

Does nutritional status influence the effects of a Multicomponent exercise program on body composition and physical fitness in older adults with limited physical function?

Ana Moradell^{1,2,3,4}, Ángel I. Fernández-García^{1,2,3,4}, David Navarrete-Villanueva^{1,2,3,5}, Jorge Pérez-Gómez^{3,6}, Eva Gesteiro^{3,7}, Ignacio Ara Royo^{8,9}, Jose Antonio Casajús^{1,2,3,5,9}, Alba Gómez-Cabello^{1,2,3,4,9,10}, Germán Vicente-Rodríguez^{1,2,3,4,9}.

¹GENUD (Growth, Exercise, NUtrition and Development) Research Group, Universidad de Zaragoza, 50009 Zaragoza, Spain.

²Agrifood Research and Technology Centre of Aragón -IA2-, CITA-Universidad de Zaragoza, 50009, Zaragoza, Spain.

³ Exercise and Health in Special Population Spanish Research Net (EXERNET).

⁴ Department of Physiatriy and Nursing, Faculty of Health and Sport Science FCSD, University of Zaragoza, 50009 Zaragoza, Spain.

⁵ Department of Physiatriy and Nursing, Faculty of Health, University of Zaragoza, 50009 Zaragoza, Spain.

⁶ HEME Research Group, University of Extremadura, 10003 Cáceres, Spain.

⁷ ImFINE Research Group, Department of Health and Human Performance, Faculty of Physical Activity and Sport Sciences-INEF, Polytechnic University of Madrid, 28040 Madrid, Spain.

⁸ CIBER of Frailty and Healthy Aging (CIBERFES), 28029 Madrid, Spain.

⁹ Biomedical Research Net in Physiopatology, Obesity and Nutricition (CIBERObn), 28029 Madrid, Spain

¹⁰ Defense University Center,50090 Zaragoza, Spain

* Correspondence: gervicen@unizar.es; Tel.: +34-876-55-37-56

ABSTRACT

The effects of physical exercise and aging on fitness may be influenced by nutritional status. This study investigates the effects of a 6-month multicomponent exercise training (MCT) on nutritional status and evaluate if this type of exercise could affect differently body composition and physical fitness depending on the nutritional status of older adults with decreased functional capacity.

Ninety-three participants (80.4 ± 6.0 y) were divided into control ($n=45$) and intervention ($n=48$) groups. The intervention consisted of a 6-month multicomponent training. Comparisons between changes in body composition and fitness during the 6-months were performed between individuals at risk of malnutrition and those well-nourished, according to the Mini Nutritional Assessment. Model mixed effect analyses were used to investigate differences after the 6 months of MCT between groups.

Well-nourished participants compared with those at risk of malnutrition had higher: arm (13.4 ± 3.5 vs 14.3 ± 3.6 repetitions) and leg strength (9.0 ± 3.0 vs 11.1 ± 3.3 repetitions), maximum walking speed (31.6 ± 13.1 vs 23.7 ± 6.3 s), agility (11.9 ± 5.8 vs 8.3 ± 2.1 s), and aerobic capacity (31.6 ± 13.1 vs 23.7 ± 6.3 m), at baseline. After the training, those without risk of malnutrition in CON decreased their nutritional status (-1.7 ± 0.7 points). Those well-nourished that performed the intervention, decreased total fat mass (-1.0 ± 0.3 kg) and body fat percentage ($-1.2 \pm 0.4\%$). Both groups of training improved similarly in all tests, except for balance, in which well-nourished showed improvements of 6.3 ± 1.9 s.

These results underline the usefulness of MCT improving physical fitness regardless of nutritional status and preventing nutritional status detriment in well-nourished older adults, who are fitter and benefit more, in terms of body composition.

HIGHLIGHTS

- Multi-component exercise program seems to be effective in delaying detriments in nutritional status of well-nourished people.
- Well-nourished older people obtain more benefits in body composition from the multicomponent exercise than those at risk of malnutrition, decreasing adiposity.
- Positive effect of multicomponent exercise was observed in physical fitness independently of nutritional status.

Key words: aging, fat mass, malnutrition, muscle strength.

1. INTRODUCTION

Multiple physiological changes occurring with aging lead to an important decline in physical function, subsequent increased risk of vulnerability and loss of autonomy (1). Some of the most remarkable changes occurs in body composition in which there is an increase in fat mass (FM) and a reduction in muscle mass, which are related with important diseases such as sarcopenia and obesity (2). Meanwhile, the implications of these changes also affect physical fitness showing an important reduction of strength, power, endurance or agility (3). To reverse these outcomes will facilitate older people to perform daily activities with autonomy and would have a positive impact in social and health systems sustainability (4).

Other important environmental factors such as a poor nutrition could also influence these aging declines. Undernourished, energy deficiencies, low protein intake and vitamin D deficiency could aggravate losses in physical function as they are needed to maintain or improve muscle mass and strength (5). Moreover, poor nutritional status has been closely related with an increased risk of being frail (6). In this way, to prevent and reverse this state has been established as a priority in the new emerging studies (7).

Physical activity and exercise have been proposed as the best strategies for active and healthy ageing for older population (8). In fact, a recent expert consensus propose as a main challenge for the near future to include exercise prescription as a mandatory part of this population's care (9). In general, multicomponent training exercise programs (MCT) have been demonstrated to be the most effective type of physical exercise for improving health in sarcopenia, osteoporosis, people with dementia and who have suffered falls and, especially in those at risk of being frail (7,9). Likewise, other beneficial effects from exercise are improvement in appetite, well-being, mood and behaviour disturbance (10,11). Thus, exercise could led to a change and potential improvement in nutritional status as other authors previously report relative to strength training program (12). Additionally, it is common a decline in food intake during aging which could be related with nutritional deficiencies such as protein, vitamins, antioxidants or polyunsaturated fatty acids which are involved in muscle synthesis (13). For this reason, it could be reasonable to believe that differences in the effects of an exercise program according to the nutritional status of this population could be found, thus, it is crucial to know how it affects and to establish the ideal nutritional levels to maximise the benefit of physical exercise. Despite this, very few studies comparing possible effects of MCT exercise programs between people with different nutritional status are scarce.

In this line, the EXERNET-Elder 3.0 study, was a project with the main objective of improving physical function and other health-related variables such as body composition in

functional frail and pre-frail older adults (14). Until now, several benefits due to this program have been reported as relation to FM (15), bone mass structure (16) and fitness (pending of publication). Nevertheless, the relationship between nutritional status and these previous health-related outcomes have been well described in the literature and the prevalence of poor nutritional status is common in this population (6). To elucidate the possible difference in the effects of these type of exercise interventions on malnourished older population could provide relevant information to move towards individualised, precision exercise prescription to improve the prevention and treatment of functional disability and frailty. Thus, main aims of the present study were: 1) to compare body composition and physical fitness between older adults with limited physical function at risk and without risk of being malnourished, 2) to study if our MCT exercise program could improve nutritional status, and 3) to study if the MCT exercise program has the same effects in those at risk and without risk of malnutrition.

2. MATERIAL AND METHODS

2.1 *Study design and participants*

This intervention study is a non-randomized control trial which was conducted in the framework of the EXERNET-Elder 3.0 project, which was carried out between 2018 and 2020. The intervention consisted of a 6-months MCT program for frail and pre-frail older adults and its main aim was to improve physical function of this population. Participants were recruited from four health care centres and three nursing homes from the city of Zaragoza, Spain. People above 65 years were screened according to their functionality with the Short Physical Performance Battery (SPPB) (17), and those scoring as moderate and slightly limitation (>4 , <10 points) (18) were selected to participate in the exercise program. Those who had cancer and/ or dementia were excluded. The whole methodology of this project has been described elsewhere (14).

Preferences and availability for the initial sample (110 participants) were considered to create the following groups: control group (CON) and training group (TRAIN). For the present study, TRAIN and CON groups were also subdivided at baseline into the following groups: with risk of being malnourished and or without risk of being malnourished. From the initial sample of 110 participants, only 93 older adults (45 CON and 48 TRAIN) completed information about risk of being malnourished (questionnaire described below) and could be included in this report.

Although it was non-randomized trial, groups were homogeneous. No baseline differences of CON and TRAIN could be seen in Supplementary 1. Additionally, according to ROBINS-I tool for assessing the risk of bias in a non-randomized study (*Cochrane Handbook for Systematic*

Reviews of Interventions version 6.2. Chapter 25, 2021), the risk of bias is low to moderate for the present research.

Personal information and other health outcomes were collected through a structured questionnaire. Specifically, the variables included in this article were as follows: mean of self-reported daily walking hours and sitting hours (19), adherence to Mediterranean diet (20) and Mini Mental Examination (for cognitive status) (21,22). Body composition measurements and physical fitness tests were performed in both groups at baseline and after 6-month MCT (23,24). Fasting blood sample tests were obtained to measure vitamin D.

The study was approved by the Hospital Universitario Fundación de Alcorcón (16/50) (Alcorcón, Spain) and was registered in *clinicaltrials.gov* (reference number: NCT03831841). All participants of the study signed an informed consent to be included. The study was developed in accordance with the Helsinki Declaration of 1961 revised in Fortaleza (2013) and the current legislation of human clinical research of Spain (Law 14/2007).

2.2 The EXERNET Elder 3.0 multicomponent exercise program

Exercise groups consisted of 8-16 older adults and all sessions were supervised by specialized instructors complying a maximum ratio of 12 participants per instructor. Participants trained three days a week for 1 hour. All sessions were organized with the following structure: 10 min of warm-up, 35-40 min of main part exercises and 10-15 min of cooldown. Exercises were focus on endurance, strength, flexibility, balance, coordination and functional capacity in daily life activities. All the intervention had a progression of the training load to ensure appropriate stimulus and to developed adaptations. Intensity of all exercises was also adapted to each participant's characteristics and functional status. The training protocol has been described in detail elsewhere (14). Meanwhile, to improve CON attendance, monthly speeches about healthy lifestyles were developed for all participants.

2.3 Mini Nutritional Assessment (MNA)

Nutritional risk was determined using the MNA questionnaire, which consists of 18 questions: the type of living accommodation, the use of regular medication, acute diseases, mobility, neuropsychological problems, pressure sores or skin ulcers, number of whole meals consumed and choice of food, daily fluid intake, possible requirement for help in eating, the perceived adequacy of food intake, weight loss during the past three months and self-perception of health. It also included measurements of body mass index (BMI) and circumferences of the mid-upper arm and calf.

According to the score obtained, the subjects were classified as “malnourished” (< 17 p), “at risk of malnutrition” ($17 - 23.5$ p), or “well-nourished” (> 23.5 p) (25). None of the participants scored as “malnourished” so only two groups were considered: “At risk of malnutrition” and “well-nourished”.

2.4 Anthropometric and body composition measurements

Anthropometric measurements were performed twice, and the mean was calculated. In cases where the difference between both measurements exceeded 0.5 cm, a third measurement was performed, and the median was calculated. A portable stadiometer with 2.10 m maximum capacity and 1 mm error margin (Seca, Hamburgo, Germany) was used to measure height. Hip, waist, mid upper arm and calf circumferences were all taken using a flexible non-elastic measuring tape Rosscraft Anthrotape (Rosscraft Innovations Inc, Vancouver, Canada). Anthropometrics measurements were performed by International Society for the Advancement of Kinanthropometry accredited researchers following its standards (26).

A body composition analyser based on Bio-Electrical Impedance Analysis (BIA) with 200 kg maximum capacity and 50 g error margin (TANITA BC-418MA, Tanita Corp., Tokyo, Japan) was used to obtain body weight (kg), FM (kg), percentage of body fat and fat-free mass. BMI was calculated. Participants came to the research center fasting and with an empty bladder. They were barefoot and wearing light clothes during the body composition measurements. All measurements were performed at same hour and conditions for all participants and evaluations.

2.5 Physical fitness assessment

The tests were always performed in the same order to ensure that all participants performed the fitness evaluations under the same conditions. Test performed were: Balance test (Flamingo’s test) (24), Strength of upper extremities (Arm Curl Test)(23), Lower-body strength test (Chair Stand test) (23), Flexibility of the upper extremities (Back Scratch Test) (23), Flexibility of the lower extremities (Chair Sit-and-Reach test) (23), Agility/ dynamic balance (8-Foot Up-and-Go test) (23), Maximum walking speed (Brisk Walking test) (24), Aerobic capacity (6-Minute Walk test) (23), Handgrip Strength (Takei TKK 5401, Tokyo, Japan). Whole description of the tests is described in detail elsewhere (14).

Relative Sit to stand muscle power test was calculated using the subject's body mass and height, chair height and the time needed to complete five sit to stand tests repetitions in 30 minutes (27).

2.6 Statistical analysis

Statistical analyses were completed using The Statistical Package for the Social Sciences v. 20.0 for Windows (SPSS, Inc, Chicago, IL., USA). Normality of the sampling distribution was study using Shapiro-Wilk tests. The level of statistical significance of all tests was set at $p < 0.05$.

Descriptive data are reported as mean \pm standard deviation, number of participants (n) or percentage (%), according to the nature of each variable. One factor Analysis of Variance (ANOVA) was used to study differences; firstly, between control and train groups in order to assess the homogeneity of groups and secondly, between those participants at risk of being malnourished and those without risk.

Model Mixed Effect Analyses were performed to compare firstly, differences in changes in the MNA score and secondly, changes in body composition and physical fitness during the 6-month MCT between groups at risk of malnutrition and those well-nourished status in CON and TRAIN separately. Changes in variables were calculated subtracting post-intervention values minus baseline values. Three different models were performed to study changes during 6 months of training in physical fitness and body composition variables; 1) adjusted by age, sex and baseline value, 2) adjusted by age, sex, baseline value, sitting and walking hours, and 3) adjusted by age, sex, baseline value and Mini Mental Examination score (cognitive status). Power analyses were also reported ($1-\beta$) for all comparisons.

3. RESULTS

3.1 Descriptive differences

Supplementary material 1 showed the homogeneity of CON and TRAIN groups. No differences were found in main variables of the study: Short Physical Performance Battery and Mini Nutritional Assessment score.

Differences at baseline between participants at risk of malnutrition and those well-nourished are shown in Table 1.

Table 1. Descriptive differences between those at risk of malnutrition and those well-nourished at the beginning of the study.

| | Whole sample | Risk of malnutrition (n=33) | Well nourished (n=60) | p-value |
|--------------------------------------|--------------|-----------------------------|-----------------------|-----------------|
| Age (y.) | 80.4±6.0 | 80.1±6.7 | 80.6±5.6 | .737 |
| SPPB (points) | 7.5±1.5 | 6.9±1.6 | 7.8±1.4 | .006 |
| Frail | 25 (27%) | 13 (40%) | 12 (20%) | .073 |
| Pre-frail | 67 (72%) | 20 (60%) | 47 (80%) | |
| ADM (points) | 7.5±1.8 | 7.4±1.9 | 7.5±1.7 | .712 |
| Walking (h/day) | 1.5±1.2 | 1.2±1.1 | 1.7±1.3 | .740 |
| Sitting time (h/day) | 6.3±2.7 | 7.0±2.8 | 5.8±2.5 | .044 |
| Mini Mental (points) | 26.1±3.2 | 25.0±3.8 | 26.7±2.6 | .018 |
| Vit D (ng/mL) | 26.7±13.9 | 25.6±11.9 | 27.4±15.0 | .568 |
| Body composition measurements | | | | |
| Weight (kg) | 73.1±14.7 | 74.4±18.9 | 72.4±11.9 | .547 |
| BMI (kg/m ²) | 29.7±5.6 | 29.9±7.3 | 29.7±4.4 | .886 |
| BF% | 37.2±7.3 | 35.3±8.3 | 38.1±6.7 | .098 |
| FM (kg) | 27.6±9.0 | 27.1±11.7 | 27.8±7.5 | .742 |
| FFM (kg) | 45.5±9.1 | 47.3±11.3 | 44.7±7.8 | .203 |
| Waist Cir (cm) | 94.0±13.0 | 95.3±17.2 | 93.0±13.0 | .526 |
| Hip Cir (cm) | 104.5±10.1 | 104.8±11.2 | 104.4±9.7 | .899 |
| Physical Fitness Assessment | | | | |
| Balance (s) | 7.0±6.7 | 6.2±8.1 | 7.6±7.5 | .425 |
| Arm Strength (rep) | 11.9±2.7 | 13.4±3.5 | 14.3±3.6 | .001 |
| Arm Flexibility (cm) | -14.8±10.9 | -16.4±14.0 | -13.9±8.8 | .280 |
| Leg Strength (rep) | 10.4±3.4 | 9.0±3.0 | 11.1±3.3 | .003 |
| Mean power (W) | 155.4±65.7 | 141.1±60.1 | 162.9±67.7 | .135 |
| Relative Power (W·kg ⁻¹) | 212.5±68.6 | 186.4±56.2 | 226.2±70.9 | .008 |
| Leg Flexibility (cm) | -13.3±11.3 | -15.6±12.5 | -12.1±10.5 | .160 |
| Agility 2,45m (s) | 9.6±4.1 | 11.9±5.8 | 8.3±2.1 | <.001 |
| Maximum Walking Speed in 30m (s) | 26.5±9.9 | 31.6±13.1 | 23.7±6.3 | <.001 |
| Endurance (m) | 357.7±104.8 | 307.7±119.1 | 383.9±86.4 | .001 |
| Handgrip Strength (kg) | 21.3±8.3 | 21.0±9.0 | 21.4±7.9 | .835 |

SPPB: Short Physical performance Battery, ADM: adherence to Mediterranean diet; Vit D: Vitamin D; BMI: Body Mass Index, BF%: Body Fat Percentage, FM: Fat Mass, FFM: Fat Free Mass, rep: repetition, Cir: Circumference. p- value describes differences between groups. All statistically significance was established at <0.05.

The initial sample of 93 participant (68 females) was divided in those at risk of malnutrition (34 individuals, 21 females) and those well-nourished (59 individuals, 47 females). Those at risk of malnutrition showed lower score in the SPPB, higher score in Mini Mental and lower sitting time than the well-nourished ones (all $p<0.05$). No significant differences were observed for body composition. However, the group at risk of malnutrition had fewer arm curl repetitions and chair stands in strength tests, as well as low relative power (all $p<0.05$). They also present less agility and lower maximum walking speed and fewer meters covered in endurance test in comparison to well-nourished participants (all $p<0.05$).

3.2. Changes in MNA after 6-month MCT

Adherence measured as percentage of assistance from the total sessions ranged from 71.2 to 97.1% for those at risk of malnutrition and from 52.9 to 98.5% those without risk. Table 2 shows changes in the MNA total score. No differences were found between CON and TRAIN when whole group was analyzed and neither within groups ($1-\beta=0.108$ (10.8%) and $1-\beta=0.329$ (32.9%), respectively). When analyses were performed dividing these groups by nutritional status those older adults without risk of malnutrition in the CON showed a worse nutritional status with a significant decrease of the total score (-1.7 ± 0.7 ; $p<0.05$), but not significant differences were found the group at risk. Statistical differences were found in changes after 6 months between this both groups, ($1-\beta=0.641$, 64%). Statistical power for all these previous non-significant analyses were ranged from 0.175 to 0.578 (17.5-57.8%).

Table 2. Differences in MNA score changes between control and training groups and among subgroups created by nutritional status (model mixed effect).

| | CONTROL | | | | TRAIN | | P-value | 1- β |
|-----------------------------|----------------------------|-----------------------|---------|------------|-----------------------------|-----------------------|---------|------------|
| Change in MNA (whole group) | -0.6 \pm 0.6 | | | | 0.3 \pm 0.6 | | .302 | .117 |
| | Risk of malnutrition (n=7) | Well-nourished (n=18) | P-value | 1- β | Risk of malnutrition (n=10) | Well-nourished (n=28) | P-value | 1- β |
| Change in MNA (by groups) | 2.8 \pm 1.4 | -1.7 \pm 0.7* | .022 | .641 | -0.7 \pm 1.4 | 0.6 \pm 0.7 | .520 | .175 |

MNA: mini nutritional assessment; *Statistical significance within groups over time; P value describes differences between groups. All statistically significance was established at <0.05 .

3.3 Changes in body composition after 6-month MCT.

Changes in body composition between pre-training and post-training adjusted by sex, age and baseline values are shown in Table 3.

Table 3. Body composition changes in older adults at risk of malnutrition and well-nourished in control and training groups between pre- and post-training periods, adjusted by baseline values, sex and age.

| | CONTROL | | | | TRAIN | | | |
|--------------------------|-----------------------------|-----------------------|----------------|------|-----------------------------|-----------------------|----------------|------|
| | Risk of malnutrition (n=11) | Well-nourished (n=21) | <i>p-value</i> | 1-β | Risk of malnutrition (n=12) | Well-nourished (n=33) | <i>p-value</i> | 1-β |
| Weight (kg) | 0.4±0.8 | -0.7±0.6 | .303 | .210 | -0.3±0.7 | -0.5±0.4 | .825 | .051 |
| BMI (kg/m ²) | 0.2±0.4 | -0.5±0.3 | .192 | .244 | -0.5±0.3 | -0.2±0.2 | .386 | .154 |
| FM (kg) | 0.2±0.8 | -0.4±0.5 | .528 | .419 | 0.2±0.6 | -1.0±0.3* | .104 | .309 |
| FFM (kg) | 0.2±0.6 | -0.2±0.4 | .669 | .064 | -0.4±0.7 | 0.6±0.4 | .211 | .295 |
| BF% (%) | 0.2±0.8 | -0.3±0.5 | .595 | .208 | 0.4±0.7 | -1.2±0.4* | .138 | .078 |
| Waist Cir.(cm) | 3.8±2.7 | 2.2±2.3 | .660 | .112 | 5.1±2.4* | 3.3±1.1* | .529 | .083 |
| Hip Cir.(cm) | 3.7±2.9 | 3.6±1.9 | .976 | .067 | 1.4±1.7 | 1.7±0.7* | .873 | .051 |

Mean differences and standard deviation reported for each body composition variable. BMI: Body Mass Index, FM: Fat Mass, FFM: Fat Free Mass, BF%: Body Fat Percentage, Cir: Circumference. *Statistically significance within groups over time. *p-value* describes differences between groups. All statistically significance was established at <0.05.

Significant decreases were observed in FM and percentage of body fat and significant increases in hip and waist circumferences only within those without risk malnutrition from the TRAIN ($p < 0.050$), with a statistical power ranged from 0.543 and 0.820 (54.3-82%). No changes were found within CON groups in those at risk of malnutrition, in those well-nourished. No significant differences between groups were observed neither in CON nor in TRAIN. The statistical power for non-significant analyses for comparisons within group were ranged from 0.052 to 0.332 (5.2-33.2%).

Model 2 (adjusted by sex, age, time spend sitting and time spend walking), compared to model 1, showed same results for body composition.

When cognitive status was added to adjust the analyses (Model 3), some differences were observed. A new statistically significant change was observed for weight, which decreased significantly in those well-nourished in TRAIN ($p < 0.05$).

3.4 Changes in physical fitness after 6-month MCT.

Table 4 shows changes in physical fitness between pre- and post-training for Model 1 (adjusted by sex, age, and baseline values).

Table 4. Fitness changes in older adults at risk of malnutrition and well-nourished in control and training groups between pre- and post-training, adjusted by baseline values, sex and age.

| | CONTROL | | | | TRAIN | | | |
|---|-----------------------------|-----------------------|----------------|------|-----------------------------|-----------------------|----------------|------|
| | Risk of malnutrition (n=11) | Well-nourished (n=21) | <i>p-value</i> | 1-β | Risk of malnutrition (n=12) | Well-nourished (n=33) | <i>p-value</i> | 1-β |
| Balance (s) | 4.6±3.1 | 1.9±2.2 | .495 | .061 | 5.5±3.0 | 6.3±1.9* | .819 | .108 |
| Arms Flexibility (cm) | 0.8±2.6 | 3.1±2.0 | .523 | .054 | 1.9±1.7 | 1.6±1.1 | .890 | .050 |
| Legs Flexibility (cm) | 2.3±2.6 | 8.5±2.0* | .087 | .324 | 5.7±2.6* | 4.5±1.7* | .705 | .064 |
| Arms Strength (rep) | 0.9±1.2 | -0.1±0.9 | .536 | .161 | 3.7±1.1* | 5.6±0.6* | .108 | .229 |
| Legs Strength (rep) | -0.5±0.9 | 1.5±0.7* | .112 | .277 | 1.9±0.7* | 3.6±0.5* | .082 | .369 |
| Mean power strength (W) | -7.9±13.8 | 11.7±11.1 | .297 | .341 | 34.8±13.4* | 52.2±7.6* | .285 | .322 |
| Relative Power Strength (W·kg ⁻¹) | -0.1±0.2 | 0.3±0.1 | .123 | .250 | 0.4±0.2* | 0.7±0.1* | .212 | .174 |
| Agility (s) | -0.4±0.6 | 1.4±0.4* | .028 | .641 | -2.0±0.4* | -2.2±0.2* | .602 | .077 |
| Maximum Walking Speed (s) | 1.7±1.7 | 1.2±1.3 | .826 | .052 | -3.4±1.0* | -4.6±0.6* | .316 | .153 |
| Endurance (m) | 1.2±26.0 | -9.1±18.6 | .757 | .060 | 15.4±24.1 | 25.7±14.9 | .733 | .061 |
| Handgrip Strength (kg) | 0.2±1.2 | 1.9±0.9* | .281 | .329 | 1.4±1.0 | 2.0±0.6* | .597 | .177 |

Mean differences and standard deviation reported for each body composition variable. Rep: repetitions. *Statistically significance within groups over time. *p-value* describes differences between groups. All statistically significance was established at <0.05.

Both groups in TRAIN (at risk malnutrition and well-nourished) showed significant improvements in leg flexibility, arm curls, chair stands, relative power, agility and maximum

walking speed (all $p < 0.05$). However, no significant changes were observed in arm flexibility within group at risk malnutrition and neither within the group of well-nourished. For balance and handgrip strength tests, only those without risk of malnutrition showed an improvement ($p < 0.05$). No statistical differences between well-nourished and risk of malnutrition groups were observed in any of the tests. The statistical power of the analyses that lead significant results ranged from 0.640 to 1.000 (64-100%) while those non-significant ranged from 0.140 to 0.540 (14-54%).

In CON, those well-nourished showed statistical improvements in leg flexibility, leg strength and handgrip strength while they spent more time spent in the agility test (all $p < 0.05$, $1-\beta$ ranged from 0.591 to 0.892, 59.1-89.2%). Those at risk did not show statistically significant changes ($1-\beta$ ranged from 0.057 to 0.173, 5.7-17.3%). Only statistical differences between those at risk of malnutrition and those well-nourished were observed for agility ($p < 0.05$).

Model 2 (adjusted by sex, age, time spend sitting and time spend walking), compared to Model 1, showed same results for body composition while there were slight differences for physical fitness. There were not statistically significant changes in those at risk of malnutrition in the TRAIN. However, an improvement was observed in the balance test in this group (6.6 ± 2.1 s; $p < 0.05$). In addition, those well-nourished increased their aerobic capacity (31.5 ± 13.1 m; $p < 0.05$). The significant differences mentioned in model 1 were maintained. No differences were found for CON comparing to model 1. Table describing these data is shown in Supplementary 2.

When cognitive status was added as a covariable (Model 3), well-nourished in TRAIN increased their aerobic capacity (29.6 ± 14.2 m), while those at risk of malnutrition in TRAIN showed an increase in balance (5.6 ± 2.0 s) (as Model 2) (all $p < 0.05$). Moreover, the statistically significant differences observed in leg strength and handgrip strength in those well-nourished in CON disappeared (compared with Model 1). Table describing these data is shown in Supplementary 3.

4. DISCUSSION

Main results obtained from the present study are; 1) older people at risk of malnutrition have lower physical fitness performance than those without risk of being malnourished while there are no differences in body composition, 2) the MCT exercise program used seems to be effective in delaying detriments in nutritional status of well-nourished people, 3) well-nourished older people obtain more benefits in body composition from the MCT than those at risk of malnutrition, as they show a decrease in adiposity, and 4) it appears that the benefits of MCTs are independent of nutritional status as there was a similar and positive effect for both TRAIN groups (those well-nourished and those at risk of malnutrition).

Nutrition is an important modifiable factor, which may influence the aging process. A poor nutritional status with energy and nutrients deficiencies could alter the physiological system and subsequently the physical function of the older adults (28). As it is common that frailty would be accompanied by malnutrition (6), important differences between those at risk of malnutrition and those well-nourished were expected to be found in this study.

First of all, MCT programs have been studied deeply during last years in order to improve health and physical function in people at risk of frailty (7). It seems to be the most effective exercise to prevent and treat some of the most important morbidities and adverse events occur in older people as describe the International Exercise Recommendations in Older Adults (ICFSR) (9). Concretely, the effects of the MCT used in this study have been previously studied in body composition (15,16) and physical fitness (pending for publication), showing positive results in this sample. In addition, the present study also demonstrates a prevention in the decline of MNA score in the TRAIN group. At least, it seems to happen for well-nourished older adults, as their pairs in CON showed a significant decrease in the MNA score. Two similar articles reported different results about nutritional status; Maltais et al. did not found a maintenance in a sample with dementia (29); however, Echevarria et al. found improvements with a guided MCT (30). Nonetheless, they did not compare possible differences between individuals who were initially at risk of malnutrition or well-nourished as in the present study. Despite they revealed slightly different results, it is reasonable to think on a relationship between exercise effects and nutritional status. However, a longer intervention would be needed to know if those at risk of malnutrition finally manage to avoid the development of malnutrition and whether the exercise intervention is effective to stop its progression as we expected.

Concerning body composition, no initial differences were observed between participants at risk of malnutrition and well-nourished. In this regard, differences in body composition showing worse values in FM and lean mass in those at risk of malnutrition, found in a sample of nonagenarians (31). The age of participants and the fact of including malnourished individuals may explain the different results. Being at risk of malnutrition is likely to be associated with a gradual deterioration during ageing, so their body composition and poor nutritional status may be changed strongly as they aged leading to set malnourished (32).

An inadequate nutrient intake followed by a weight loss, low muscle mass and low muscle synthesis is common in malnourished people and could compromise MCT effects. Present study shows a decrease in adiposity in well-nourished elderly but not in those at risk of malnutrition in the TRAIN. These results could be explained by an increase in inflammation (33,34), and could suggest that people at risk of being malnourished may need to combine this intervention with an adequate nutrition in order to reach the enough nutritional requirements, allowing them to achieve

same results as their pairs. However, no comparable studies to contrast our results were found, as the vast majority of them do not focus on physical exercise alone, neither compare people with and without risk of being malnourished, which could be a critical previous step to determine how to prevent the onset of malnutrition. Moreover, it has not to be missed that those at risk of malnutrition also presented longer time of sitting hours, which could be related with the difference baseline fitness levels as well as with the different effects of MCT in body composition, as well as with the different baseline fitness levels.

Nevertheless, while no changes were found for muscle mass during the intervention, significant improvements were observed in most of physical performance tests due to the MCT used in both groups (well-nourished and those at risk of malnutrition). Concretely, improvements were found in agility, maximum walking speed, upper and lower limb strength, relative power, and leg flexibility. No significant difference was found in aerobic capacity. It can be thought that here have no occurred an important metabolic and cardiovascular adaptations, such as increased VO_2 or mitochondrial biogenesis. It could happen because exercise was more focus in daily activities and time spent on improving endurance was not enough. However no publish results reveal that when all sample was considered, the train group showed improvements in this variable. For balance, at first it seemed to improve only in well-nourished individuals but when cognitive status was considered it increased significantly in both groups highlighting the relationship between balance and cognitive status (35). Similarly, another study concluded that dynamic balance, but not static balance, was associated with malnutrition (36), which could be explaining why in Model 1, those at risk do not improve results in the Flamingo's test, and also why initial differences were not observed initial differences (36). Moreover, it seems that although it was not significant, leg strength increased more in well-nourished than the group at risk which is in line to the results found by Kamo et al (37). These authors revealed that malnutrition was a negative factor which affects functional fitness changes after a resistance training (37). Despite that, our results support the idea that MCT produces neuromuscular adaptations without an increasing muscle mass and thus, those at risk of being malnourished could need more time to obtain the same effects than well-nourished. However, it is reasonable to think that an adequate nutritional intake could also improve results in the group at risk, although they seemed to be similar. In this line, lower intakes of proteins have been observe in the group at risk of malnutrition (13). On the other hand, in CON, significant changes were observed only in those at no risk, which seems to be more susceptible to aging at least in agility, showing significant difference with the group at risk. Nevertheless, the well-nourished group reported improvements in leg strength and flexibility, which could be influenced by the fact that they were under a middle evaluation along these 6 months. As their pairs at risk of malnutrition did not present same changes a possible explanation for these fluctuations is their good nutritional status which suggest that they meet the recommended nutrient intakes for having muscle adaptations.

Some limitations of this study should be mentioned. Firstly, a randomization of the sample was not possible as it was difficult to change older adult routines, and some participants refused to participate in TRAIN group. Therefore, groups were created according to the volunteers' preferences/availability in order to maximize attendance. Despite this fact, groups formed were homogeneous and the risk of bias assessed for this study pointed between low to moderate. Groups according to the MNA were created specifically for this study so important differences were observed in the number of participants in each subgroup (well-nourished and at risk of malnutrition). Analysis was not conducted under the intention to treat frame, which may lead to time bias or survival bias. Even though, sample sizes were similar in other studies. Therefore, studies with larger number of participants should be developed to establish deeper conclusions as the statistical power of our analyses was very low in some comparisons. Besides, adherence apparently did not affect the final results. Body composition measurements in this study were performed using BIA and even when all measurements were standardized to avoid possible bias (38). Other confounders not considered, such as pharmacology and nutrient intake or dietary quality may be interfering in the results. It should be highlighted that from the best of our knowledge, the MCT used is the one with the longest intervention period in this topic. Even though no one in TRAIN revoked their participation and the percentage of attendance was high, it was difficult to encourage attendance for CON, which may lead to bias. Moreover, all participants (both in CON and TRAIN) have requested to participate in an intervention group again in a new phase of the project.

5. CONCLUSION

To sum up, some differences between older adults at risk of malnutrition and well-nourished are observed in relation to physical fitness. The implementation of a MCT program seems to prevent a decrease in the nutritional status in well-nourished older adults. Moreover, although both groups seem to increase their physical performance similarly, well-nourished seemed to obtain more benefits from the MCT as they present additionally, a decrease of their adiposity and an increase in balance which are not observed in those at risk. For all these reasons, future research focusing on nutritional status of participants, maximize the training period or including nutritional interventions that led to positive effects on nutritional status, could help to prevent pathologies, dependence, or the need of care and improve not only quality of life in this population but also individual and social sustainability.

Funding: This study was funded by “Ministerio de Economía, Industria y Competitividad” (DEP2016-78309-R), “Centro Universitario de la Defensa de Zaragoza” (UZCUD2017-BIO-01),

Biomedical Research Networking Center on Frailty and Healthy Aging (CIBERFES) and FEDER funds from the European Union (CB16/10/00477).

Acknowledgments: The authors are grateful to all the collaborators, nursing homes, health centers and participants whose cooperation and dedication made this study possible. A. M. F. received a PhD grant from “Gobierno de Aragón” (2016-2021). D. N. received a grant from “Gobierno de Aragón” (DGAIU/1/20). A. F. G. received a grant from the Spanish Government (BES-2017-081402).

Declaration of Interest: The authors declare no conflict of interest.

REFERENCES

1. Fulop T, Larbi A, Witkowski JM, McElhaney J, Loeb M, Mitnitski A, et al. Aging, frailty and age-related diseases. *Biogerontology*. 2010;11(5):547–63.
2. Gomez-Cabello, A, Vicente-Rodríguez, G, Vila-Maldonado S, Casajus JA, Ara I. Aging and body composition: the sarcopenic obesity in Spain. *Nutr Hosp*. 2012;27(1):22–30.
3. Vopat BG, Klinge SA, McClure PK, Fadale PD. The Effects of Fitness on the Aging Process. *J Am Acad Orthop Surg*. 2014 Sep;22(9):576–85.
4. Hajek A, Bock J-O, Saum K-U, Matschinger H, Brenner H, Holleczeck B, et al. Frailty and healthcare costs-longitudinal results of a prospective cohort study. *Age Ageing*. 2018 Mar;47(2):233–41.
5. Shlisky J, Bloom DE, Beaudreault AR, Tucker KL, Keller HH, Freund-Levi Y, et al. Nutritional Considerations for Healthy Aging and Reduction in Age-Related Chronic Disease. *Adv Nutr*. 2017 Jan;8(1):17–26.
6. Soysal P, Veronese N, Arik F, Kalan U, Smith L, Isik AT. Mini Nutritional Assessment Scale-Short Form can be useful for frailty screening in older adults. *Clin Interv Aging*. 2019;14:693–9.
7. Angulo J, El Assar M, Bustos AÁ, Rodríguez-Mañas L. Physical activity and exercise: Strategies to manage frailty. *Redox Biol*. 2020;101513.
8. Fiuza-Luces C, Garatachea N, Berger NA, Lucia A. Exercise is the real polypill. *Physiology*. 2013;
9. Izquierdo M, Merchant RA, Morley JE, Anker SD, Aprahamian I, Arai H, et al. International Exercise Recommendations in Older Adults (ICFSR): Expert Consensus Guidelines. *J Nutr Health Aging*. 2021;
10. Michel JP, Cruz-Jentoft AJ, Cederholm T. Frailty, Exercise and Nutrition. Vol. 31, *Clinics in Geriatric Medicine*. 2015.
11. Anton SD, Hida A, Mankowski R, Layne A, Solberg LM, Mainous AG, et al. Nutrition and Exercise in Sarcopenia. *Curr Protein Pept Sci*. 2018;19(7):649–67.
12. Schreier MM, Bauer U, Osterbrink J, Niebauer J, Iglseider B, Reiss J. Fitness training for the old and frail. Effectiveness and impact on daily life coping and self-care abilities. *Z*

Gerontol Geriatr. 2016 Feb;49(2):107–14.

13. Moradell A, Fernández-García ÁI, Navarrete-Villanueva D, Sagarra-Romero L, Gesteiro E, Pérez-Gómez J, et al. Functional Frailty, Dietary Intake, and Risk of Malnutrition. Are Nutrients Involved in Muscle Synthesis the Key for Frailty Prevention? Vol. 13, *Nutrients* . 2021.
14. Fernández-García ÁI, Gómez-Cabello A, Moradell A, Navarrete-Villanueva D, Pérez-Gómez J, Ara I, et al. How to Improve the Functional Capacity of Frail and Pre-Frail Elderly People? Health, Nutritional Status and Exercise Intervention. The EXERNET-Elder 3.0 Project. *Sustainability*. 2020 Aug 3;12(15):6246.
15. Moradell A, Navarrete-Villanueva D, Fernández-García ÁI, Sagarra-Romero L, Marín-Puyalto J, Pérez-Gómez J, et al. Effects of a multicomponent exercise program, a detraining period and dietary intake prediction of body composition of frail and pre-frail older adults from the exernet elder 3.0 study. *Sustainability*. 2020 Nov 26;12(23):9894.
16. Moradell A, Navarrete-Villanueva D, Fernández-García ÁI, Marín-Puyalto J, Gómez-Bruton A, Pedrero-Chamizo R, et al. Role of Dietary Intake and Serum 25(OH)D on the Effects of a Multicomponent Exercise Program on Bone Mass and Structure of Frail and Pre-Frail Older Adults. *Nutrients*. 2020 Oct;12(10).
17. Guralnik JM, Simonsick EM, Ferrucci L, Glynn RJ, Berkman LF, Blazer DG, et al. A Short Physical Performance Battery Assessing Lower Extremity Function: Association With Self-Reported Disability and Prediction of Mortality and Nursing Home Admission. *J Gerontol*. 1994 Mar 1;49(2):M85–94.
18. Izquierdo M. Prescripción de ejercicio físico. El programa Vivifrail como modelo. *Nutr Hosp*. 2019 May 17;36.
19. Lopez-Rodriguez C, Laguna M, Gomez-Cabello A, Gusi N, Espino L, Villa G, et al. Validation of the self-report EXERNET questionnaire for measuring physical activity and sedentary behavior in elderly. *Arch Gerontol Geriatr*. 2017 Mar;69:156–61.
20. Schroder H, Fito M, Estruch R, Martinez-Gonzalez MA, Corella D, Salas-Salvado J, et al. A short screener is valid for assessing Mediterranean diet adherence among older Spanish men and women. *J Nutr*. 2011 Jun;141(6):1140–5.
21. Folstein MF, Folstein SE, McHugh PR, Lobo A, Saz P, Marcos G, et al. Revalidation and standardization of the cognition mini-exam (first Spanish version of the Mini-Mental

- Status Examination) in the general geriatric population. *Med Clin (Barc)*. 1999;112(20):767–74.
22. Folstein MF, Folstein SE, McHugh PR. “Mini-mental state”: a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12(3):189–98.
 23. Rikli RE, Jones CJ. *Senior Fitness Test Manual*. Human Kinetics; 2013.
 24. Consejo Superior de Deportes. Ministerio de Educación y Ciencia. Eurofit : test europeo de aptitud física. Madrid. 1992.
 25. Vellas B, Guigoz Y, Garry PJ, Nourhashemi F, Bennahum D, Lauque S, et al. The Mini Nutritional Assessment (MNA) and its use in grading the nutritional state of elderly patients. *Nutrition*. 1999 Feb;15(2):116–22.
 26. Tim Olds Arthur Stewart, Lindsay Carter Mike M-JAS. *International Standards for Anthropometric Assessment*. Internatio. 2011.
 27. Alcazar J, Losa-Reyna J, Rodriguez-Lopez C, Alfaro-Acha A, Rodriguez-Mañas L, Ara I, et al. The sit-to-stand muscle power test: An easy, inexpensive and portable procedure to assess muscle power in older people. *Exp Gerontol*. 2018 Oct;112:38–43.
 28. O’Connell ML, Coppinger T, McCarthy AL. The role of nutrition and physical activity in frailty: A review. *Clin Nutr ESPEN*. 2020;35(xxxx):1–11.
 29. Maltais M, Rolland Y, Haÿ P-E, Armaingaud D, Cestac P, Rouch L, et al. The Effect of Exercise and Social Activity Interventions on Nutritional Status in Older Adults with Dementia Living in Nursing Homes: A Randomised Controlled Trial. *J Nutr Health Aging*. 2018;22(7):824–8.
 30. Echeverria I, Amasene M, Urquiza M, Labayen I, Anaut P, Rodriguez-Larrad A, et al. Multicomponent Physical Exercise in Older Adults after Hospitalization: A Randomized Controlled Trial Comparing Short- vs. Long-Term Group-Based Interventions. *Int J Environ Res Public Health*. 2020 Jan 20;17(2):666.
 31. Pereira da Silva A, Matos A, Valente A, Gil Â, Alonso I, Ribeiro R, et al. Body composition assessment and nutritional status evaluation in men and women Portuguese centenarians. *J Nutr Health Aging*. 2016;20(3):256–66.
 32. Cuervo M, García A, Ansorena D, Sánchez-Villegas A, Martínez-González MA,

- Astiasarán I, et al. Nutritional assessment interpretation on 22 007 Spanish community-dwelling elders through the Mini Nutritional Assessment test. *Public Health Nutr.* 2009/01/01. 2009;12(1):82–90.
33. Ticinesi A, Meschi T, Lauretani F, Felis G, Franchi F, Pedrolli C, et al. Nutrition and Inflammation in Older Individuals: Focus on Vitamin D, n-3 Polyunsaturated Fatty Acids and Whey Proteins. *Nutrients.* 2016 Mar 29;8(4):186.
 34. Dalle S, Rossmeislova L, Koppo K. The Role of Inflammation in Age-Related Sarcopenia. *Front Physiol.* 2017 Dec 12;8:1045.
 35. Mahoney JR, Verghese J. Does Cognitive Impairment Influence Visual-Somatosensory Integration and Mobility in Older Adults? *Journals Gerontol Ser A.* 2020 Feb 14;75(3):581–8.
 36. Ramsey KA, Meskers CGM, Trappenburg MC, Verlaan S, Reijnierse EM, Whittaker AC, et al. Malnutrition is associated with dynamic physical performance. *Aging Clin Exp Res.* 2019/08/19. 2020 Jun;32(6):1085–92.
 37. Kamo T, Ishii H, Suzuki K, Nishida Y. The impact of malnutrition on efficacy of resistance training in community-dwelling older adults. *Physiother Res Int.* 2019 Jan;24(1):e1755.
 38. Safer U, Tasci I, Binay Safer V, Doruk H. Is segmental bioelectrical impedance analysis a valid tool to assess muscle mass in the elderly? *Vol. 13, Geriatrics & gerontology international. Japan;* 2013. p. 1085–6.