Effect of Resistance Training on Immunological Parameters of Healthy Elderly Women

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ABSTRACT

RASO, V., G. BENARD, A. J. DA SILVA DUARTE, and V. M. NATALE. Effect of Resistance Training on Immunological Parameters of Healthy Elderly Women. Med. Sci. Sports Exerc., Vol. 39, No. 12, pp. 2152–2159, 2007. **Purpose:** To determine the effect of a 12-month moderate resistance training program on phenotypic and functional immunological parameters of previously sedentary, clinically healthy, elderly women. **Methods:** A total of 42 clinically healthy, sedentary females (aged 60–77 yr old) were randomly assigned to either a moderate-intensity resistance training program or a control group during a 12-month longitudinal, randomized, controlled, intervention study. Resistance training program consisted of three sets of 12 repetitions at 54.9% ± 2.4% 1RM for five different exercises performed three times per week during 12 months. Natural killer cell cytotoxic activity (NKCA), lymphoproliferative response to the mitogen phytohemagglutinin (PHA), and quantification of the lymphocytes (CD3+, CD3+CD19+, CD56+) and subpopulations (CD4+, CD8+, CD56dim, CD56bright) as well as cellular expression molecules (CD25+, CD28+, CD45RA+, CD45RO+, CD69+, CD95+, HLA-DR+) were determined by immunological assays. **Results:** The experimental group increased muscle strength in 44% and 48% after 6 and 12 months, respectively (P < 0.05). There were no statistically significant differences between the groups or according to the time for quantitative (CD3+, CD3+CD19+, CD56+, CD4+, CD8+, CD45RA+, CD45RO+, CD56dim, CD56bright, CD95+, CD28+, CD25+, CD69+, HLA-DR+) and functional immunological parameters (natural killer cell cytotoxic activity and lymphoproliferative response). **Conclusion:** A 12-month moderate resistance training program increases muscle strength, but it does not change immune phenotypic and functional parameters of previously sedentary, clinically healthy, elderly women. **Key Words:** AGING, EXERCISE, IMMUNOSENESCENCE, IMMUNE SYSTEM, MUSCLE STRENGTH

With aging, the immune system undergoes a remodeling process termed immunosenescence (14), whereby the sustained, lifelong exposure to a plethora of antigens (bacterial, viral, exogenous, self) leads to various immunological alterations. Among these are a gradual decline of naïve T cells (37), increase of DR expression on T lymphocytes (15), accumulation of memory T cells and effector CD8+CD28− T cells, disturbances in the T-cell repertoire and consequently reduced lymphoproliferative responses to mitogens and antigens (20,27), and decreases in Fas-mediated T-cell apoptosis (40). There is also a general consensus that NK cells from elderly humans show decreased cytotoxic capacity on a per cell basis (24,32). Additionally, some observations suggest that as many components of immunity wane with advanced age because of sustained antigenic stress over an individual’s lifespan, there is a shift to a chronic, proinflammatory state. As a consequence, effector and memory cells gradually replace naïve cells, and expanded effector and memory T cells secrete increased amounts of proinflammatory cytokines such as IL-6 (12,13).

There is good evidence corroborating the use of exercise as a strategy to ameliorate physiological age-associated changes as well as an adjuvant strategy in the disease therapy (5,39). In general, aerobic exercise has been largely employed, but more recently, resistance exercise has been suggested, especially for the elderly population, because of its better effect on the functional capacity to perform activities of daily living regardless of health status (4,8,16,21,25,28,29,34,38). Subsequently, aerobic and resistance exercise have also been suggested to counter immunosenescence (5,18,39). Long-term cross-sectional studies have shown that the lymphoproliferative response to nonspecific stimuli (e.g., PHA) (1,34) are significantly higher in elderly runners when compared with sedentary individuals. This enhancement was paralleled by higher interleukin 2 (IL-2) (1,34), interferon gamma (IFN-γ), and IL-4 production (34), but lower IL-3, IL-6, and IL-12 serum levels (1). Overall, these findings may suggest a better immunological performance of these elderly runners.
However, many of the available prospective and experimental studies have used different designs and exercise protocols and have assessed distinct immunological parameters, giving rise to heterogeneous results. Most of them were based on a short-term follow-up, evaluated few immunological parameters, and used varying inclusion criteria protocols. In contrast with the cross-sectional studies mentioned above, lymphoproliferative response to mitogens remained unchanged, whereas natural killer cell cytotoxic activity (NKCA) either improved or remained stable in prospective and experimental exercise studies (8,16,25,28,29,38). Woods et al. (38) observed a non-significant increase in NKCA after a 6-month intervention aerobic exercise program in apparently healthy elderly, but they saw no or only modest increases in some other immune parameters, including mitogen lymphoproliferative responses. More recently, McFarlin et al. (21) have shown that resting NKCA increases as a result of a vigorous resistance training program in elderly women. Kapasi et al. (16) found that the expression of the costimulatory molecule CD28 in frail, elderly, nursing home–dwelling women was not affected by an intervention exercise program, in contrast to findings from acute exercise studies that have shown decreased expression (4). The heterogeneous effects of aging on the expression of activation markers, such as the decrease in CD25 expression and increase in HLA-DR expression in frail elderly subjects (9), were not countered by exercise (16).

Thus, considering the heterogeneity of the data on the association between several aspects of the immunity in the elderly and long-term regular physical exercise, our aim was to determine the effects of a 12-month resistance training program on the immune phenotypic and functional parameters of previously sedentary, clinically healthy, elderly women. A light to moderate exercise training program was chosen because it has been shown to provide better immunological benefits than vigorous exercise programs (5,39).

METHODS

Subject recruitment and enrollment. This study was approved by the institutional board of the Hospital das Clínicas, Faculty of Medicine, University of São Paulo, Brazil, and all subjects gave their written consent before their inclusion in the study. Seventy-three volunteers, aged 60–77 yr old, were initially recruited from the community to participate in this study. They underwent a standard clinical and physical examination before being admitted to the study to determine their health status, which included (I) current and past detailed health status; (II) 12-lead electrocardiogram; (III) cardiopulmonary exercise testing; (IV) body composition by bioelectrical impedance technique; and (V) laboratory parameters according to the SENIEUR protocol (19).

Of these, 31 were excluded because they presented either abnormal laboratory tests on the SENIEUR protocol or other biochemical parameters (cholesterol, triglycerides, glycemia), or one or more of the following criteria: (I) participation in a regular physical activity program in the previous 3 months; (II) undergoing alternative dietetic therapy; (III) undernourishment or obesity, (IV) cigarette smoking; (V) cardiovascular, pulmonary, metabolic, chronic infectious, or autoimmune diseases; (VI) central or peripheral nervous system disorders; (VII) treatment for, or history of, cancer; (VIII) chronic use of corticosteroids; (IX) any kind of surgery in the previous 3 months; (X) forced bed rest in the previous 3 months; or (XI) any orthopedic limitation to perform resistance exercises.

Forty-two volunteers were cleared for participation, reported their willingness to be randomly assigned to two treatment conditions (experimental or control group), and agreed not to participate in exercise programs outside the study.

Acclimation period to resistance training program. This period consisted of three sets of 12 repetitions for five different exercises (seated bench press, latissimus pull-down, seated row, leg extension, and leg press (Biodelta Equipments, São Paulo, Brazil)), three times a week. Initially, volunteers performed the exercises without any load (first to second week), and, subsequently (third to fourth week), the load was determined according to the rating of perceived exertion (6–8 (CR-10)). During this period, volunteers learned how to perform all exercises correctly, carry out adequate respiratory technique (expiration in concentric phase), perform each exercise with adequate velocity of execution (1- to 2-s concentric and 2- to 3-s eccentric action), and take adequate rest intervals (120-s intersets and 180-s interexercises). About 5–10 min of upper- and lower-extremity mobility and stretching exercises preceded and followed all resistance exercise sessions during the acclimation and resistance training periods.

Resistance training program. The resistance training program consisted of three sets of 12 repetitions at 60% of the one-repetition maximum (1RM) for the above-mentioned exercises, performed three times a week during 12 months. The program required 60 min·d⁻¹ for 144 sessions, which were performed at our rehabilitation center under the supervision of one of the authors (V.R.). 1RM was determined as the maximum amount of weight a subject could lift just once using the proper technique; it was retested and adjusted every 6 wk for all exercises, to provide constant stimuli during the entire program. The proper technique was defined as the subject performing each resistance exercise using the specified muscle groups and without using momentum or changes in body position to help to apply the force. Control group volunteers were tested to determine their 1RM at baseline and after every 6 months (baseline, 6 months (6M), and 12 months (12M)). For this, each control group volunteer participated in a familiarization period (repeated in each period (baseline, 6M, and 12M)) consisting of the participation in three sessions comprising three sets of 12 repetitions of the same exercises.
The intensity of training was calculated according to the load employed for each exercise by the volunteers. Volunteers trained at 54.9 ± 2.4% 1RM (53.2 ± 3.3% (latissimus pull-down) to 55.0 ± 2.3% (seated row)) during the study. Volunteers were also informed that they would be excluded if they missed two consecutive sessions in the same week. Control group volunteers participated once a month in health-related meetings during the study period (12 months).

**Blood collection and white blood cells count.** Volunteers were instructed not to ingest solid or liquid foods containing caffeine, chocolate, or cola-based products 48 h before blood collection. They were also informed not to participate in any exercise sessions and not to perform any moderate or vigorous physical activity 48 h before blood sampling.

On each occasion, volunteers came to the laboratory at 7:00 a.m., having fasted overnight. After a 30-min rest period in the sitting position, antecubital venous blood samples were obtained at baseline and at 6- and 12-month time points. Blood collected in a nonheparinized syringe was dispensed into evacuated tubes with EDTA. Blood samples collected through a heparinized syringe were used for the lymphoproliferative response and NKCA assays after an interval of no more than 4 h. Blood samples (EDTA) for differential blood count were kept refrigerated until analysis later on the same day on a Cell-Dyn 3500 cell analysis system (Coulter Corp., Miami, FL).

**Flow cytometry.** Two hundred microliters of whole blood was incubated for one-, two-, or three-color immunophenotyping, using appropriate combinations of monoclonal antibodies (Becton-Dickinson, Miami, FL) conjugated to fluorescein isothiocyanate (FITC (CD25, CD45RA, CD95)), phycoerythrin (PE (CD19, CD28, CD45RO, CD69, HLA-DR)), or phycoerythrin-cyanine (PE-Cy-5 or PCy-5 (CD3, CD4, CD8, CD56)). Conjugated monoclonal antibodies (MAB) were used were CD3(PCy-5)/CD4(FITC)/CD8(PE) and CD3(FITC)CD19(PE). Conjugated mouse antibodies purified PBMC were adjusted to 10^6 cells/ml and incubated with radiolabeled K562 cells. K562 cells were maintained in RPMI 1640 supplemented with 10% FBS, gentamicin (40 μg/mL), and Heps buffer (Sigma), at 37°C with 5% CO2. The plates were incubated at 37°C for 72 h in an atmosphere of 5% CO2 and were then pulsed with 1 μCi per well of 3H-thymidine (6.7 Ci/mmol, ICN Biomedicals, Irvine, CA), 18 h before harvesting onto glass-fiber filter paper (Skatron Cell Harvester, Norway). Five milliliters of scintillation fluid was added to the filters, and they were counted in a β-plate scintillation counter (Wallac Oi, Turku, Finland). The control count was subtracted from the mitogenic count and expressed as counts per minute.

**NKCA.** A radioactive chromium release assay using the standard NK-sensitive K562 cell line was used to measure NKCA. The human erythromyeloid leukemia-derived cell line K562 was maintained in RPMI 1640 supplemented with 10% FBS, gentamicin (40 μg/mL), and Heps buffer (Sigma), at 37°C with 5% CO2. Freshly isolated Ficoll-purified PBMC were adjusted to 1 x 10^6 cells per milliliter in CM and then serially diluted at 40:1, 20:1, 10:1, and 5:1 effector-to-target (E:T) ratios. The PBMC were placed into 96-well round-bottom microtiter plates and incubated with radiolabeled K562 cells. K562 cells were labeled with 100 μCi 10^-6 cells of sodium 51 chrome (51Cr; ICN Biomedicals, Irvine, CA) for 1 h in a shaking 37°C waterbath. After a 4-h incubation at 37°C and 5% CO2, the plates were centrifuged at 100g for 5 min. The supernatant (100 μL) was transferred to polypropylene tubes, and the released radioactivity was counted in a parallel with each sample. A minimum of 5000 cells were analyzed on a Coulter XL-MCL (Coulter Corp., Miami, FL), and data analyses were performed using XL System II software. Lymphocyte analyses were performed by gating on the lymphocyte region based on forward and side light scatter. Lymphocyte numbers within each subset were obtained by multiplying the lymphocyte count by the percentage of the respective subset.

**Peripheral blood mononuclear cells.** Peripheral blood mononuclear cells (PBMC) were isolated from heparinized whole blood by Ficoll-Hypaque (Pharmacia, Uppsala, Sweden) density gradient centrifugation. They were then diluted in RPMI (GIBCO, Carlsbad, CA) with 5% heat-inactivated fetal calf serum (FCS, Sigma-Aldrich), gentamicin (40 μg/mL), glutamine (200 mM), and 2-mercaptoethanol (5 x 10^-5 M) (complete medium (CM)).

**Lymphoproliferative response.** Lymphoproliferative response was measured by 3H-thymidine incorporation after (PHA) stimulation. The freshly isolated PBMC were adjusted to 2 x 10^6 cells per milliliter, and 100 μL of the suspension was plated in triplicate wells of a 96-well, round-bottomed microplate (Costar, Cambridge, MA). PHA was diluted to a final concentration of 5 μg/mL. The plates were incubated at 37°C for 72 h in an atmosphere of 5% CO2 and were then pulsed with 1 μCi per well of 3H-thymidine (6.7 Ci/mmol, ICN Biomedicals, Irvine, CA), 18 h before harvesting onto glass-fiber filter paper (Skatron Cell Harvester, Norway). Five milliliters of scintillation fluid was added to the filters, and they were counted in a β-plate scintillation counter (Wallac Oi, Turku, Finland). The control count was subtracted from the mitogenic count and expressed as counts per minute.

**TABLE 1. Main clinical characteristics of the elderly women in the experimental and control groups.**

<table>
<thead>
<tr>
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<th>Experimental Group</th>
<th>Control Group</th>
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<tr>
<td></td>
<td>Baseline 6 months</td>
<td>12 months</td>
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<tr>
<td>Body weight (kg)</td>
<td>60 ± 9</td>
<td>60 ± 9</td>
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<tr>
<td>BMI (kg m^-2)</td>
<td>24 ± 4</td>
<td>24 ± 7</td>
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<tr>
<td>%FAT</td>
<td>31 ± 5</td>
<td>31 ± 5</td>
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<tr>
<td>FFM (%)</td>
<td>70 ± 9</td>
<td>68 ± 5</td>
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<tr>
<td>Muscle strength (kg)</td>
<td>109 ± 11</td>
<td>161 ± 23†</td>
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<td>Mean ± standard error of mean; BMI, body mass index; %FAT, percentage of fat; FFM, fat-free mass.</td>
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* Significantly different from the control group at the same time point; † significantly different between baseline and the other time points.
gamma counter (1275 minigamma, LKB-Wallac, Turku, Finland). Total release was determined in wells containing $^{51}$Cr-labeled cells with RPMI 1640, 10% FBS with 10% triton X-100. Spontaneous release was always less than 10% of total release. NKCA was calculated by using the mean value of triplicate determinations for each E:T ratio and expressed as percentage lysis, calculated as follows:

\[ \% \text{ lysis} = \frac{(\text{mean experimental counts per minute} - \text{mean spontaneous counts per minute})}{(\text{mean maximum counts per minute} - \text{mean spontaneous counts per minute})} \times 100 \]

Statistical analysis. The sample size was determined according to $\alpha = 0.05$ and $\beta = 0.20$ to find effect size as a result of training (performed using the SigmaStat software, Jandel Scientific, San Rafael, CA). Repeated-measures ANOVA was used for 2 (group) $\times$ 3 (time) factor analysis. Tukey’s post hoc test was used when a significant effect was observed. Significance level adopted was $P < 0.05$. All analyses were performed using SPSS 10.0 for Windows package (SPSS, Inc., Chicago, IL). Data are presented as means $\pm$ standard deviations (SD).

RESULTS

Randomization. Mean adherence level during the study period was $80 \pm 8\%$ and was not different between

<table>
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<th>TABLE 2. Naive (CD45RA$^+$) and memory (CD45RO$^+$) T cells and NK cell subtypes of the elderly women in the experimental and control groups.</th>
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<tbody>
<tr>
<td><strong>Experimental Group</strong></td>
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<tr>
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</tr>
<tr>
<td>CD4$^+$CD45RA$^+$</td>
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<tr>
<td>CD8$^+$CD45RA$^+$</td>
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<tr>
<td>CD4$^+$CD45RO$^+$</td>
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<td>CD8$^+$CD45RO$^+$</td>
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<tr>
<td>CD56$^{dim}$</td>
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<tr>
<td>CD56$^{bright}$</td>
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<tr>
<td><strong>Control Group</strong></td>
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<tr>
<td>CD4$^+$CD45RA$^+$</td>
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<td>CD8$^+$CD45RA$^+$</td>
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<td>CD8$^+$CD45RO$^+$</td>
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<tr>
<td>CD56$^{dim}$</td>
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<td>CD56$^{bright}$</td>
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Mean = standard error of mean of cells per microliter of peripheral blood.
the PRE-6M and 6M-12M periods. Every volunteer in the experimental group attended at least two sessions per week during the whole period of study. Energy intake and expenditure, profile of mood state, and quality of life (environmental, physical, psychological, and social domains) were preserved throughout the study period in both groups, and there were no significant differences between them regardless of time (data not shown). Random assignment to the experimental and control groups resulted in similar age (67 ± 5 and 68 ± 3 yr old), body height (155 ± 6 and 157 ± 7 cm), and body composition (Table 1). There was no identified resistance training program–induced effect on body composition, as observed in Table 1.

**Muscle strength.** The resistance training program induced a significant increase in muscle strength scores (1RM leg press plus 1RM seated row (6 and 12 months vs baseline, \( P < 0.0001 \)). In addition, the experimental group presented higher scores than did the control group after 6 (\( P = 0.0001 \)) and 12 months (\( P = 0.007 \)) of exercise (Table 1).

**Immunological parameters.** There were no significant differences between the two groups at any time point for total lymphocyte number or its subsets (CD3\(^+\), CD4\(^+\), CD8\(^+\), CD19\(^+\), and CD56\(^+\) cells), nor were there any resistance training program–induced changes in these cell subsets (Fig. 1). The CD4\(^+\) and CD8\(^+\) cell subsets were further evaluated for the expression of naïve and memory markers. As expected, CD4\(^+\) and CD8\(^+\) cells comprised more memory (CD45RO\(^+\)) than naïve (CD45RA\(^-\)) cells in both the experimental and control groups at the start of the study; the resistance training program did not significantly affect this parameter (Table 2). We also assessed the level of expression of the NK cell marker, CD56, because CD56\(^{dim}\) cells represent more mature and functional cells than do their CD56\(^{bright}\) counterpart. As expected for healthy, aged donors, CD56\(^{dim}\) largely predominated in both groups, with no effect of the resistance training program on such numbers at any time point (Table 2).

Aging has been shown to affect the expression of some costimulatory molecules, such as CD28 and CD95, and/or activation markers, such as CD25, CD69, and HLA-DR. There was no difference in the numbers of CD4\(^+\) and CD8\(^+\) cells expressing CD28 or CD95 or coexpressing both molecules in the two groups during the study period, nor was there a detectable effect of the exercise program on their expression (Table 3). The activation markers CD25\(^+\), CD69\(^+\), and HLA-DR\(^+\) were expressed by the same proportions of CD3\(^+\), CD4\(^+\), and CD8\(^+\), CD56\(^{dim}\), and CD56\(^{bright}\) cells of the two volunteer groups, and before versus after (6 or 12 months) the start of the resistance training program (data not shown).

We also analyzed two lymphocyte function assays. There were no significant differences in the lymphoproliferative response to PHA and NKCA in the experimental group before and after 12 months of the resistance training program (Fig. 2). Both groups (experimental and control groups) also presented similar results at baseline and at 12 months (Fig. 2).

**DISCUSSION**

Our study provides evidence that a 12-month, moderate resistance training program produces significant improvement in muscle strength of healthy, elderly women without
either detrimental or positive effects on selected indexes of immune system function. We did not find any study in the literature that had assessed the response of such a large number of immunological variables to a long-term training program (≥12 months) regardless of the mode used in elderly people.

Physical exercise has been proposed as an intervention to restore immune function in older populations. In general, long-term exercise interventions seem the most promising. Exercise-related improvements have been reported with respect to antibody titer, T cell function, macrophage response, alterations of the T_{H1}/T_{H2} cytokine balance, the level of proinflammatory cytokines, and changes in naïve/memory cell ratio (1,6,34).

Resistance training promotes improvements in muscle strength and endurance and increases muscle mass, but little is known about the immune responses to resistance exercise in elderly people. The effect of resistance training on immune function in the elderly has been investigated in a limited number of studies. Most of them found that 8–12 wk of resistance training programs had minimal effects on resting inflammatory, innate, or acquired immune parameters, as assessed by analysis of peripheral blood (3,10,11,20,21,28,29).

Defects in T cell function are the most dramatic, are the most consistently demonstrated, and are frequently found to be responsible for deficiencies in defensive immunity at both the cellular and humoral levels in the elderly (27). In general, cross-sectional studies assessing highly active elderly subjects have demonstrated higher in vitro T cell responses to polyclonal stimulation when compared with sedentary elderly subjects (1,34). Unfortunately, prospective human studies have failed to demonstrate a consistent improvement of lymphoproliferative response in older adults (28,29,38). Most studies have involved a short-term period (≤24 wk); more long-term training programs in the elderly are required to confirm the results of cross-sectional studies. Particularly with regard to the effect of resistance training on T cell proliferation, three studies have analyzed this parameter and did not find any change in lymphocyte function (10,28,29). Similarly, we were not able to detect improvement in lymphoproliferative response after the resistance training program. We believe this finding is not attributable to the intensity of exercise used in our study, because Miles et al. (23), studying different intensities of resistance training in young women, have concluded that anaerobic intensity is associated with increased strength and workload but not with changes in T cell proliferation responses. This is also consistent with studies that have shown a lack of improvement in immune function with high-intensity exercises (5,39). On the other hand, a few studies have used interventional aerobic exercise programs that apparently did not promote stronger immunological effects than did resistance training programs (10,16,22,25,26,29,34). Keylock et al. (17), in a cross-sectional study, did not observe increments in cell-mediated responses in high, physically fit elderly compared with low, physically fit individuals, although the antibody response to a vaccination protocol in the former elderly group was enhanced. Nieman et al. (26) have verified that highly conditioned, elderly subjects show higher NKCA and lymphoproliferative response in the baseline, but a moderate cardiorespiratory training program improved these immune parameters further. In addition, Woods et al. (38) also did not find changes in the cellular immunity parameters such as lymphoproliferative responses and NK cell activity of elderly subjects undergoing 6 months of moderate aerobic exercise training. Furthermore, a concern may be raised regarding some prospective studies that have detected a better immunological response of physically active individuals when compared with sedentary individuals, because the extent to which several other healthy behaviors commonly associated with the physically active lifestyle could have influenced the immune system responses was not determined (33).

The number of total T cells (CD3+) decreases slightly with age, whereas the CD4+ and CD8+ cell number remains unchanged or decreases slightly with aging. However, these modifications are not enough to compromise the immune function (27). Normally, no significant changes in CD3+, CD4+, CD8+, CD3−CD19+, and CD3+CD16−CD56+ cell numbers have been identified as well as in the CD4:CD8 ratio when elderly people who participated in an aerobic or a resistance training program, regardless of the health status of the volunteers (8,10,28,29,39), and our results regarding these parameters are in agreement with the majority of the literature. The difficulties in demonstrating the impact of exercise on the size of cell compartments is illustrated by the study of Kapasi et al. (16), who have shown a small but significant increase in CD8+ (5%) cells in frail, elderly, nursing home residents after 8 wk of an aerobic and resistance exercise program that was subsequently lost when evaluated at 32 wk. Indeed, according to Bates-Jensen et al. (2), these minor changes are not sufficient to provoke an immune enhancement or, eventually, immunosuppression, which could modify the clinical susceptibility to infections.

The ratio of antigen-experienced memory T lymphocytes to naïve T lymphocytes increases with age as a result of thymus involution and the consequent decrease in the number of naïve T lymphocytes. This phenotype change would be coupled with a predicted reduced ability to respond to new antigens (27). The present study represents the first long-term, randomized, controlled trial on resistance training in elderly people that analyzed the number of CD4+ and CD8− naïve and memory cells. In this study, no effect on naïve and memory cells could be demonstrated. This is in contrast with the study by Woods et al. (38), which showed a nonsignificantly increased tendency in CD4+CD45RA+ and CD8+CD45RA+ cells, as well as a decrease in CD4+CD45RO+ cells in apparently healthy...
elderly subjects who practiced aerobic exercise for 6 months.

Age-associated changes in the composition of T cell subpopulations also include decreased levels of CD28+ cells and increased levels of CD95+ cells. However, CD28 costimulation most often protects against apoptosis, even that caused by the ligation of CD95 (FAS) on the T cell surface, and CD28-negative cells may be more susceptible to apoptosis (27). CD95+ and CD28+ expression did not change after the intervention. Our results were similar to those observed by Kapasi et al. (16), who did not identify a positive effect on costimulatory molecule CD28+ expression in frail elderly. There are no other studies regarding exercise intervention and CD95+.

The aging process increases the number of apparently activated T cells (HLA-DR+, CD25+, although possibly not CD69+) as well as the number of activated natural killer cells (30,35). The meaning of these findings in the immunosenescence process is not completely understood. Our results demonstrate that CD25+, CD69+, and HLA-DR+ also seem unresponsive to exercise training, regardless of the cell subtype (CD3+, CD4+, CD8+, CD56dim, CD56bright). Similar observations have been made in frail, elderly subjects (16).

NK cells make up 10–20% of the peripheral blood human lymphocyte population. NK cells can be divided into CD56bright NK cells (low cytotoxicity) and CD56dim NK cells (most mature, and high cytotoxicity) (35). We did not find changes in CD56dim, CD56bright either, or in NKCA. Recently, McFarlin et al. (21) have shown that a vigorous resistance training program increases resting NKCA in elderly women. This discrepancy with our data may be accounted for by the different study designs: their study employed a progressive resistance training that reached higher-intensity exercises for only 10 wk. In fact, the majority of the available evidence seems to demonstrate that resistance training programs do not improve NKCA (3,10). Thus, our results are in agreement with other studies showing that resistance training performed by healthy elderly does not alter resting NK number or function.

Although some research on aerobic exercise training has suggested improvements in the immune system for elderly subjects (8,25,34), we did not find any major effects of resistance training on the immune parameters of healthy, elderly subjects. However, published data are still controversial, and this may be related to the criteria used to select healthy, old individuals (7), by the training strategy (5,39), and by differences between human populations, depending on ethnicity or geographical region (31). We have tried to minimize these intervening factors by using a randomized, controlled design and the SENIEUR protocol to reinforce the eligibility criteria (7). Questionnaires on behavioral, nutritional, and psychosocial aspects were also applied, showing no intragroup (baseline vs 6 and 12 months) or intergroup differences (data not shown). In addition, our study was designed to address a moderate resistance training program for a longer period as compared with most exercise studies that have used vigorous-intensity exercise (i.e., > 80% 1RM) for short periods, because this higher intensity would probably not be well tolerated in a 12-month program. We believe that this program may fit better to the common daily circumstances of elderly people than would vigorous exercise programs. Thus, our study suggests that a 12-month, moderate resistance training program produces significant improvement in muscle strength but that it does not improve immune phenotypic and functional parameters of previously sedentary, clinically healthy elderly women. It is possible that for exercise programs based on moderate-intensity resistance training, long-term follow-up (i.e., two or more years) is necessary for achievement of identifiable immunological benefits in a selected group of healthy elderly. This group likely presented a more preserved immune function and, consequently, a higher ceiling for exercise-mediated improvements in immune function. Thus, further studies are warranted to verify whether other aging populations with clinical characteristics different from those of our highly selected population, such as frail elderly subjects, are more susceptible to the immunological benefits potentially provided by our exercise program.

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