknown in individuals with knee OA. Given the association between muscle mass and disease progression and other clinical features in OA (10–13), especially in older patients, investigating the effects of BFRT on quadriceps muscle mass constitutes an important clinical question in OA management.

Therefore, the aim of this study was to compare the effects of BFRT to more traditional RT on lower-limb muscle strength and mass, functionally, pain and quality of life in women with OA. We hypothesized that BFRT would result in similar benefits as compared with conventional high-intensity RT while inducing less pain.

**METHODS**

**Study design.** This is a randomized controlled trial conducted between January 2011 and July 2013 in Sao Paulo, Brazil. This study was approved by the local ethical committee and all participants signed an informed consent form before participation. All of the procedures were in accordance with the Helsinki Declaration revised in 2008. The trial was registered at clinicaltrials.gov as NCT01483131. This article was reported according to CONSORT guidelines (25).

Patients were ranked in tertiles according to their 1-RM in the leg press exercise, then they were randomized by a computer-generated code into one of the following conditions: (i) high-intensity resistance training (HI-RT); (ii) low-intensity resistance training (LI-RT), and (iii) LI-RT with blood flow restriction (BFRT).

At baseline (PRE) and after 12 wk of training (POST), we assessed 1-RM leg press and knee extension, physical function (as assessed by timed-stands test [TST] and timed-up-and-go [TUG] tests), quadriceps cross-sectional area (CSA), and self-reported quality of life (as assessed by Short Form Health Survey [SF-36] and Western Ontario and McMaster Universities Osteoarthritis Index [WOMAC]). Self-reported adverse events were recorded throughout the protocol. Experimental design is illustrated elsewhere (see Supplemental Digital Content 1, Experimental design, http://links.lww.com/MSSE/B161).

**Patients.** Women (age between 50 and 65 yr) diagnosed with knee OA according to the American College of Rheumatology criteria (26) were selected to participate in the study. Exclusion criteria were as follows: (i) participation in physical exercise training over the past year; (ii) cardiovascular diseases and/or musculoskeletal disturbances which precluded exercise participation; (iii) Kellgren–Lawrence radiographic grade of 1 or 4; (iv) knee pain numeric Visual Analog Score less than 1 or greater than 8; (v) use of non-steroidal anti-inflammatory drugs over the past three months; (vi) intra-articular infiltration with hyaluronic acid and corticosteroids infiltration over the past 6 months. We decided to include female patients only in this trial, as knee OA is more prevalent in women than in men (1) and to account for sex variability in important variables, such as muscle strength and mass. Table 1 shows the patients’ main features.

**Resistance training programs.** Resistance training was performed in an intrahospital gymnasium (Laboratory of Assessment and Conditioning in Rheumatology, School of Medicine, University of Sao Paulo). Exercise sessions occurred two times a week and were monitored by a fitness professional. The RT program was comprised of bilateral leg press and knee extension exercises using conventional strength training machines (Nakagym®, Sao Paulo, Brazil).

To acquaint the subjects to their training protocols, the first week of training was performed as follows: HI-RT performed four sets of 10 repetitions at 50% 1-RM, whereas LI-RT performed four sets of 15 repetitions at 20% 1-RM. From the second week on, training intensity was increased to 80% and 30% 1-RM for HI-RT and LI-RT, respectively, and from the fifth week on, all groups increased the number of sets performed for each exercise from four to five. Training intensity and load progression for BFRT was exactly the same as those of LI-RT, however, BFRT trained with an air cuff placed at the inguinal fold (width 175 mm × length 920 mm − inflated to 70% of the pressure needed to provide complete blood flow restriction, see description below) to provide partial blood flow restriction. Importantly, the air cuff and, hence, blood flow restriction, was sustained throughout the entire training sessions, including rest intervals, and was released immediately after the end of the session.

A 1-min rest period was allowed between sets for all groups. Exercise load was adjusted every 4 wk by reassessing patients’ 1-RM. Training intensity and blood flow restriction increments are comprehensively described elsewhere (Supplemental Digital Content 2, Progression of training loads, http://links.lww.com/MSSE/B162). A member of the research staff monitored the adherence to the exercise program on a session basis.

**Determination of the blood flow restriction pressure.** Patients were asked to lie on a supine position while
resting comfortably. A vascular Doppler probe (DV-600; Marted, São Paulo, Brazil) was placed over the tibial artery to capture its auscultatory pulse. For the determination of the cuff pressure (mm Hg) necessary for complete blood flow restriction (i.e., pulse elimination pressure), an air cuff was attached to the patient’s thigh (i.e., inguinal fold region), and then inflated up to the point in which the auscultatory pulse was interrupted. Cuff pressure used during the training protocol was determined as 70% of the necessary pressure for complete blood flow restriction in a resting condition. The average cuff pressure necessary for complete blood flow restriction was 139.2 ± 10.8 mm Hg, and average cuff pressure used throughout the training protocol was 97.4 ± 7.6 mm Hg.

**Strength and functional tests.** Before the 1-RM test, two light warm-up sets interspaced by 2 min were performed. Afterward, patients had up to five attempts to achieve the 1-RM load with a 3-min interval between attempts. The 1-RM tests were conducted for the leg press and knee extension exercises according to previous description (27).

Physical function was measured by the TST and the TUG test. An initial reference image was obtained to determine the perpendicular distance from the greater trochanter of the femur to the inferior border of the lateral epicondyle of the femur, which was defined as the segment length. Quadriceps CSA was measured at 50% of the segment length with 0.8 cm slices. Scanning characteristics were as follows: 120 kV, 300 mA, rotation time of 0.75 s, and a field of view of 500 mm. Quadriceps images were traced in triplicates by a specialized researcher who was blinded to the treatment, and their mean values were used for further analysis. Quadriceps CSA measurement’s CV was 0.73%.

**Self-reported quality of life assessment.** Pain, stiffness, and physical function were measured by WOMAC. This instrument is validated and recommended by the Osteoarthritis Research Society as the measure of choice when assessing health status in older adults with knee OA (31). Rating scale ranges from 0 (none) to 4 (extreme), with higher total scores indicating greater dysfunction. Quality of life was also assessed through SF-36, which is a multipurpose, short-form health survey with 36 questions. It yields a profile of functional health and well-being scores as well as psychometrically-based physical and mental health summary measures, with the higher total scores indicating better health condition (32).

**Sample size calculation and statistical analysis.** Sample size was estimated with the assistance of the G-Power® software (version 3.1.2). Based on data from a previous meta-analysis reporting effects of BFRT on muscle strength in untrained individuals (20), we determined that 12 patients would be needed to provide 95% power (α = 0.05) for muscle strength in our untrained population of OA patients would be needed to provide 95% power (α = 0.05).

### Table 1. Patients’ baseline characteristics and drug regimen.

<table>
<thead>
<tr>
<th>Groups</th>
<th>HI-RT (n = 16)</th>
<th>LI-RT (n = 16)</th>
<th>BFRT (n = 16)</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td>Age (yr)</td>
<td>59.9 ± 4</td>
<td>60.7 ± 4</td>
<td>66.3 ± 3</td>
<td>0.8672</td>
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<tr>
<td>Weight (kg)</td>
<td>74.2 ± 16</td>
<td>71.0 ± 13</td>
<td>77.9 ± 7</td>
<td>0.5021</td>
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<tr>
<td>Height (cm)</td>
<td>159.9 ± 5</td>
<td>157.0 ± 5</td>
<td>160.8 ± 8</td>
<td>0.2553</td>
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<tr>
<td>BMI (kg m⁻²)</td>
<td>30.3 ± 5</td>
<td>29.9 ± 3</td>
<td>30.2 ± 3</td>
<td>0.8944</td>
</tr>
<tr>
<td>VAS (cm)</td>
<td>5.3 ± 1</td>
<td>5.1 ± 1</td>
<td>5.2 ± 1</td>
<td>0.9323</td>
</tr>
<tr>
<td>Disease duration, years since diagnosis</td>
<td>4.4 ± 3</td>
<td>4.7 ± 3</td>
<td>4.4 ± 3</td>
<td>0.9594</td>
</tr>
<tr>
<td>Kellgren–Lawrence radiographic grade, n (%)</td>
<td>2 11 (69)</td>
<td>9 (56)</td>
<td>10 (62)</td>
<td>0.9154</td>
</tr>
<tr>
<td>3 5 (31)</td>
<td>7 (44)</td>
<td>6 (38)</td>
<td>0.6974</td>
<td></td>
</tr>
<tr>
<td>Drugs, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antihypothyroid</td>
<td>1 (6)</td>
<td>2 (12)</td>
<td>2 (12)</td>
<td>0.8278</td>
</tr>
<tr>
<td>Antibulcer</td>
<td>1 (6)</td>
<td>1 (6)</td>
<td>1 (6)</td>
<td>0.9913</td>
</tr>
<tr>
<td>Antihypertensive</td>
<td>5 (31)</td>
<td>5 (31)</td>
<td>7 (44)</td>
<td>0.8679</td>
</tr>
<tr>
<td>Antidepressant</td>
<td>2 (12)</td>
<td>1 (6)</td>
<td>4 (25)</td>
<td>0.6734</td>
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<tr>
<td>Antidiabetic</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (6)</td>
<td>0.5889</td>
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<tr>
<td>Symptomimetic</td>
<td>0 (0)</td>
<td>1 (6)</td>
<td>0 (0)</td>
<td>0.4970</td>
</tr>
<tr>
<td>Immunosuppressive</td>
<td>1 (6)</td>
<td>1 (6)</td>
<td>3 (19)</td>
<td>0.4529</td>
</tr>
<tr>
<td>Hypocholesteromic</td>
<td>0 (0)</td>
<td>2 (12)</td>
<td>3 (19)</td>
<td>0.2243</td>
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<tr>
<td>Myorelaxant</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>2 (12)</td>
<td>0.1951</td>
</tr>
<tr>
<td>Antiarthritic</td>
<td>2 (12)</td>
<td>5 (31)</td>
<td>8 (50)</td>
<td>0.5740</td>
</tr>
<tr>
<td>Glucosamine</td>
<td>2 (12)</td>
<td>3 (19)</td>
<td>4 (25)</td>
<td>0.6377</td>
</tr>
<tr>
<td>Chondroitin</td>
<td>2 (12)</td>
<td>3 (19)</td>
<td>2 (12)</td>
<td>0.8228</td>
</tr>
<tr>
<td>Diacerein</td>
<td>0 (0)</td>
<td>2 (12)</td>
<td>7 (44)</td>
<td>0.5568</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD and level of significance (P). No significant differences were observed between groups at baseline.

BMI, body mass index; VAS, Visual Analog Score.
patients. As muscle strength was our primary outcome and the most reported adaptation to BFRT, sample size calculation was based on this parameter.

Data were analyzed using intention-to-treat principles. Dependent variables were tested by mixed models with repeated measures using the software SAS® version 9.3. Tukey post hoc was used for multicomparisons purpose. Additionally, a secondary per protocol analysis was conducted using delta scores (i.e., changes from PRE to POST tests). Groups baseline (PRE) values were compared and found similar (P > 0.05). Additionally, PRE values influence on change scores (PRE to POST) were tested, and no significant effects were found, possible between-group differences in delta changes were tested by a one-way analysis of variance. Tukey post hoc was used when necessary. Effect sizes (ES) (per protocol approach) were calculated according to Cohen (1992). Fisher’s test was applied to assess the possible between-group differences in the proportion of patients who dropped out due to reasons potentially attributed to the interventions (e.g., persistent pain, injuries, fatigue). Finally, an exploratory analysis (Pearson’s r) was conducted on any possible associations between training-induced changes in quadriceps muscle CSA or increases in strength with the remaining clinical variables (e.g.; functionality, pain, quality of life, stiffness). Significance level was previously set at P < 0.05. Data are presented as mean ± SD, except when stated otherwise.

RESULTS

Patients. The flow of patients is illustrated in Figure 1. Of the 379 patients who were screened for participation, 48 met the inclusion criteria. These patients were ranked into tertiles according to their 1-RM leg press and then randomly assigned to either HI-RT (n = 16), LI-RT (n = 16), or BFRT (n = 16). Throughout the trial, six patients were excluded from HI-RT due to both intervention-related and non–intervention-related reasons (exercise-induced keen pain: n = 4; personal reasons: n = 2). Four patients were excluded from LI-RT due to non–intervention-related reasons (inguinal hernia: n = 1; personal reasons: n = 3), and four patients were excluded from BFRT due to non–intervention-related reasons (rectal nodule, n = 1; upper-respiratory tract infection, n = 1; upper respiratory infection, n = 1).
personal reasons, n = 2). Adherence rate to training protocol were 90%, 85%, and 91% for HI-RT, LI-RT, and BFRT, respectively (considering completed case data).

**Muscle strength and functional tests.** The 1-RM leg press and 1-RM knee extension were similar between HI-RT, LI-RT, and BFRT at baseline (P = 0.94 and P = 0.72 for leg press and knee extension, respectively). Within-group increases in 1-RM leg press (Fig. 2C) were found only in HI-RT (+33%, ES = 0.82, P < 0.0001; +22%, ES = 0.83, P < 0.0001, respectively) and BFRT (+26%, ES = 1.01, P < 0.0001; +23%, ES: 0.86, P < 0.0001). In contrast, 1-RM leg press (+8%, ES = 0.23, P = 0.22) and 1-RM knee extension (+7%, ES = 0.21, P = 0.23) remained unaltered after the intervention in LI-RT. Despite significant within-group effects, both leg press and knee extension 1-RM were similar across groups at POST (P > 0.05).

Importantly, delta analysis revealed that HI-RT (P < 0.0001) and BFRT (P = 0.0004) had significantly greater increases in 1-RM leg press when compared with LI-RT (Fig. 2B). Similarly, HI-RT and BFRT had greater increases in 1-RM knee extension (P = 0.0004 and P = 0.0005, respectively) when compared with LI-RT (Fig. 2D). Of note, no significant differences between HI-RT and BFRT were observed (P > 0.05), indicating a similar effect between treatments.

Baseline scores in TST and TUG tests were comparable between groups (P = 0.61 and P = 0.71, respectively). Within-group comparisons revealed significant improvements in TST in HI-RT and BFRT (+14%, ES = 0.52, P < 0.0001 and +7%, ES = 0.43, P = 0.01, respectively) after the intervention, whereas LI-RT showed no significant change (+5%, ES = 0.32, P = 0.31) (Fig. 3A). Despite significant within-group effects, no interaction effects were found and groups were comparable at POST (P > 0.05). Delta analysis demonstrated that HI-RT had greater performance in TST than LI-RT (P = 0.04); no significant differences were noted between BFRT and LI-RT and BFRT and HI-RT (all P > 0.05) (Fig. 3B).

In respect of the TUG, no within- or between-group differences were noted (all P > 0.05) (Fig. 3C). Additionally, delta analysis did not show any significant difference between the three groups (all P > 0.05) (Fig. 3D).

**Quadriceps CSA.** There were no significant differences between groups at PRE (P = 0.77). Importantly, significant within-group increases in CSA were observed only in HI-RT (+8%, ES = 0.54, P < 0.0001) and BFRT (+7%, ES = 0.39, P < 0.0001), but not in LI-RT (+2%, ES = 0.12, P = 0.52) (Fig. 4A). Despite this, groups were not significantly different at POST (P > 0.05); importantly, delta analysis showed significantly greater increases in CSA in HI-RT and BFRT than LI-RT (P = 0.007 and P = 0.02) (Fig. 4B). Finally, no significant difference was noted between HI-RT and BFRT (P > 0.05), evidencing a comparable effect between treatments for this variable.

**Pain and self-reported quality of life.** The WOMAC and SF-36 data can be found in Table 2. All groups were comparable at PRE for all WOMAC subscales (i.e., pain,
stiffness, physical function, and total) (all P > 0.05). The WOMAC pain score was significantly reduced in LI-RT and BFRT (−45%, ES = −0.79, P = 0.001 and −39%, ES = −0.79, P = 0.02, respectively), but not in HI-RT (−31%, ES = −0.54, P = 0.19). WOMAC stiffness score was significantly reduced in BFRT (−44%, ES = −1.12, P = 0.013), but not in HI-RT and LI-RT (−41%, ES = −1.11, P = 0.53 and −32%, ES = −0.55, P = 0.286, respectively). The WOMAC physical function score was significantly improved in BFRT and HI-RT (−49%, ES = −1.30, P = 0.019 and −42%, ES = −1.18, P = 0.02), but not in LI-RT (−42%, ES = −0.69, P = 0.09). The WOMAC total score was significantly improved from PRE- to POST-test in all groups (HI-RT, −39%, ES = −1.23, P = 0.016; LI-RT, −42%, ES = −0.79, P = 0.005; BFRT: −46%, ES = −1.3, P = 0.008).

There were no significant differences within or between groups for any domain from SF-36, nor any significant differences between delta scores (all P > 0.05).

Finally, we found significant associations between changes in leg extension 1-RM and change scores in stiffness and physical function subscales (r = 0.4, P = 0.02 and r = 0.37, P = 0.03, respectively) and total score in WOMAC (r = 0.37, P = 0.03), and a trend toward significance in its association with changes in TST scores (r = 0.31, P = 0.07). Changes in CSA were significantly associated with changes in TST scores (r = 0.5, P = 0.002), and a trend toward

FIGURE 3—Functional tests. Panels A and C show data from timed-stands and timed-up-and-go tests, respectively, PRE and POST the exercise training protocol. * indicates P < 0.05 for within-group comparisons. Panels B and D show delta changes (pretraining to posttraining) in TST and TUG, respectively. *P < 0.05 when compared with LI-RT. Data are presented as mean and ± SD.

FIGURE 4—Quadriceps CSA. Panel A shows quadriceps CSA PRE and POST the exercise training protocol. *P < 0.05 for within-group comparisons. Panel B shows delta changes in quadriceps CSA (pretraining to posttraining). *P < 0.05 when compared with LI-RT. Data are presented as mean and ± SD.
significant associations were found between changes in CSA and changes in stiffness subscale in WOMAC (r = 0.3, P = 0.09). No significant associations were found between changes in leg press 1-RM and any of the parameters; however, a trend toward significance was found in its association with changes in scores in stiffness and physical function subscales (r = 0.3, P = 0.09 and r = 0.3, P = 0.09) and total score in WOMAC (r = 0.3, P = 0.08).

**Adverse events.** Four patients (of 16) from HI-RT were excluded throughout the follow-up due to exercise-induced knee pain. Fischer’s exact test revealed that this incidence was significantly superior to that of either BFRT (P = 0.03) or LI-RT (P = 0.03) (none in either group). No other adverse events were self-reported.

### DISCUSSION

The main findings of this study are that BFRT was similarly effective as HI-RT in increasing lower-limb maximum dynamic strength, quadriceps CSA, and functionality in knee OA patients. Additionally, both training methods were able to improve WOMAC physical function subscale whereas BFRT, but not HI-RT, significantly improved WOMAC pain and stiffness subscales. Importantly, HI-RT resulted in a significant number of withdrawals.

Knee OA often encompasses diminished muscle strength and mass, which is accompanied by pain and reduced quality of life. Therefore, given the importance of quadriceps muscle strength and mass on disease progression, functionality, and quality of life (5,6,8,9,15,19), both the American College of Rheumatology (33) and the European League Against Rheumatism (34) consider RT a first-line therapy in OA management. To maximize training-induced adaptations, the American College of Sports Medicine recommends moderate- to high-load RT (>65% 1-RM) (17), which constitutes an important drawback when dealing with knee OA patients, as pain is often a limitation while attempting to exercise at higher intensities (18). In this respect, BFRT has emerged as a potential alternative to HI-RT, as it allegedly allows patients to exercise at much lower intensities (~20%–40% 1-RM) while experiencing similar muscle adaptations (20,22).

In the present study, lower-limb maximum dynamic strength, as measured by leg press and knee extension 1-RM, and functionality were increased to a similar extent with BFRT and HI-RT, whereas no changes were found in LI-RT. This is in line with previous studies in different populations (20,21). For instance, we and others have shown BFRT to be equally effective as HI-RT in increasing lower-limb 1-RM in young (22) and healthy elderly (21,35) individuals. In diseased populations, we have also shown BFRT to be a promising adjuvant therapy in dermatomyositis and polymyositis (36), as well as in a patient with inclusion body myositis (37), which corroborates our findings.

Regarding OA management, there is preliminary evidence showing that BFRT was able to induce gains in muscle strength in women with risk factor for knee OA (23). However, no comparison to an HI-RT group was provided, hampering further inferences on BFRT efficacy. The only study to investigate BFRT on OA patients also reported comparable increases in muscle strength between BFRT and HI-RT, with slightly greater relative changes than those found herein (24). It is important to note that only isometric strength was assessed, which although informative, is less complex than a more physiological test, such as the maximum dynamic muscle strength test employed in our study. This, in association with the apparent lack of familiarization procedure in the study by Bryk et al., may, at least partially, explain the difference in magnitude between studies (despite a similar response pattern between training protocols). Additionally, the authors included neither an intensity-matched nonocclusion group nor muscle mass assessments, limiting their conclusions.

In this respect, BFRT has been suggested as an effective method for increasing lower-limb lean mass. In fact, similar muscle mass accrual has been shown after BFRT when compared with HI-RT in both young (22) and elderly (21). Additionally, we have previously shown BFRT to be able to induce increases in muscle mass in severely diseased individuals (36,37), which is now extended to OA patients. In the present study, we found comparable increases in quadriceps CSA between BFRT and HI-RT, with no change in LI-RT. This novel finding is of substantial clinical relevance and advances the literature significantly as quadriceps muscle mass is an important feature in knee OA. In fact, a greater loss in lower extremity lean mass has been observed in women with knee OA when compared with healthy controls (9). This reduction in muscle mass is also associated with disease progression (10), pain (11), and with both presence and severity of age-related OA (12). Finally, thigh lean muscle mass is related to knee extensor and flexor power in women with knee OA (38), which has direct implications for strength and functionality (6,7,9); therefore, targeting

### TABLE 2. Self-reported quality of life.

<table>
<thead>
<tr>
<th></th>
<th>PRE</th>
<th>POST</th>
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<tbody>
<tr>
<td>WOMAC—pain</td>
<td>7.2 ± 2.2</td>
<td>4.6 ± 3.1</td>
</tr>
<tr>
<td>HI-RT</td>
<td>7.9 ± 3.9</td>
<td>4.0 ± 2.6*</td>
</tr>
<tr>
<td>BFRT</td>
<td>6.9 ± 3.3</td>
<td>4.0 ± 2.9*</td>
</tr>
<tr>
<td>WOMAC—stiffness</td>
<td>3.5 ± 1.2</td>
<td>2.0 ± 1.8</td>
</tr>
<tr>
<td>HI-RT</td>
<td>2.8 ± 1.4</td>
<td>1.8 ± 1.7</td>
</tr>
<tr>
<td>BFRT</td>
<td>3.6 ± 1.5</td>
<td>2.1 ± 1.5*</td>
</tr>
<tr>
<td>WOMAC—physical function</td>
<td>25.9 ± 9.3</td>
<td>14.6 ± 9.2</td>
</tr>
<tr>
<td>HI-RT</td>
<td>24.4 ± 12.9</td>
<td>12.7 ± 7.7*</td>
</tr>
<tr>
<td>BFRT</td>
<td>21.0 ± 8.5</td>
<td>10.3 ± 6.9*</td>
</tr>
<tr>
<td>WOMAC—total</td>
<td>31.5 ± 12.0</td>
<td>17.1 ± 11.2*</td>
</tr>
<tr>
<td>SF-36—mental health</td>
<td>65.4 ± 20.7</td>
<td>71.1 ± 23.1</td>
</tr>
<tr>
<td>HI-RT</td>
<td>69.0 ± 15.7</td>
<td>78.5 ± 19.3</td>
</tr>
<tr>
<td>BFRT</td>
<td>68.0 ± 23.8</td>
<td>79.3 ± 12.0</td>
</tr>
<tr>
<td>SF-36—physical health</td>
<td>55.7 ± 16.9</td>
<td>61.8 ± 15.5</td>
</tr>
<tr>
<td>HI-RT</td>
<td>57.0 ± 15.9</td>
<td>66.0 ± 20.3</td>
</tr>
<tr>
<td>BFRT</td>
<td>60.4 ± 16.1</td>
<td>73.4 ± 13.5</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD. *P < 0.05 for within-group comparisons.
not only quadriceps strengthening, but also lean mass, is key in OA management.

In line with our findings regarding muscle strength and mass, functionality was significantly improved after training in both BFRT and HI-RT (as measured by TST). Maintaining functionality is one of the main goals in OA treatment. Impaired physical function is associated with restrictions in physical performance of daily activities for independent living and is considered a predictor of disability (39). The findings of the present study support the use of BFRT interventions in knee OA, as it favors preservation of independence and, thus, quality of life in these patients while inducing less strain in the affected joints and, consequently, less pain. In fact, although WOMAC scores for physical function were significantly improved in both BFRT and HI-RT, subscale WOMAC pain was significant and positively changed only after BFRT, supporting our contention. Another relevant finding was that 25% of the sample enrolled in the conventional HI-RT intervention protocol withdrew from study due to exercise-related pain, whereas no adverse events were noted during BFRT. It is likely that lower joint stress and lesser pain may exert a differential effect on the long-term adherence to exercise in knee OA patients, which would be of clinical significance though proper investigation is currently lacking. Additionally, arterial blood pressure was monitored before and after each training session, and no clinically relevant alterations were observed (data not shown). Similarly, resting blood pressure was not affected by the 12-wk intervention (data not shown), adding to the safety argument of BFRT for this population. In fact, BFRT has previously been deemed safe in a variety of populations, with minimal incidence of adverse events (40), though professional assistance and proper control of training variables are necessary. Data on the safety of BFRT in patients with cardiovascular disease are still scarce.

Given the effect increases in muscle strength and/or mass may have on clinical parameters in knee OA, we decided to investigate any possible associations between these variables. Importantly, these results are exploratory and limited by the low sample size; nonetheless, it is interesting to observe positive associations between physiological and clinical variables in a population of knee OA patients. This is somehow expected, as previous studies have indicated positive associations between muscle mass and strength with pain and functionality (6–8,10,11).

Finally, it is imperative to emphasize that the discussion of our findings is based on within-group changes and between-group comparisons in delta scores, the latter being a secondary analysis in our model. Even though no significant between-group differences were found, this is mitigated by the much larger ES observed in both BFRT and HI-RT when compared with LI-RT, and the observable similarity in data behavior pattern over time, with BFRT and HI-RT presenting very similar response patterns. Moreover, although we ran a priori power analysis for sample size calculation, it is very likely that the study is actually underpowered based on a posteriori power analysis, which may explain the lack of interaction effects.

In conclusion, the present study demonstrated similar effects between BFRT and HI-RT in increasing muscle strength, quadriceps muscle mass, and functionality in older female knee OA patients. Importantly, BFRT was also able to improve pain while using lower loads and inducing less joint stress, emerging as a feasible and effective therapeutic adjuvant in OA management.

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