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Effects of Multicomponent Exercise on Immunity, Antibodies, and Physical Activity in Older Adults After COVID-19 Vaccination: An RCT-Feasibility Study

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Abstract

Background

Immunosenescence contributes to reduced vaccine responsiveness and chronic low-grade inflammation in older adults. Although regular physical exercise has been associated with improved immune function, evidence regarding the feasibility and immunological effects of multicomponent exercise training (MET) following COVID-19 vaccination remains limited. This pilot randomized feasibility trial aimed to assess the feasibility of implementing a 10-week MET program and to explore its effects on functional fitness, physical activity, anthropometric measures, lipid profile, and immuno-inflammatory markers in community-dwelling older adults after COVID-19 vaccination.

Methods

Twenty-three community-dwelling older adults (≥60 years) completed this randomized pilot feasibility trial and were allocated to either a MET group (n = 10) or a Behavior Change Program (BCP) group (n = 13). Both interventions lasted 10 weeks. Pre- and post-intervention assessments included functional fitness (Short Physical Performance Battery), physical activity levels, anthropometric measures, lipid and protein profiles, immunoglobulins (IgA, IgM, IgG), and cytokines (IL-2, IL-6, IL-10, TNF-α, and IFN-γ).

Results

The intervention proved feasible, with satisfactory adherence among participants completing the program and no exercise-related adverse events. The MET group demonstrated significant improvements in functional fitness ($p = 0.002$; $d = 1.90$). Although physical activity levels showed a positive trend, changes did not reach statistical significance. Significant reductions in IL-2, IL-6, and TNF-α were observed following MET (all $p \leq 0.05$), whereas the BCP group exhibited increased IL-6 concentrations together with higher IL-2/IL-10 and IL-6/IL-10 ratios, suggesting a shift toward a more pro-inflammatory profile. Moderate-to-large effect sizes were also observed for improvements in selected lipid parameters, although most biochemical changes were not statistically significant.

Conclusions

This pilot feasibility trial demonstrated that a 10-week multicomponent exercise program can be safely implemented in community-dwelling older adults following COVID-19 vaccination and provides preliminary evidence of beneficial effects on functional fitness and selected immuno-inflammatory markers. Given the small sample size, these findings should be interpreted cautiously and confirmed in adequately powered randomized controlled trials.

Key Words

Community-dwelling; Exercise immunology; Immunoglobulin; Inflammaging; Physical function; Vaccine

Introduction

Cellular senescence and chronic low-grade inflammation ("inflammaging") are hallmarks of biological ageing and play a central role in the progressive decline of immune function (Di Micco et al., 2021). This age-related deterioration of the immune system, commonly referred to as immunosenescence, is characterized by impaired innate and adaptive immune responses, including reduced antigen presentation, diminished antibody production by B lymphocytes, lower vaccine responsiveness, and increased susceptibility to infectious diseases (Duggal et al., 2019). In addition to compromising host defence mechanisms, immunosenescence contributes to persistent systemic inflammation and to the development and progression of several age-related chronic conditions (Conti et al., 2020).

The COVID-19 pandemic highlighted the vulnerability of older adults to severe infectious diseases. Owing to age-associated immune dysfunction, older individuals experienced disproportionately higher rates of hospitalization, complications, and mortality following SARS-CoV-2 infection (Fulop et al., 2022; Al-Qudimat et al., 2023). Although vaccination has substantially reduced the burden of COVID-19, vaccine-induced immune responses remain highly heterogeneous in older adults because of immunosenescence, reinforcing the need for complementary non-pharmacological strategies capable of optimizing immune function after vaccination (Santoro et al., 2021).

Regular physical activity and structured exercise are among the most effective non-pharmacological interventions for promoting healthy ageing. Previous studies have demonstrated that regular exercise improves neuromuscular and cardiovascular function (Izquierdo et al., 2021), reduces the incidence of upper respiratory tract infections (Scudiero et al., 2021), attenuates immunosenescence (Cao Dinh et al., 2019; Minuzzi et al., 2017), and positively modulates both innate and adaptive immune responses (Salimans et al., 2022). Maintaining recommended levels of physical activity has also been associated with lower systemic inflammation, enhanced immune surveillance, and improved responses to both influenza and COVID-19 vaccines (Furtado et al., 2021; Silva et al., 2023). These benefits appear to be mediated, at least in part, by exercise-induced production of myokines and other immunomodulatory molecules capable of regulating inflammatory pathways.

Despite these advances, important knowledge gaps remain. Most previous studies have investigated isolated aerobic or resistance exercise, acute exercise responses, or physically active populations, whereas evidence regarding structured multicomponent exercise programmes performed after COVID-19 vaccination remains limited. Furthermore, few randomized studies have simultaneously examined functional performance together with lipid profile, immunoglobulins, circulating cytokines, and cytokine balance in community-dwelling older adults. Consequently, the multidimensional effects of multicomponent exercise on post-vaccination immune and inflammatory responses in this population are still insufficiently understood.

Therefore, this randomized pilot feasibility study aimed (i) to evaluate the feasibility of implementing a 10-week multicomponent exercise training (MET) programme in community-dwelling older adults following COVID-19 vaccination and (ii) to explore its effects on functional fitness, physical activity levels, anthropometric measures, lipid profile, immunoglobulins, and immuno-inflammatory markers. We hypothesized that the MET programme would be feasible to implement, achieve satisfactory adherence, improve functional fitness and physical activity levels, and promote a more favourable immuno-inflammatory profile than a Behaviour Change Programme (BCP).

Material and Methods

Study design

This study was designed as a two-arm randomized pilot feasibility trial to investigate the feasibility and preliminary effects of a 10-week multicomponent exercise training (MET) programme on functional, biochemical, and immunological outcomes in community-dwelling older adults following COVID-19 vaccination. Participants were randomly allocated to either the MET intervention group or a Behaviour Change Programme (BCP) control group.

The study was conducted between December 2022 and April 2023 in Jequié, Bahia, Brazil, and followed the principles of the Declaration of Helsinki for research involving human participants. The manuscript was prepared in accordance with the CONSORT 2010 Statement and the CONSORT extension for randomized pilot and feasibility trials.(Cuschieri, 2019).

Participants and Eligibility Criteria

Community-dwelling older adults registered in the Family Health Strategy (FHS) of the urban area of Jequié, Bahia, Brazil, were invited to participate in the study. Recruitment was conducted through the local primary healthcare services, and individuals were screened for eligibility before enrolment.

Eligible participants were required to: (i) be aged 60 years or older; (ii) be registered in the Family Health Strategy; (iii) have completed the recommended COVID-19 vaccination schedule; (iv) be able to walk independently, with or without an assistive device; and (v) provide written informed consent.

Participants were excluded if they presented medical conditions contraindicating physical exercise, including unstable cardiovascular disease, severe musculoskeletal disorders, uncontrolled hypertension, symptomatic hypotension, uncontrolled diabetes mellitus, recent fractures, severe cognitive impairment preventing participation in the assessments or exercise sessions, or any other clinical condition considered by the research team to preclude safe participation in the intervention.

2.3. Recruitment and Randomization

Participants were recruited from Family Health Strategy (FHS) units located in the urban area of Jequié, Bahia, Brazil. Recruitment was conducted through the local primary healthcare services, and all potentially eligible individuals were invited to participate. Eligibility was confirmed through clinical screening according to the predefined inclusion and exclusion criteria, and written informed consent was obtained prior to baseline assessments.

Following enrolment, participating FHS units were randomly allocated to either the Multicomponent Exercise Training (MET) group or the Behaviour Change Programme (BCP) group, thereby determining the allocation of eligible participants. Random allocation was performed before the beginning of the intervention to minimize selection bias and ensure comparable study groups.

Due to the nature of the intervention, neither participants nor exercise professionals could be blinded to group allocation. However, all outcome assessments were conducted according to standardized protocols, using identical procedures at baseline and post-intervention to minimize measurement bias.

2.4. Sample Size

As this study was designed as a randomized pilot feasibility trial, the primary objective was to evaluate the feasibility and obtain preliminary estimates of the intervention effects rather than to provide definitive hypothesis testing. Nevertheless, an a priori sample size estimation was performed using G*Power software (version 3.1.9.2), considering an α error probability of 0.05, statistical power of 80%, and a 95% confidence level. Based on these assumptions, a minimum of 15 participants per group was estimated to provide adequate preliminary data for the proposed analyses (Kang, 2021).

Initially, 222 older adults were screened for eligibility. Following application of the inclusion and exclusion criteria, 46 participants were considered eligible for randomization. Six individuals withdrew before the intervention commenced, resulting in 40 participants initially allocated to the two study groups. As expected in a community-based pilot trial involving older adults, participant attrition occurred during follow-up, and 23 participants completed both baseline and post-intervention assessments, constituting the final analytical sample.

2.5. Ethical Considerations

This study forms part of the broader research project previously described by Rocha et al. (2024). The research protocol was reviewed and approved by the appropriate Institutional Research Ethics Committee (approval number: XXXXXXX) and was conducted in accordance with the ethical principles established in the Declaration of Helsinki and the Guidelines for Exercise Science Research (Shephard, 2002).

All participants received detailed verbal and written information regarding the objectives, procedures, potential risks, and expected benefits of the study before providing written informed consent. Participant confidentiality and anonymity were strictly maintained throughout all stages of data collection, analysis, and reporting. Personal information was handled according to applicable ethical and legal requirements, and participation was entirely voluntary, with participants being free to withdraw from the study at any time without prejudice.

2.6. Outcome Measures

Outcome assessments were performed at baseline (pre-intervention) and immediately following completion of the 10-week intervention (post-intervention). All assessments were conducted during the morning by trained researchers following standardized protocols. Sociodemographic information was collected during face-to-face interviews at participants' homes, whereas physical performance assessments and blood sample collection were performed at the Family Health Strategy (FHS) facilities. Participants were instructed to attend the assessment sessions after an overnight fast and to refrain from vigorous physical activity for at least 24 hours before blood collection.

The primary objective of this pilot trial was to assess the feasibility of implementing the intervention. Secondary outcomes included anthropometric characteristics, physical activity levels, functional fitness, biochemical parameters, and immunological and inflammatory biomarkers.

2.6.1. Sociodemographic and Anthropometric Variables

Sociodemographic information, including age and sex, was collected using standardized questionnaires. Body weight and height were measured using calibrated equipment according to standardized procedures, and body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). Anthropometric assessments were performed at baseline and after completion of the intervention.

2.6.2. Clinical Characteristics

Clinical status was assessed using the Charlson Comorbidity Index (CCI), a validated instrument that estimates disease burden based on the presence of chronic comorbidities. In the present study, twelve comorbid conditions were considered, generating a weighted score in accordance with the original methodology described by Charlson et al. (1994). Higher scores indicate greater clinical complexity and comorbidity burden.

2.6.3. Physical Activity Assessment

Habitual physical activity was assessed using the validated Brazilian version of the International Physical Activity Questionnaire (IPAQ). The questionnaire evaluates the frequency, duration, and intensity of physical activity performed during the previous seven days across four domains: occupational activities, active transportation, household activities, and leisure-time physical activity (Matsudo et al., 2001). Total physical activity was expressed as metabolic equivalent task minutes per week (MET-min/week), providing an estimate of overall physical activity behaviour.

2.6.4. Functional Fitness

Functional fitness was evaluated using the Short Physical Performance Battery (SPPB), a widely validated instrument for assessing lower-extremity physical performance in older adults (Guralnik et al., 1994). The SPPB comprises three components: standing balance, usual gait speed over four metres, and the five-times chair stand test. Each component is scored from 0 to 4, resulting in a total score ranging from 0 to 12, with higher scores indicating better functional performance. According to established criteria, total scores were classified as very low (0–3), low (4–6), moderate (7–9), or good (10–12) functional performance.

2.6.5. Biochemical Analysis

Venous blood samples were collected at baseline and immediately after completion of the intervention following an overnight fast. Serum samples were processed according to standardized laboratory procedures.

Biochemical analyses included total protein, albumin, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), non-HDL cholesterol, triglycerides, and the triglyceride-to-HDL ratio (TG/HDL). All biochemical measurements were performed using automated enzymatic-colorimetric methods following the manufacturer's recommendations (do Amaral et al., 2024).

2.6.6. Immunological and Inflammatory Biomarkers

Serum concentrations of the pro-inflammatory cytokines interleukin (IL)-2, IL-6, tumour necrosis factor-alpha (TNF-α), and interferon-gamma (IFN-γ), together with the anti-inflammatory cytokine IL-10, were quantified using commercially available enzyme-linked immunosorbent assay (ELISA) kits according to the manufacturers' instructions. Serum samples were stored at −80°C until analysis.

Specific immunoglobulin responses against SARS-CoV-2 were assessed by measuring IgA, IgM, and IgG antibodies using an adapted in-house ELISA methodology. To further characterize the inflammatory balance, cytokine ratios (IL-2/IL-10, IL-6/IL-10, TNF-α/IL-10, and IFN-γ/IL-10) were subsequently calculated and analysed.

Whenever available, detailed information regarding ELISA kits (manufacturer, catalogue number, analytical sensitivity, and intra- and inter-assay coefficients of variation) should be included to facilitate reproducibility.

2.7. Multicomponent Exercise Training (MET)

The Multicomponent Exercise Training (MET) programme was adapted from the VIVIFRAIL® programme (Izquierdo, 2019), an evidence-based exercise intervention specifically developed to improve functional capacity, muscular strength, balance, mobility, and overall physical performance in older adults.

The intervention consisted of 20 supervised exercise sessions delivered over a 10-week period (two sessions per week), with each session lasting approximately 50 minutes. All sessions were conducted in a climate-controlled room at the Family Health Strategy (FHS) facilities and were supervised by two certified Physical Education professionals previously trained in the intervention protocol.

Each exercise session comprised three sequential components:

1. Functional warm-up, consisting of time-based exercises designed to improve mobility, coordination, and dynamic balance;

2. Neuromuscular training, including multi-joint exercises targeting the principal movement patterns (push, pull, squat, gait and balance), performed in three sets of 12–20 repetitions. Exercise intensity was progressively increased throughout the intervention by adjusting exercise complexity, volume, and execution time;

3. Cool-down, consisting of flexibility and stretching exercises for the upper and lower limbs, with each stretch maintained for approximately 10–30 seconds.

Exercise intensity was individually monitored throughout the intervention using the Adapted Borg Rating of Perceived Exertion (RPE) Scale (Shariat et al., 2018), allowing participants to self-regulate exercise intensity according to their functional capacity while maintaining the planned progression of the programme.

To ensure intervention standardization, all exercise sessions followed the same protocol and were delivered according to a predefined progression schedule. A detailed description of the exercises, progression criteria, and weekly training programme is provided in Supplementary Table S1**,** following the Template for Intervention Description and Replication (TIDieR) recommendations.

2.8. Behaviour Change Programme (BCP)

Participants allocated to the Behaviour Change Programme (BCP) received a structured educational intervention based on the VAMOS ("Active Life, Better Health") programme (Konrad et al., 2022), designed to promote healthy lifestyle behaviours and encourage long-term adoption of regular physical activity.

The intervention consisted of four group sessions delivered over a two-month period (two sessions per month), each lasting approximately 60–90 minutes. Sessions were conducted by a multidisciplinary team comprising professionals and students from the fields of Physical Education, Psychology, and Medicine.

Educational sessions addressed topics including the health benefits of regular physical activity, healthy eating habits, behavioural strategies to overcome barriers to exercise, motivation, self-management, and the importance of family and social support for maintaining an active lifestyle. Interactive discussions and group participation were encouraged throughout the intervention.

To improve reproducibility, the educational content delivered during each session is summarized in Supplementary Table S2**.**

2.9. Feasibility Outcomes and Intervention Adherence

As this study was designed as a pilot feasibility trial, feasibility outcomes were assessed throughout the intervention. These included participant recruitment, retention, intervention adherence, programme completion, and the occurrence of adverse events.

Attendance was recorded at every exercise session by the supervising instructors. Participants attending at least 75% of the prescribed exercise sessions were considered adherent to the intervention protocol and were eligible for the post-intervention assessments.

Participants who missed consecutive sessions were contacted by telephone and, whenever necessary, through home visits to encourage continued participation and identify potential barriers to adherence (Spiteri et al., 2019). Retention rate and reasons for withdrawal were documented throughout the study. Any adverse events occurring during the intervention were also recorded and monitored.

2.10. Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics (Version XX; IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD) for normally distributed data or median and interquartile range (IQR) for non-normally distributed variables.

Normality was assessed using the Shapiro–Wilk test, while homogeneity of variances was evaluated using Levene's test.

Within-group comparisons between baseline and post-intervention measurements were performed using paired Student's *t*-tests for normally distributed variables or Wilcoxon signed-rank tests for non-parametric data. Between-group comparisons were performed using independent Student's *t*-tests or Mann–Whitney *U* tests, as appropriate.

Effect sizes were calculated using Cohen's *d* and interpreted as small (0.20–0.49), moderate (0.50–0.79), or large (≥0.80). Because this was an exploratory pilot feasibility trial with a limited sample size, emphasis was placed on effect sizes and the magnitude of observed changes rather than solely on statistical significance.

All statistical tests were two-tailed, with statistical significance established at $p < 0.05$. Owing to the exploratory nature of this pilot study, adjustments for multiple comparisons were not performed.

Analyses were conducted on participants who completed both baseline and post-intervention assessments (per-protocol analysis). Missing data resulting from participant withdrawal were not imputed.

Results

3.1. Participant Flow and Feasibility

A total of 222 community-dwelling older adults were screened for eligibility, of whom 46 met the predefined inclusion criteria and were considered eligible for participation. Six participants withdrew before the intervention commenced, resulting in 40 participants initially allocated to the Multicomponent Exercise Programme (MEP) (n = 20) or the Behaviour Change Programme (BCP) (n = 20).

During the intervention period, participant attrition resulted in complete baseline and post-intervention assessments for 23 participants, including 10 individuals in the MEP group and 13 in the BCP group (Figure 1).

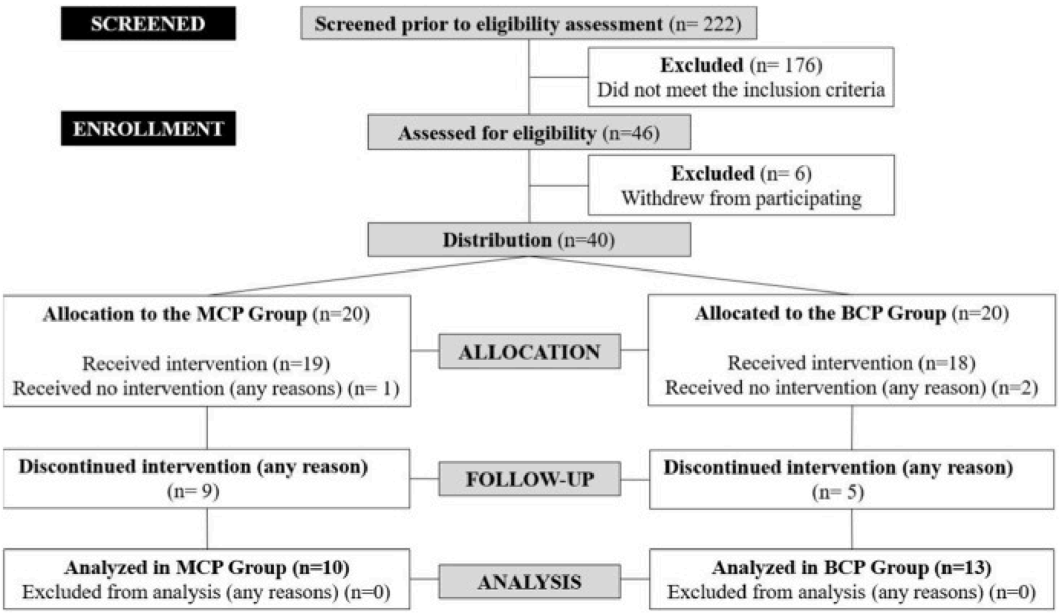

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Figure 1. CONSORT Flowchart.

Overall feasibility outcomes are summarized in Supplementary Table S3**.** Recruitment was completed within the planned study period, and both interventions were successfully implemented in the primary healthcare setting. No serious or exercise-related adverse events were reported throughout the study. Participant retention and adherence supported the feasibility of implementing supervised multicomponent exercise in community-dwelling older adults following COVID-19 vaccination.

3.2. Baseline Characteristics

Baseline demographic, anthropometric, clinical, and functional characteristics of the participants are presented in Table 1**.** No statistically significant differences were observed between groups regarding age, stature, body mass, body mass index, or Charlson Comorbidity Index (all $p > 0.05$), indicating comparable demographic and clinical profiles at study entry. However, participants allocated to the BCP group presented significantly higher Lawton Index of Functional Status (LIFS) scores than those allocated to the MEP group ($p = 0.0209$), suggesting slightly greater functional independence at baseline.

Table 1. General characteristics of total sample, experimental (MEP) and control (BCP) groups at baseline

	To sample (n=23)	MEP (n=10)	BCP n=13)	P value
	M(±SD)	M(±SD)	M(±SD)	
Chronological age (years)	71.09 ± 5.51	70.4 ± 5.70	71.6 ± 5.53	0.6180
Stature (cm)	153.0 ± 6.40	159.0 ± 9.92	152.0 ± 7.40	0.8609
Body mass (kg)	63.37 ± 12.75	62.82 ± 12.43	64.08 ± 13.47	0.9562
Body mass index (kg·m^{-2})	26.37 ± 5.25	24.76 ± 4.42	27.74 ± 5.60	0.9307
Charlson comorbidity (A±SD)	4.70±1.94	3.8±1.75	5.38±1.85	0.319
LIFS scale (total score)	11.74 ± 3.35	10.3 ± 2.67	12.8 ± 3.48	***0.0209***

Notes: **p≤0.01; *p≤0.05; **Acronyms: M =** mean; **SD =** standard and deviation; **LIFS =** Lawton Index of Functional Status; **MEP =** Multicomponent exercise program; **BCP=** Behavior change program.

3.3. Anthropometric Characteristics, Physical Activity and Functional Fitness

Changes in anthropometric variables, physical activity levels and functional performance following the intervention are summarized in Table 2.

Table 2. Anthropometric, Functional fitness and levels of PA scores pre- and post- MEP and BCP groups after 8-weeks

	MEP (Pre) (n=10)	MEP (Post) (n=13)	P value	Cohen's D	Practical relevance	BCP (Pre) (n=10)	BCP (Post) (n=13)	P value	Cohen's D	Practical relevance
	M (±SD)					M (±SD)				
Stature (cm)	159±9.92	159±9.92	1.000	0.00	Negligible	152.0±7.40	152.0±7.40	1.000	0.00	Negligible
Body mass (kg)	62.4±12.2	63.2±12.8	0.700	0.11	Small	64.1±18.6	64.1±13.6	0.700	0.15	Small
BMI (kg·m^{-2})	24.6±4.48	24.9±4.45	0.800	0.07	Small	27.7±5.60	27.7±5.62	0.950	0.02	Small
CW	88.2±13.12	90.15±14.04	0.500	0.14	Small	93.69±13.21	94±13.92	0.800	0.06	Small
CH	95.4±7.09	97.3±7.42	0.400	0.26	Small	101.08±11.12	100.46±11.65	0.600	0.14	Small
Levels of PA	856±680	1294±1528	0.180	0.45	Small	1278±1240	665±596	0.270	0.47	Small
SPPB tests	10.2±0.63	11.4±0.84	0.008*	1.90	High	8.46±1.56	8.85±0.89	0.015*	0.22	Small

Notes: Body Mass was analyzed using the Wilcoxon test. The remaining variables were analyzed using the student t-test; **p≤0.01; *p≤0.05; **Acronyms: M** = mean; **SD** = standard and deviation; **cm =** centimeter; **kg =** kilograms; **kg·m^{-2} =** kilogram per square meter; **SPPB =** short physical performance battery; **PA =** physical activity; **BMI =** body mass index; **CW =** waist circumference; **CH =** hips circumference; **MEP =** Multicomponent exercise program; **BCP=** Behavior change program.

Anthropometric variables remained stable throughout the intervention in both study groups. No significant changes were observed in body mass, body mass index, waist circumference or hip circumference following either intervention (all $p > 0.05$), with effect sizes ranging from negligible to small.

Physical activity levels demonstrated a positive trend in participants allocated to the MEP programme, increasing from 856 ± 680 to 1294 ± 1528 MET-min/week, whereas the BCP group showed a reduction from 1278 ± 1240 to 665 ± 596

MET-min/week. Although these changes did not reach statistical significance, the magnitude and direction of change differed between interventions, with small effect sizes observed in both groups.

Functional performance, assessed using the Short Physical Performance Battery (SPPB), improved significantly following both interventions. However, participants in the MEP group demonstrated a markedly greater improvement, increasing from 10.2 ± 0.63 to 11.4 ± 0.84 points (p = 0.008), corresponding to a large effect size (d = 1.90). In contrast, the BCP group showed only modest improvements, from 8.46 ± 1.56 to 8.85 ± 0.89 points (p = 0.015), with a small effect size (d = 0.22). These findings indicate that the multicomponent exercise programme produced substantially greater gains in functional capacity than the behavioural intervention alone.

3.4. Biochemical Profile

Changes in biochemical parameters are presented in Figure 2.

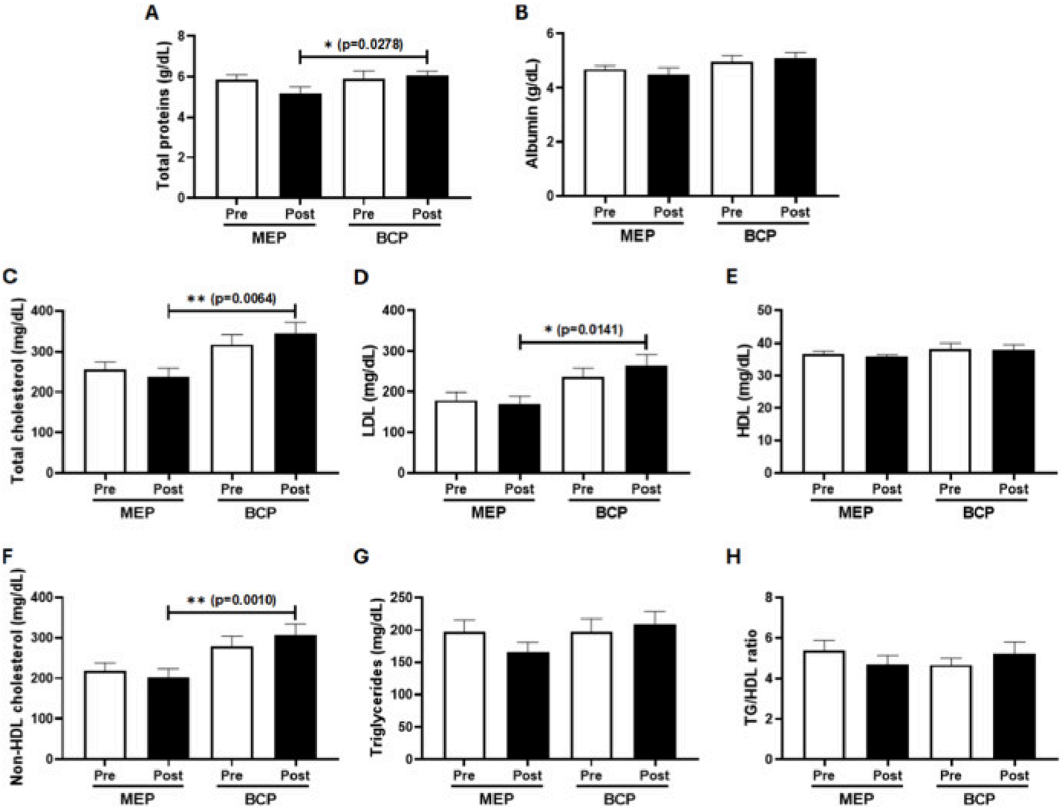

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Figure 2. Circulating Protein and Lipid Profile in Older Adults Pre- and Post-Intervention. Mean (±SD) circulating levels of (A) total protein, (B) albumin, (C) total cholesterol, (D) LDL cholesterol, (E) HDL cholesterol, (F) non-HDL cholesterol, (G) triglycerides, and (H) the triglycerides/HDL ratio (TG/HDL) were analyzed for the MEP and BCP groups. Intragroup and intergroup analyses were conducted. Effect sizes were calculated using Cohen's d. Acronyms: LDL = low-density lipoprotein, HDL = high-density lipoprotein, TG = triglycerides, MEP = multicomponent exercise program, BCP = behavior change program.

Overall, most biochemical variables remained stable following the intervention. Nevertheless, participants allocated to the MEP group demonstrated a more favourable lipid profile after the intervention than those assigned to the BCP group. In particular, lower concentrations of total cholesterol, LDL cholesterol and non-HDL cholesterol were observed following the exercise programme, whereas no comparable improvements were identified in the control group. Although several within-group changes did not reach statistical significance, moderate-to-large effect sizes suggested clinically meaningful improvements in lipid metabolism following multicomponent exercise.

3.5. Immunological and Inflammatory Biomarkers

The effects of both interventions on circulating cytokines and SARS-CoV-2-specific immunoglobulins are illustrated in Figure 3.

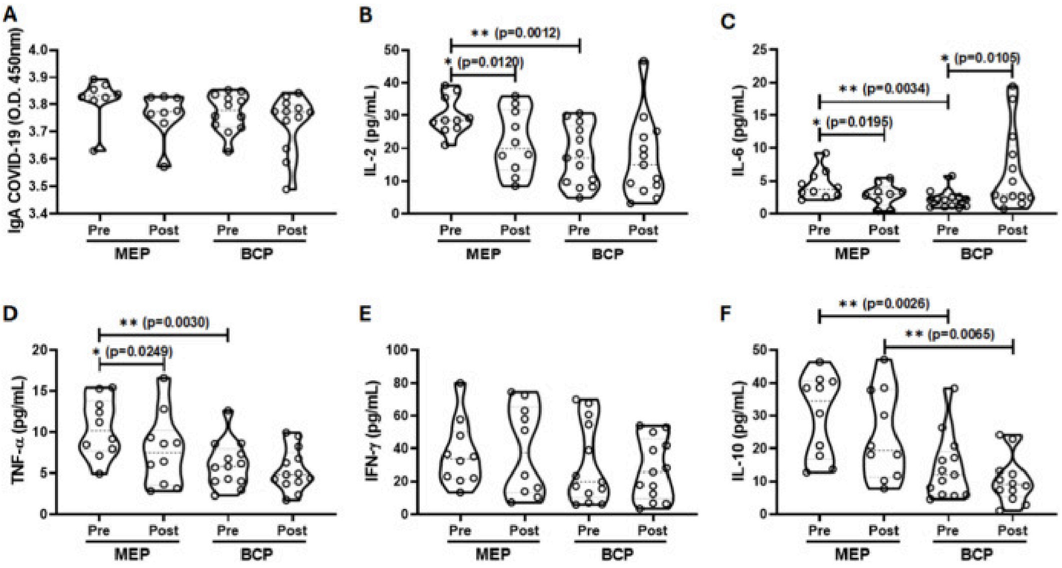

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Figure 3. Inflammatory and Anti-Inflammatory Cytokine Levels Pre- and Post-Intervention. Mean (±SD) circulating levels of (A) SARS-CoV-2-specific IgA, (B) IL-2, (C) IL-6, (D) TNF-α, (E) IFN-γ, and (F) IL-10 were analyzed for the MEP and BCP groups. Intragroup and intergroup analyses were conducted. Effect sizes were calculated using Cohen's d. Acronyms: IL = interleukin, TNF-α = tumor necrosis factor-alpha, IFN-γ = interferon-gamma, MEP = multicomponent exercise program, BCP = behavior change program.

Distinct immunological responses were observed between study groups. Participants allocated to the MEP programme exhibited significant reductions in circulating IL-2, IL-6 and TNF-α concentrations following the intervention, whereas participants in the BCP group demonstrated a significant increase in IL-6 levels over the same period.

At baseline, circulating concentrations of IL-2, IL-10 and TNF-α were higher in the MEP group than in the BCP group. Following completion of the intervention, only IL-10 remained significantly higher in the exercise group, suggesting partial normalization of the inflammatory profile after multicomponent exercise.

No statistically significant changes were observed for SARS-CoV-2-specific IgA concentrations or IFN-γ in either intervention group.

3.6. Cytokine Ratios

Changes in cytokine balance are presented in Figure 4.

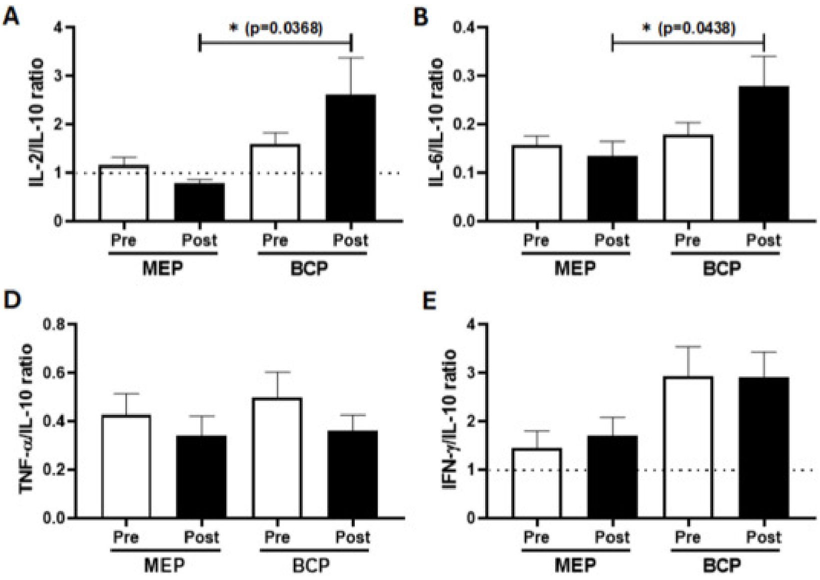

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Figure 4. Pro-/Anti-Inflammatory Cytokine Ratios Pre- and Post-Intervention. Mean (±SD) ratios of (A) IL-2/IL-10, (B) IL-6/IL-10, (C) TNF-α/IL-10, and (D) IFN-γ/IL-10 was calculated for the MEP and BCP groups. Intragroup and intergroup analyses were conducted. Effect sizes were calculated using Cohen's d. Acronyms: IL = interleukin, TNF-α = tumor necrosis factor-alpha, IFN-γ = interferon-gamma, MEP = multicomponent exercise program, BCP = behavior change program.

Analysis of cytokine ratios demonstrated divergent inflammatory responses between interventions. Participants allocated to the BCP group exhibited significant increases in both the IL-2/IL-10 and IL-6/IL-10 ratios following the intervention, indicating a shift towards a more pro-inflammatory cytokine profile. Conversely, these ratios remained stable in participants undertaking the multicomponent exercise programme.

No statistically significant changes were identified for the TNF-α/IL-10 or IFN-γ/IL-10 ratios in either study group.

Overall, the findings indicate that the multicomponent exercise programme was feasible to implement and was associated with greater improvements in functional performance together with favourable modulation of selected inflammatory biomarkers when compared with the behavioural intervention.

Discussion

The present randomized pilot feasibility trial investigated the feasibility and preliminary effects of a 10-week multicomponent exercise programme in community-dwelling older adults following COVID-19 vaccination. Overall, the findings demonstrate that the intervention was feasible and safe to implement within a primary healthcare setting and was associated with improvements in functional performance together with favourable modulation of selected inflammatory biomarkers. Although the limited sample size precludes definitive conclusions, the observed effect sizes support the potential clinical relevance of multicomponent exercise as a strategy to promote healthy ageing.

Functional Performance

The most robust finding of the present study was the improvement in functional performance following participation in the multicomponent exercise programme. Participants allocated to the MEP group demonstrated a significant increase in SPPB scores, accompanied by a large effect size (d = 1.90), whereas improvements observed in the BCP group were considerably smaller. Since the SPPB is widely recognised as one of the strongest predictors of disability, institutionalisation and mortality in older adults, improvements of this magnitude may have important implications for maintaining independence and quality of life.

These findings are consistent with previous investigations demonstrating that multicomponent exercise programmes effectively improve lower-limb strength, balance, gait performance and functional mobility in older populations (Izquierdo et al., 2021; Cadore and Rodríguez-Mañas, 2013). Unlike interventions focusing exclusively on resistance or aerobic training, multicomponent exercise simultaneously targets several physiological systems that contribute to functional capacity, making it particularly suitable for community-dwelling older adults.

Although habitual physical activity increased following the intervention, these changes did not reach statistical significance. This finding is not unexpected considering the relatively short intervention period and the limited statistical power of a pilot study. Nevertheless, the positive trend observed suggests that participation in structured exercise programmes may encourage more active lifestyles beyond supervised sessions.

Immunological and Inflammatory Responses

The principal novelty of the present study lies in the observed modulation of inflammatory biomarkers following the multicomponent exercise intervention. Significant reductions in circulating IL-2, IL-6 and TNF-α concentrations were identified in participants allocated to the exercise programme, whereas the behavioural intervention was associated with increased IL-6 concentrations and less favourable cytokine ratios.

Ageing is characterised by chronic low-grade inflammation, commonly referred to as inflammaging, which contributes to immunosenescence and increases susceptibility to infectious diseases, cardiovascular disorders and functional decline (Duggal et al., 2019; Di Micco et al., 2021, Lindo et al, 2024). Among the cytokines evaluated, IL-6 has consistently been identified as one of the most important biomarkers of biological ageing and poor health outcomes in older adults. Therefore, the reduction in IL-6 observed following multicomponent exercise may represent an important biological adaptation, although confirmation in larger randomized trials is required.

Similarly, reductions in TNF-α reinforce the anti-inflammatory potential of regular exercise. Previous studies have demonstrated that repeated exercise sessions promote the release of anti-inflammatory myokines, improve metabolic regulation and reduce chronic activation of inflammatory pathways (Cao Dinh et al., 2019; Salimans et al., 2022). The present findings are consistent with this growing body of evidence and suggest that structured multicomponent exercise may contribute to attenuating age-related inflammatory processes following COVID-19 vaccination.

Particularly interesting was the analysis of cytokine ratios. While participants in the behavioural intervention demonstrated increases in both the IL-2/IL-10 and IL-6/IL-10 ratios, these markers remained stable following multicomponent exercise. Since cytokine ratios provide information regarding the balance between pro- and anti-inflammatory responses, these observations further support the hypothesis that exercise contributes to maintaining a more favourable inflammatory profile.

No significant changes were observed in SARS-CoV-2-specific IgA concentrations. This finding may indicate that the intervention period was insufficient to modify vaccine-specific humoral immunity or that exercise exerts greater influence on inflammatory regulation than on antibody concentrations. Similar observations have been reported in previous studies evaluating immune adaptations to exercise in older adults (Furtado et al., 2021; Silva et al., 2023).

Lipid Profile

Although within-group biochemical changes were generally modest, participants allocated to the exercise programme demonstrated lower post-intervention concentrations of total cholesterol, LDL cholesterol and non-HDL cholesterol compared with the behavioural intervention. Moderate-to-large effect sizes suggest that these changes may be clinically relevant despite the absence of statistically significant differences for some variables.

These findings agree with previous evidence indicating that regular exercise contributes to improved lipid metabolism and cardiovascular health in older adults (Furtado et al., 2021; Rodrigues et al, 2024). Nevertheless, because this was a pilot study with a limited sample size and relatively short intervention period, these observations should be interpreted cautiously until confirmed in adequately powered randomized clinical trials.

Feasibility of the Intervention

Beyond its preliminary physiological findings, this study demonstrates that implementation of a supervised multicomponent exercise programme within the Family Health Strategy was feasible and safe. Recruitment was completed successfully, participants tolerated the intervention well, and no serious or exercise-related adverse events were reported. These findings reinforce the practicality of implementing structured exercise programmes within primary healthcare services using relatively simple and low-cost resources.

Strengths and Limitations

This study has several strengths. It is one of the few randomized pilot feasibility trials investigating the combined effects of multicomponent exercise on functional performance, lipid metabolism and immuno-inflammatory biomarkers in older adults following COVID-19 vaccination. The multidimensional assessment of physical, biochemical and immunological outcomes provides a comprehensive overview of the potential benefits of structured exercise in this population.

Several limitations should also be acknowledged. First, the relatively small sample size limits statistical power and the generalisability of the findings. Second, participant attrition reduced the final analytical sample and may have introduced selection bias. Third, dietary habits, sleep quality and other lifestyle factors were not controlled and could have influenced inflammatory and metabolic outcomes. Fourth, physical activity was assessed using a self-reported questionnaire, which is inherently susceptible to recall bias. Finally, the relatively short intervention period may not have been sufficient to detect changes in all biochemical and immunological markers.

Future Directions

Future randomized controlled trials involving larger samples, longer intervention periods and objective measures of physical activity are warranted to confirm these preliminary findings. Further research should also investigate whether multicomponent exercise enhances long-term vaccine responsiveness, immune resilience and healthy ageing in community-dwelling older adults.

Conclusion

This randomized pilot feasibility trial demonstrated that a 10-week multicomponent exercise programme is a feasible and safe intervention for community-dwelling older adults following COVID-19 vaccination. The programme was successfully implemented within a primary healthcare setting, with satisfactory participant retention and no serious exercise-related adverse events.

Although the study was not powered to establish definitive clinical efficacy, the findings provide preliminary evidence that multicomponent exercise may improve functional performance while promoting favourable modulation of selected inflammatory biomarkers, particularly IL-2, IL-6 and TNF-α. In contrast, no meaningful changes were observed in SARS-CoV-2-specific IgA concentrations, suggesting that the intervention may exert a greater influence on inflammatory regulation than on vaccine-specific humoral responses.

Given the exploratory nature of this pilot study and its limited sample size, these findings should be interpreted with caution. Nevertheless, they support the feasibility of conducting larger randomized controlled trials to determine the effectiveness of multicomponent exercise in improving functional capacity, immune regulation and healthy ageing in older adults.

CRediT authorship contribution statement

André Luís Lacerda Bachi: Resources. **Marcelo Rossi:** Resources. **Albená Nunes-Silva:** Investigation. **Francisco José Barbas Rodrigues:** Writing – review & editing. **Jônatas Bussador do Amaral:** Funding acquisition. **Antonio Felipe Souza-Gomes:** Formal analysis. **Guilherme Eustáquio Furtado:** Data curation. **Bruna Maria Palotino-Ferreira:** Conceptualization. **Saulo Vasconcelos:** Formal analysis. **Clarice Alves dos Santos:** Software. **Juliana da Silva Oliveira:** Methodology

Uncited reference

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Patient Consent Statement

The authors confirm that written informed consent was obtained from all participants prior to their enrolment in the study.

Before providing consent, all participants received comprehensive verbal and written information regarding the study objectives, procedures, potential risks, expected benefits, and their right to withdraw from the study at any time without penalty.

The study protocol was reviewed and approved by the appropriate Institutional Research Ethics Committee (Approval No. XXXXXXX) and was conducted in accordance with the ethical principles of the Declaration of Helsinki and the Guidelines for Exercise Science Research.

The signed informed consent forms are securely held by the investigators and will be made available to the journal upon reasonable request, where permitted by applicable ethical and legal requirements.

Data Availability

The data supporting the findings of this study are available upon reasonable request.

Participant Consent Statement

All participants in this study provided informed written consent prior to participation in the research.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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