applied sciences

Article

The Effect of 6-Month Complex Exercise on Serum Bone Metabolism: Focused on the Elderly over 75 Years Old

A-Ram Kim [1], So-Eun Lee [2], Yoo-Jin Shim [1,*] and Seung-Wook Choi [1,*]

[1] Department of Sport Leisure, Sungshin Women's University, Bomun-ro 34da-gil, Seongbuk-gu, Seoul 02844, Korea
[2] College of Wesley Creative Convergence, Hyupsung University, Hwaseong-si 18330, Korea
* Correspondence: zini9498@naver.com (Y.-J.S.); swchoi@sungshin.ac.kr (S.-W.C.); Tel.: +82-2-920-7650 (S.-W.C.)

Abstract: Korea already entered the aging society (August 2017), in which 14% of the population is 65 years or older, and it is expected to enter as a super-aged society, in which 20% of the population is elderly at the world's fastest rate by 2025. This means that a health management plan is needed to effectively manage the health of the elderly in preparation for the upcoming super-aging society. Therefore, this study analyzed the effects of exercise on serum osteocalcin, bone ALP, and estradiol, which are representative indicators of bone formation after six months of complex exercise, and confirmed the usefulness of exercise programs and biochemical indicators for the elderly in late years to provide basic data for the prevention of osteoporosis. The subjects of this study were the elderly in late years (exercise group = 14, control group = 15), those 75 years or older in Korea, who performed complex exercises twice a week for six months. As a result of analyzing the effect of exercise performance on osteocalcin in the elderly in late years for six months in this study, no significant difference was found. However, osteocalcin decreased by 7.7% in the control group and increased by 18.66% in the exercise group, while ALP increased by 18.92% in the control group and significantly increased by 69.81% in the exercise group. As a result of analyzing the effect on estradiol, there was no significant difference, but it decreased by 55.09% in the control group and decreased by 1.85% in the exercise group. Based on the results showing that exercise clearly plays a positive role in improving bone density even for middle- and late-aged elderly people, in the future, the exercise will be useful to maintain and improve health related to the skeleton of the elderly through the combined participation of aerobic, resistance, and balance exercises. In addition, it is necessary to conduct repeated studies targeting the elderly of various age groups to evaluate the effects of exercise according to period and gender.

Keywords: complex exercise; osteocalcin; ALP; estradiol; elderly over 75 years

Citation: Kim, A.-R.; Lee, S.-E.; Shim, Y.-J.; Choi, S.-W. The Effect of 6-Month Complex Exercise on Serum Bone Metabolism: Focused on the Elderly over 75 Years Old. *Appl. Sci.* **2022**, *12*, 11373. https://doi.org/10.3390/app122211373

Academic Editor: Grazia Maugeri

Received: 13 October 2022
Accepted: 7 November 2022
Published: 9 November 2022

1. Introduction

Korea already entered the aging society (August 2017), in which 14% of the population is 65 years or older, and is expected to enter a super-aging society in 2025 at the world's fastest rate, in which 20% of the population is elderly [1]. Ahead of the super-aged society, now the elderly are intensely interested in health and aging prevention while pursuing healthy life expectancy; not simply living long, but living long healthily. This period is where physical function changes are experienced with increasing age [2]. In Korea, 84.0% of the total elderly were diagnosed with chronic diseases that persist for three months or longer, and those with two or more chronic diseases account for 54.9% of the total elderly [3]. This means that health management measures are needed to effectively manage the health of the elderly in preparation for the upcoming super-aging society [4].

Osteoporosis attracts attention along with high blood pressure, diabetes, hyperlipidemia, arthritis, and back pain, which are representative chronic diseases in Korea. In particular, osteoporotic fractures increase in frequency with age and increase the possibility of morbidity and mortality due to fractures, so the management of bone density is vital for the elderly [5].

It was reported that the risk of fracture is 2.9–7.4 times higher in the hip joint and 3.8–7.4 times higher in the spine for the elderly with osteoporosis compared to those who have no osteoporosis [6]. It is known that these risk factors for osteoporosis include demographic factors such as age, race, gender, and menopause, medical factors such as diseases and drugs, and lifestyle factors such as nutritional deficiencies and sedentary lifestyle [7], and a recent study reported that it is closely related to the appropriate body circumference in old age [8]. On the other hand, it is reported that every 0.44 falls in osteoporotic female patients increases the risk of hip fracture by 1.5 times, and the risk of death within 2 years is reported to increase by about 2.1 times [9,10].

In fact, according to NHANES in the United States, about 50% of women and 12% of men over 85 years old had osteoporosis prevalence [11], and 93% of women over 80 years of age used to have at least one fracture. In Korea, the number of fracture patients by age group over the past five years was 37.4% in their 80s (annual average 8.3%) in 2020, 26.3% in their 60s (annual average 6.0%), and 14.1% (annual average 3.4%) in their 70s compared to 2016. The number of patients treated for fractures was more for women than men from the age of 50 or older [12]. Additionally, in the UK, NHS pays GBP 4.4 billion annually for fragility fractures [13]. In the United States, it is estimated that they paid USD 57 billion for osteoporosis in 2018, and this shows that more than 95 billion US dollars per year will be required till 2040 [14]. An effective osteoporosis prevention strategy is essential in view of the increase in life expectancy worldwide and the burden that osteoporosis-induced fractures put on society, medical systems, and individuals.

For the prevention and treatment of osteoporosis, it is a general guideline to recommend quitting smoking, calcium intake, and exercise in addition to drugs. In particular, studies showing that taking a bed rest that does not support body weight may cause loss of bone density, and significant changes in bone composition relatively explains the need for exercise [15]. Therefore, many studies for activities using a single body part [16], such as exercise [17–21], walking [22,23], or sports [24] focusing on specific types of physical activity, were carried out with middle-aged women, adolescents, and men. However, despite the transitional period of functional loss [25], studies focusing on the elderly in the late years are not sufficient. There are still many different opinions on the effect of exercise on improving performance the bone density of the elderly.

Starting from the age of 75, due to a decrease in daily living ability and physical strength, depending on others, or needing to use an orthosis or cane, the service must be provided in a different way according to the characteristics of the age [26], but most of the studies for exercise programs [27–30] were conducted for all age groups without any age classification.

In the case of response to osteoporosis treatment, a long-term study is necessary because bone density tests appear 1 to 2 years later, and bone remodeling does not work well due to aging [31]. In the case of biochemical bone markers, there is an advantage in that the treatment effect can be checked within a short period of time by showing a change of 30 to 70% within 3 to 6 months [32].

Therefore, this study analyzed the effects of exercise on serum osteocalcin (OC), bone ALP [33], and estradiol, which are representative indicators of bone formation after six months of complex exercise, and analyzed the exercise program and biochemical indicators. This study aims to provide basic data for the prevention of osteoporosis of the elderly by confirming the usefulness of the exercise program and biochemical markers.

2. Methods

2.1. Subjects of the Research

The subjects of this study were women, who were randomly selected and assigned to the elderly aged 75 years or older (exercise group = 14, control group = 15) who used one public health center located in S city, South Korea. Prior to the study, an orientation was held to explain the test and exercise, and the subjects understood the purpose and method of the study, and had no problems with verbal communication and decision making, and had no physical defects or diseases. In addition, those who took drugs, smoked, drank alcohol, etc., for a long time were excluded from the subjects. This experimental protocol was approved by the Institutional Review Committee of Sungshin Women's University (SSWUIRB-2021-015) and was conducted with prior consent of all participants. Thirty-six elderly women were selected, but seven women who failed to participate in the study till the end were excluded. The characteristics of the participants are as follows <Table 1>.

Table 1. Characteristics of the study participants.

Variable	Control Group (Mean ± SE)	Exercise Group (Mean ± SE)	*p*-Value
Age (year)	80.80 ± 2.37	81.14 ± 3.98	0.429
Height (cm)	154.59 ± 2.14	155.14 ± 3.05	0.992
Weight (kg)	57.68 ± 3.15	59.26 ± 4.14	0.791

2.2. Measuring Items and Methods

2.2.1. Physical Examination

In the case of height, using a digital extensometer (NeoGMTEC Co., Ltd., Seoul, Korea), the subject was asked to keep the eyes in a horizontal position and chin in the upright position, and then the vertical distance from the sole to the two vertices was measured (measurement values were recorded in units of 0.1 cm). In addition, in the case of bodyweight, after undressing, it was placed in the center of the scale and recorded to one decimal place, and the unit was recorded in kg.

2.2.2. Blood Analysis

To measure osteocalcin, bone ALP and estradiol (E2), 5 mL of blood was collected from the antecubital vein using a disposable syringe between 8 and 9 am on the same day under fasting for 2 h. After clotting at room temperature for more than 30 min, centrifugation was performed at 3000 rpm (or $3500\times g$) for 5 to 10 min, and the supernatant was transferred to an EP tube and then measured.

2.2.3. Exercise Program

The complex exercise was performed twice a week for six months. For exercise intensity, the exercise duration was gradually adjusted to an exercise intensity of 45–55% of HRRmax, considering that the study subject were elderly women over 75 years old, using Karvonen's formula. Resistance exercise was performed at 11–14 RM, for three sets. In the case of balance exercise, a single leg standing exercise for 1 to 2 min, rest for 30 s, and other various movements (including movements such as single leg standing with another leg lifting forward, lifting aside, lifting back, and bening), was performed for the duration of the single leg standing and the frequency was gradually increased. The exercise was conducted in a public health center, and one professional instructor guided then exercise for 6 months. The exercise consisted of a 5 min warm-up exercise, 5 min cool-down exercise, and the main exercise. The main exercise was a complex exercise and consisted of 20 min of aerobic exercise, 20 min of resistance exercise, and 10 min of balance exercise. The exercise program is as follows <Table 2>.

Table 2. The 6-month complex exercise program for the elderly aged over 75 years.

Variable	Type		Time	Frequency	Intensity
Warm-up exercise	Stretching		5 min	Twice a week	RPE 2~3
Main exercise	Aerobic exercise	Walking in place 7 m shuttle walking	20 min		HRmax 45~55%
	Resistance exercise	Biceps curl, triceps curl, side band squat, kick back, knee up	20 min		11~14 RM 3 set
	Balance exercise	One-leg standing	10 min		
Cool-down exercise	Stretching		5 min		RPE 2~3

2.2.4. Data Processing

All data measured in this study were expressed as descriptive statistics (mean, standard error of the mean: SE) using the upper statistical program of SPSS PC + for window (version 22.0), and the detailed processing method is as follows:

Mean (M) and standard deviation (SD) were calculated for all variables, one-way ANOVA was performed to check the interaction between groups and measurement time, and a *t*-test was performed before and after the group's analysis. The significance level was set as $\alpha = 0.05$.

2.3. Data Procesing

(1) Shapiro–Wilk was conducted for a preliminary normality test for the exercise group and the control group. After carrying out the normality test, a statistical method was applied according to the nonparametric analysis (Wilcoxon, Mann–Whitney) and the parametric analysis (paired *t*-test and independent *t*-test).

(2) In order to verify the difference in changes observed in the dependent variables within each group with normality, a paired *t*-test was performed. In addition, in order to examine the difference in variables by the measurement period between the groups, an independent *t*-test was conducted.

(3) Wilcoxon was carried out in order to verify the difference in changes in dependent variables within each group without normality, while Mann–Whitney was conducted in order to inquire into the difference in variables by the measurement period between the groups.

(4) The two-way repeated measures ANOVA was performed to make a simultaneous analysis of the differences in the mean of dependent variables between two groups (exercise group and control group) and between two tests (pre-test and post-test).

(5) The significance level of all statistical analyses was set to <0.05.

3. Result

The mean and standard deviation of osteocalcin, bone ALP, and estradiol in each group can be summarized as follows <Table 3>.

Table 3. Changes in osteocalcin after 6-month compound exercise.

Variable		Pre	Post	*p*
Osteocalcin (ng/mL)	control group	9.18 ± 3.09	8.47 ± 3.54	0.603
	exercise group	8.04 ± 3.93	9.54 ± 5.48	0.683
ALP (ug/L)	control group	10.15 ± 3.91	12.07 ± 3.71	0.181
	exercise group	7.75 ± 4.47	13.16 ± 4.43	0.003
Estradiol (pg/mL)	control group	11.29 ± 12.17	5.07 ± 0.25	0.946
	exercise group	14.09 ± 12.76	13.83 ± 13.77	0.325

3.1. Results of Osteocalcin

The 6-month complex exercise analysis results are shown in Table 2 and Figure 1. In the case of osteocalcin, the control group was 9.18 ± 3.09 ng/mL before exercise and 8.47 ± 3.54 ng/mL after exercise, and the exercise group was 8.04 ± 3.93 ng/mL before exercise and 9.54 ± 5.48 ng/mL after exercise, showing no significant difference in both groups.

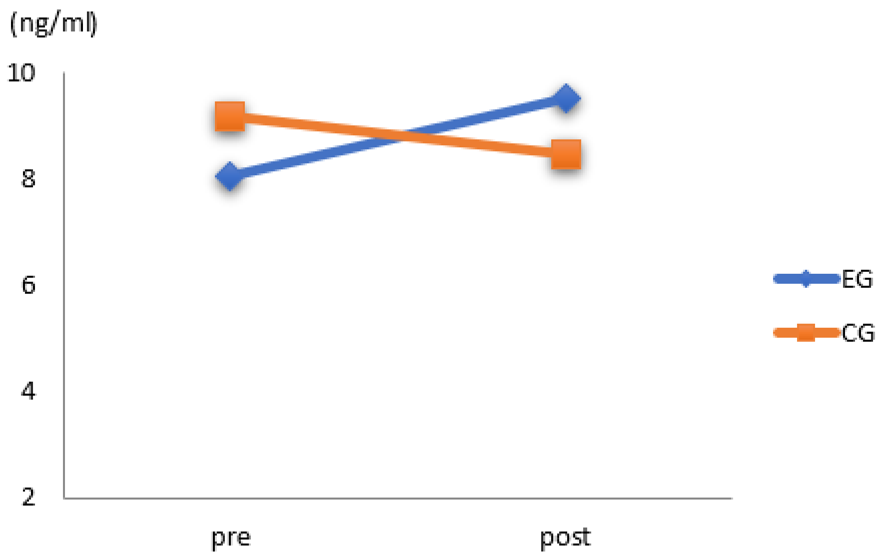

Figure 1. Osteocalcin changes.

As a result of analyzing the interaction effect according to the group, the F statistic value was 0.001, the F statistic value according to the measurement period was 0.132, and the F statistic value for the interaction between the group and the measurement period was 1.057, which was not significant at all <Table 4, Figure 1>.

Table 4. Results of two-way ANOVA analysis of osteocalcin.

Variable	*SS*	*df*	*MS*	*F*	*p Value*	*p eta-sq*
Corrected model	19.433	3	6.479	0.389	0.762	0.021
Intercept	4492.615	1	4492.615	269.520	0.000	0.833
Group	0.017	1	0.017	0.001	0.978	
Time	2.200	1	2.200	0.132	0.718	
Group × Time	17.623	1	17.623	1.057	0.308	
Error	900.124	54	16.669			
Total	5418.120	58				
Corrected total	919.557	57				

3.2. Results of ALP

The result of the 6-month complex exercise analysis is shown in Table 2 and Figure 1. In the case of ALP, there was no significant difference in the control group at 10.15 ± 3.91 ug/L before exercise and 12.07 ± 3.71 ug/L after exercise, but in the exercise group, it was 7.75 ± 4.47 ug/L before exercise and 13.16 ± 4.43 ug/L after exercise, showing a significant difference.

As a result of analyzing the interaction effect according to the group, the F statistic value was not significant at 0.365, and the F statistic value was 11.359, indicating a significant difference as a result of testing whether it affects ALP according to the measurement period <Table 5, Figure 2>.

Table 5. Results of two-way ANOVA analysis of ALP.

Variable	*SS*	*df*	*MS*	*F*	*p Value*	*p eta-sq*
Corrected model	238.357	3	79.452	4.651	0.006	0.205
Intercept	6734.303	1	6734.303	394.229	0.000	0.880
Group	6.241	1	6.241	0.365	0.548	0.007
Time	194.030	1	194.030	11.359	0.001	0.174
Group × Time	44.197	1	44.197	2.587	0.114	0.046
Error	922.440	54	17.082			
Total	7917.280	58				
Corrected total	1160.797	57				

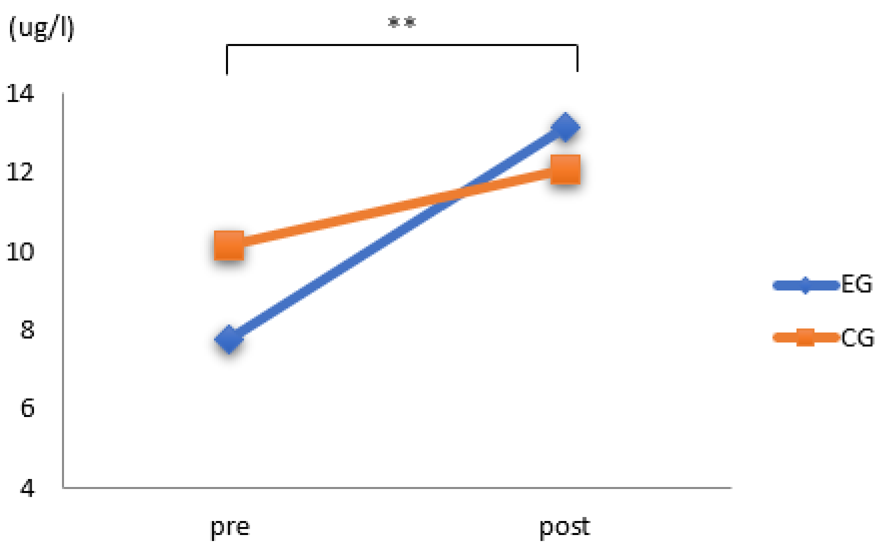

Figure 2. ALP changes (** $p < 0.01$).

3.3. Results of Estradiol

The result of the 6-month complex exercise analysis is shown in Table 2 and Figure 1. For estradiol, the control group was 11.29 ± 12.17 pg/mL before exercise and 5.07 ± 0.25 pg/mL after exercise, and the exercise group was 14.09 ± 12.76 pg/mL before exercise and 13.83 ± 13.77 pg/mL after exercise, which showed no significant difference between both groups.

As a result of analyzing the interaction effect according to the group, the F statistic value was 0.001, the F statistic value according to the measurement period was 0.132, and the F statistic value for the interaction between the group and the measurement period was 1.057, which did not show a significant difference <Table 6, Figure 3>.

Table 6. Results of two-way ANOVA analysis of estradiol.

Variable	*SS*	*df*	*MS*	*F*	*p Value*	*p eta-sq*
Corrected model	775.176	3	258.392	2.096	0.111	0.104
Intercept	7097.473	1	7097.473	57.580	0.000	0.516
Group	484.524	1	484.524	3.931	0.053	0.068
Time	152.235	1	152.235	1.235	0.271	0.022
Group × Time	128.428	1	128.428	1.042	0.312	0.019
Error	6656.249	54	123.264			
Total	14409.880	58				
Corrected total	7431.424	57				

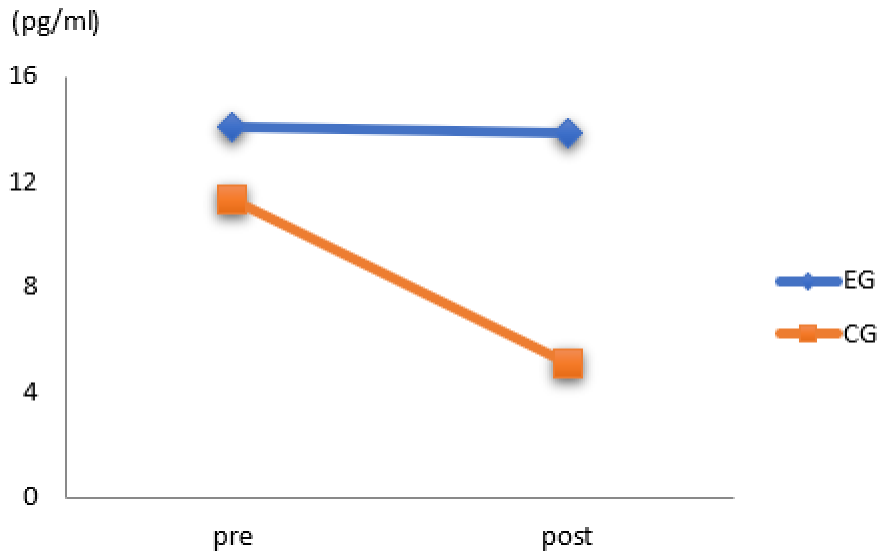

Figure 3. Estradiol changes.

4. Discussion

This study analyzed the effects of an exercise program on the representative serum osteocalcin, bone ALP, and estradiol as indicators of bone formation after 6 months of complex exercise for elderly women aged 75 years or older using public health centers in order to provide a basis for its use.

This study analyzed the effect of exercise performance on osteocalcin for six months in the elderly in late years. Although there was no significant difference, osteocalcin in the control group decreased by 7.7%, and osteocalcin in the exercise group increased by 18.66%. Osteocalcin differs depending on aerobic exercise and resistance exercise [34]. As a result of 16 weeks of resistance exercise in postmenopausal women, it was reported that there was no change in osteocalcin, an indicator of bone formation [35], and there was also a report [36] that postmenopausal women's exercise treatment did not change with osteocalcin. Additionally, exercise performance in postmenopausal women increases bone mineral density, but does not change serum osteocalcin levels [37]. However, according to Smith et al. [38], osteocalcin increased when anaerobic exercise was performed for 1 to 2 months [39], and low-intensity and high-intensity ladders for 6 weeks in mature male rats. As a result of exercise, the serum osteocalcin concentration was significantly increased in both groups compared to the control group, but bone density was significantly increased only in the high-intensity exercise group. Therefore, it is judged that exercise performance plays a positive role in improving maximum bone mass and bone density [40].

It was reported that ALP is a representative index reflecting the activity of osteoblasts [41] and can be used as an index of bone metabolism in subjects without liver disease or metabolic disease.

As a result of analyzing the effect of exercise performance on ALP for six months in the elderly in late years in this study, the control group increased by 18.92%, and the exercise group significantly increased by 69.81%. This study, together with Rudberg et al. [42], which reported that bone-type alkaline phosphatase increased dramatically as a result of performing a bicycle ergometer with an average age of 57 years old, a report which claimed that the concentration of BALP was high [43], a report which claimed that the bone BALP increased after 12 weeks compared to pre-exercise only in the aqua aerobic exercise group [13], and the report of Swissa-Sivan et al. [44], which claimed that growing rats after swimming exercise for 12 weeks showed bone density higher by 13%, and bone content higher by 10% and 67% higher ALP than the control group, respectively, proved that the exercise is effective for the bone density increase in the elderly in late years.

However, serum osteocalcin and ALP were increased at the time of menopause due to the compensatory process by the osteogenesis inhibitory action [45–47] and osteoporosis.

The analysis results on the pattern of the bone formation index change according to exercise treatment in postmenopausal women with prognoses are still not clear. Therefore, along with a number of reports [48,49], which claim that the effect on bone metabolism is different depending on the type of exercise, it is also affected by the duration of exercise [47]. To use it as an analysis index of metabolism, further analysis is required, including many cases in the future.

Among endocrine hormones, aging-related hormones include growth hormone, DHEA-S (dehydroepiandrosterone sulfate), and estrogen, and these hormones show a decrease in secretion with aging [49]. After menopause, estradiol (E2), which accounts for most estrogen, is not produced, and trace levels of E2 appear [50]. This study analyzed the effect of complex exercise performance on estradiol for 6 months in the elderly in late years. Although no significant difference was found, the control group decreased by 55.09%, and the exercise group decreased by 1.85%.

Lanfrancok et al. [51] found that estrogen increased significantly in both male and female elderly in a study conducted with resistance exercise for the elderly, whereas [52] showed that estradiol decreased after completing 12 weeks of a complex exercise program. In addition, with the application of a 12-week circular exercise program [53], an elastic resistance exercise program using a rip trainer [54], and an aerobic exercise program [55], it is reported that there is a positive improvement effect by increasing E2.

Therefore, it was found that although women hardly produce E2 as they age and enter menopause, regular physical activity can synthesize trace amounts of E2 [54].

In this study, estradiol decreased in both groups, but the exercise group showed a slight decrease compared to the control group, so exercise is judged to be able to delay the decrease in estradiol levels due to aging.

Bone is sensitive to external mechanical stimuli, as well as to metabolic changes in the body to cause changes in activity. Changes in bone metabolism that cause increases and decreases in bone mass include genetic factors [56], as well as environmental factors, such as nutrition [57] and exercise [58], causing a significant impact on inactivity environments, such as space flight [59] or weightlessness [60], promoting bone mass loss. However, regular moderate exercise maintains or increases bone mass and is known to cause the disease [20]. Physical activity and exercise play a role in preserving bone density by increasing osteoblast activity [61], and Nuti et al. [62] also found that exercise patterns differed in growth, adolescence, and old age. However, there was an increase in bone density due to exercise. In addition, many studies show that exercise is associated with bone formation [63–66] and it is reported that the exercise has a significant effect on improving bone mineral density [67].

Looking at the above results in general, it is necessary to maintain and promote physical activity for health management of the elderly, and strategies to increase the current low rate of physical activity are required. Therefore, it is necessary to understand the physical characteristics and physical activity of the elderly. Since this study was limited to the female elderly, it is necessary to secure subjects of various age groups, including male elderly, in the future study. The rate of aging varies from person to person [68], and the physical response and adaptation to physical activity may vary according to age [69], and diseases of the elderly also vary according to age. For this reason, the exercise program should be conducted differently by dividing the elderly by age.

5. Conclusions

This study is an experimental study, which attempted to check the effect of an exercise program on osteocalcin, ALP, and estradiol in middle and late-stage elderly (over 75 years old), and was effective in maintaining and improving osteocalcin, ALP, and estradiol.

It will be important to improve bone metabolism-related health and other health through continuous participation in exercise by developing and providing an exercise program for the elderly based on the results that exercise clearly plays a positive role in improving bone mineral density even for middle- and late-stage elderly people.

Such efforts can be an alternative that can efficiently cope with various problems caused by the increase in the elderly population at a low cost. In the future, it will be necessary to conduct a long-term program of at least 6 months or longer and carry out repeated studies on elderly people of various age groups to evaluate the effects of exercise according to period and gender.

Author Contributions: Conceptualization, A.-R.K.; Data curation, S.-E.L.; Formal analysis, A.-R.K.; Investigation, S.-E.L.; Resources, Y.-J.S.; Software, Y.-J.S.; Supervision, S.-W.C.; Writing—original draft, A.-R.K.; Writing—review & editing, S.-W.C. All authors have read and agreed to the published version of the manuscript.

Funding: This work was supported by the Ministry of Education of the Republic of Korea and the National Research Foundation of Korea (NRF-2020S1A5B5A17089936).

Institutional Review Board Statement: This experimental protocol was approved by the Institutional Review Committee of Sungshin Women's University (SSWUIRB-2021-015) and informed to and received the consent of all participants.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

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

References

1. Statistics Korea. Social Indicators in Korea. 2021. Available online: https://kostat.go.kr/portal/korea/kor_nw/1/1/index.board?bmode=read&aSeq=403253 (accessed on 29 September 2021).
2. Milanovic, Z.; Jorgić, B.; Trajković, N.; Sporis, P.S.; James, N. Age-related decrease in physical activity and functional fitness among elderly men and women. *Clin. Interv. Aging* **2013**, *549*. [CrossRef] [PubMed]
3. Korea Institute for Health and Social Affairs. *2020 Survey of the Elderly*; Korea Institute for Health and Social Affairs: Seoul, Korea, 2021.
4. Nieto-Riveiro, L.; Groba, B.; Miranda, M.C.; Concheiro, P.; Pazos, A.; Pousada, T.; Pereira, J. Technologies for participatory medicine and health promotion in the elderly population. *Medicine* **2018**, *97*, e1079. [CrossRef] [PubMed]
5. Kanis, J.A. The burden of osteoporosis. *J. Endocrinol. Investig.* **1999**, *22*, 583–588. [CrossRef] [PubMed]
6. Bliuc, D.; Alarkawi, D.; Nguyen, T.V.; Eisman, J.A.; Center, J.R. Risk of subsequent fractures and mortality in elderly women and men with fragility fractures with and without osteoporotic bone density: The Dubbo Osteoporosis Epidemiology Study. *J. Bone Miner. Res.* **2015**, *30*, 637–646. [CrossRef] [PubMed]
7. Pouresmaeili, F.; Kamalidehghan, B.; Kamarehei, M.; Goh, Y.M. A comprehensive overview on osteoporosis and its risk factors. *Ther. Clin. Risk Manag.* **2018**, *14*, 2029. [CrossRef]
8. Chao, Y.P.; Kao, T.W.; Chen, W.L.; Peng, T.C.; Wu, L.W. Mid-arm muscle circumference as an indicator of osteoporosis in community-dwelling older men. *Arch. Gerontol. Geriatr.* **2020**, *87*, 103998. [CrossRef]
9. Schwartz, A.V.; Nevitt, M.C.; Brown Jr, B.W.; Kelsey, J.L. Increased falling as a risk factor for fracture among older women: The study of osteoporotic fractures. *Am. J. Epidemiol.* **2005**, *161*, 180–185. [CrossRef]
10. Lee, S.R.; Ha, Y.C.; Kang, H.; Park, Y.G.; Nam, K.W.; Kim, S.R. Morbidity and mortality in Jeju residents over 50-years of age with hip fracture with mean 6-year follow-up: A prospective cohort study. *J. Korean Med. Sci.* **2013**, *28*, 1089–1094. [CrossRef]
11. Gallagher, C.M.; Kovach, J.S.; Meliker, J.R. Urinary cadmium and osteoporosis in US women $\geq$50 years of age: NHANES 1988–1994 and 1999–2004. *Environ. Health Perspect.* **2008**, *116*, 1338–1343. [CrossRef]
12. Health Insurance Review & Assessment Service. 2021. Available online: https://www.hira.or.kr/bbsDummy.do?pgmid=HIRAA020041000100&brdScnBltNo=4&brdBltNo=10478&pageIndex=1 (accessed on 22 November 2021).
13. IOF. Broken Bones, Broken Lives UK. 2018. Available online: https://www.iofbonehealth.org/impact-osteoporosis (accessed on 10 February 2019).
14. Lewiecki, E.M.; Ortendahl, J.D.; Vanderpuye-Orgle, J.; Grauer, A.; Arellano, J.; Lemay, J.; Singer, A.J. Healthcare policy changes in osteoporosis can improve outcomes and reduce costs in the United States. *JBMR Plus* **2019**, *3*, e10192. [CrossRef]
15. Smith, S.M.; Zwart, S.R.; Heer, M.A.; Baecker, N.; Evans, H.J.; Feiveson, A.H.; Shackelford, L.C.; Leblanc, A.D. Effects of artificial gravity during bed rest on bone metabolism in humans. *J. Appl. Physiol.* **2009**, *107*, 47–53. [CrossRef]
16. Babatunde, O.O.; Bourton, A.L.; Hind, K.; Paskins, Z.; Forsyth, J.J. Exercise interventions for preventing and treating low bone mass in the forearm: A systematic review and meta-analysis. *Arch. Phys. Med. Rehabil.* **2020**, *101*, 487–511. [CrossRef] [PubMed]
17. Marín-Cascales, E.; Alcaraz, P.E.; Ramos-Campo, D.J.; Rubio-Arias, J.A. Effects of multicomponent training on lean and bone mass in postmenopausal and older women: A systematic review. *Menopause* **2018**, *25*, 346–356. [CrossRef]
18. Park, H.Y. *The Effect of Physical Exercise Type on Bone Metabolism and Inflammatory Markers in Elderly Women*; Hanyang University: Seoul, Korea, 2016.

19. De Kam, D.; Smulders, E.; Weerdesteyn, V.; Smits-Engelsman, B.C.M. Exercise interventions to reduce fall-related fractures and their risk factors in individuals with low bone density: A systematic review of randomized controlled trials. *Osteoporos. Int.* **2009**, *20*, 2111–2125. [CrossRef] [PubMed]
20. Howe, T.E.; Shea, B.; Dawson, L.J.; Downie, F.; Murray, A.; Ross, C.; Creed, G. Exercise for preventing and treating osteoporosis in postmenopausal women. *Cochrane Database Syst. Rev.* **2011**. [CrossRef] [PubMed]
21. Martyn-St James, M.; Carroll, S. A meta-analysis of impact exercise on postmenopausal bone loss: The case for mixed loading exercise programmes. *Br. J. Sport. Med.* **2009**, *43*, 898–908. [CrossRef]
22. Ma, D.; Wu, L.; He, Z. Effects of walking on the preservation of bone mineral density in perimenopausal and postmenopausal women: A systematic review and meta-analysis. *Menopause* **2013**, *20*, 1216–1226. [CrossRef]
23. Martyn-St James, M.; Carroll, S. Meta-analysis of walking for preservation of bone mineral density in postmenopausal women. *Bone* **2008**, *43*, 521–531. [CrossRef]
24. Abrahin, O.; Rodrigues, R.P.; Marçal, A.C.; Alves, E.A.C.; Figueiredo, R.C.; Sousa, E.C.D. Swimming and cycling do not cause positive effects on bone mineral density: A systematic review. *Rev. Bras. Reumatol.* **2016**, *56*, 345–351. [CrossRef]
25. Beger, T.; Yavuzer, H. Yaslilik ve yaslilik epidemiyolojisi. *Klin. Gelisim* **2012**, *25*, 1–3.
26. Kang, H.Y.; Seo, N.S.; Kim, Y.H. Health pattern of elderly according to age group who living alone in an urban area. *J. Korean Acad. Nurs.* **2004**, *34*, 1057–1068. [CrossRef] [PubMed]
27. Kim, O.J. The effects of integrated movement program on the health and quality of life for the elderly in rural areas. *Korean J. Sports Sci.* **2020**, *29*, 279–288. [CrossRef]
28. Jang, S.H.; Hwang, B.D.; Yoon, H.J.; Lee, S.K. Effect of exercise program on grip strength, balance and bone mineral density of the elderly women in rural community. *J. Korea Contents Assoc.* **2009**, *9*, 214–223. [CrossRef]
29. Lee, S.G.; Park, S.K. The effects of a video strength exercise on grip strength, balance, TUG in the frail elderly women. *J. Korean Soc. Phys. Med.* **2013**, *8*, 91–98. [CrossRef]
30. Jang, J.H.; Kim, J.C.; Kang, S.H.; Ko, J.U. Changes of physical fitness variables after 12-Week health promotion exercise program in elderly women: One-year follow-up. *J. Korean Assoc. Phys. Educ. Sport Girls Women* **2016**, *30*, 221–236. [CrossRef]
31. Shin, J.H.; Hwang, Y.N.; Kim, W.W.; Kim, H.S.; Song, S.W. The relationship between the level of serum lipids and bone metabolism among pre and postmenopausal women. *Korean J. Obes.* **2007**, *16*, 162–169.
32. Bonnick, S.L.; Shulman, L. Monitoring osteoporosis therapy: Bone mineral density, bone turnover markers, or both? *Am. J. Med.* **2006**, *119*, S25–S31. [CrossRef]
33. Johansen, J.S.; Riss Delmas, P.D.; Chritianen, C. Clinical indication for bone mineral measurements. *J. Bone Miner. Res.* **1988**, *4*, 1–28.
34. Woitge, H.W.; Friedmann, B.; Suttner, S.; Farahmand, I.; Müller, M.; Schmidt-Gayk, H.; Seibel, M.J. Changes in bone turnover induced by aerobic and anaerobic exercise in young males. *J. Bone Miner. Res.* **1998**, *13*, 1797–1804. [CrossRef]
35. Ryan, A.S.; Treuth, M.S.; Hunter, G.R.; Elahi, D. Resistive training maintains bone mineral density in postmenopausal women. *Calcif. Tissue Int.* **1998**, *62*, 295–299. [CrossRef]
36. Yasumura, S.; Aloia, J.F.; Gundberg, C.M.; Yeh, J.; Vaswani, A.N.; Yuen, K.; Cohn, S.H. Serum osteocalcin and total body calcium in normal pre-and postmenopausal women and postmenopausal osteoporotic patients. *J. Clin. Endocrinol. Metab.* **1987**, *64*, 681–685. [CrossRef] [PubMed]
37. Kohrt, M.W.; Snead, B.D.; Slatopolsky, E.; Birge, S.J., Jr. Additive effects of weight-bearing exercise and estrogen on bone mineral density in older women. *J. Bone Miner. Res.* **1995**, *10*, 1303–1311. [CrossRef] [PubMed]
38. Smith, M.Z.; Goettsch, B.M.; Van Ramshorst, R.D.; O'brien, J.A.; Jaque, S.V.; Sumida, K.D. Resistance training and bone mineral density during growth. *Int. J. Sport. Med.* **2008**, *29*, 316–321. [CrossRef] [PubMed]
39. Banfi, G.; Lombardi, G.; Colombini, A.; Lippi, G. Bone metabolism markers in sports medicine. *Sport. Med.* **2010**, *40*, 697–714. [CrossRef]
40. Ahn, N.Y.; Kim, K.J. Utility of Bone Metabolic Markers, Serum and Salivary Cortisol Concentration for Exercise Training Effect Analysis in Elderly with Osteoporosis. *Exerc. Sci.* **2016**, *25*, 1–9. [CrossRef]
41. Leung, K.S.; Fung, K.P.; Sher, A.H.; Li, C.K.; Lee, K.M. Plasma bone-specific alkaline phosphatase as an indicator of osteoblastic activity. *J. Bone Jt. Surg. Br. Vol.* **1993**, *75*, 288–292. [CrossRef]
42. Rudberg, A.; Magnusson, P.; Larsson, L.; Joborn, H. Serum isoforms of bone alkaline phosphatase increase during physical exercise in women. *Calcif. Tissue Int.* **2000**, *66*, 342–347. [CrossRef]
43. Lee, C.J. The Effects of Resistance Training to Health-Related Fitness. Growth Hormone. Bone Metabolism & Bone Mineral Density by Grades of Male's High School Students. Ph.D. Thesis, Graduate School of Pusan National University, Busan, Korea, 2005.
44. Swissa-Sivan, A.; Azoury, R.; Statter, M.; Leichter, I.; Nyska, A.; Nyska, M.; Samueloff, S. The effect of swimming on bone modeling and composition in young adult rats. *Calcif. Tissue Int.* **1990**, *47*, 173–177. [CrossRef]
45. Gundberg, C.M.; Looker, A.C.; Nieman, S.D.; Calvo, M.S. Patterns of osteocalcin and bone specific alkaline phosphatase by age, gender, and race or ethnicity. *Bone* **2002**, *31*, 703–708. [CrossRef]
46. Delmas, P.D. Biochemical markers of bone turnover for the clinical investigation of osteoporosis. *Osteoporos. Int.* **1993**, *3*, 81–86. [CrossRef]
47. Van Hoof, V.O.; De Broe, M.E. Interpretation and clinical significance of alkaline phosphatase isoenzyme patterns. *Crit. Rev. Clin. Lab. Sci.* **1994**, *31*, 197–293. [CrossRef] [PubMed]

48. Eliakim, A.; Raisz, L.G.; Brasel, J.A.; Cooper, D.M. Evidence for increased bone formation following a brief endurance-type training intervention in adolescent males. *J. Bone Miner. Res.* **1997**, *12*, 1708–1713. [CrossRef] [PubMed]
49. Humphries, B.; Newton, R.U.; Bronks, R.O.G.E.R.; Marshall, S.O.N.J.A.; McBRIDE, J.E.F.F.; Triplett-McBride, T.R.A.V.I.S.; Sly, N. Effect of exercise intensity on bone density, strength, and calcium turnover in older women. *Med. Sci. Sport. Exerc.* **2000**, *32*, 1043–1050. [CrossRef] [PubMed]
50. Burger, H.G.; Hale, G.E.; Robertson, D.M.; Dennerstein, L. A review of hormonal changes during the menopausal transition: Focus on findings from the Melbourne Women's Midlife Health Project. *Hum. Reprod. Update* **2007**, *13*, 559–565. [CrossRef]
51. Lanfranco, F.; Gianotti, L.; Giordano, R.; Pellegrino, M.; Maccario, M.; Arvat, E. Ageing, growth hormone and physical performance. *J. Endocrinol. Investig.* **2003**, *26*, 861–872. [CrossRef]
52. Ahn, K.J. *12-Week Combined Exercise Program on Bone Mineral Density and Sex Hormone in the Elderly*; Chungbuk National University: Cheongju, Korea, 2008.
53. Lee, J.H. *Effects of Circuit Exercise on Physical Fitness, Blood Ipids and Estrogen in Elderly Women*; Jeju National University: Jeju, Korea, 2010.
54. Kim, Y.S.; Jeong, C.K.; Kang, H.S. The Effect of Elastic Resistance Exercise and Protein Intake on Functional Fitness and Aging Hormone in Elderly women. *J. Korean Soc. Study Phys. Educ.* **2016**, *21*, 111–124.
55. Kim, C.H.; Lee, J.W.; Han, S.I. The Effect of Exercise Type Performance in Elderly Women on The Aging Hormone and De-pression Factor. *J. Korea Soc. Wellness* **2013**, *8*, 373–386.
56. Zmuda, J.M.; Sheu, Y.T.; Moffett, S.P. Genetic epidemiology of osteoporosis: Past, present, and future. *Curr. Osteoporos. Rep.* **2005**, *3*, 111–115. [CrossRef]
57. Mundy, G.R. Nutritional modulators of bone remodeling during aging. *Am. J. Clin. Nutr.* **2006**, *83*, 427S–430S. [CrossRef]
58. Ferrari, S. Osteoporosis: A complex disorder of aging with multiple genetic and environmental determinants. *World Rev. Nutr. Diet.* **2005**, *95*, 35. [CrossRef]
59. Ohshima, H. Bone loss and bone metabolism in astronauts during long-duration space flight. *Clin. Calcium* **2006**, *16*, 81–85. [PubMed]
60. Iwamoto, J.; Takeda, T.; Sato, Y. Interventions to prevent bone loss in astronauts during space flight. *Keio J. Med.* **2005**, *54*, 55–59. [CrossRef] [PubMed]
61. Villareal, D.T.; Fontana, L.; Weiss, E.P.; Racette, S.B.; Steger-May, K.; Schechtman, K.B.; Holloszy, J.O. Bone mineral density response to caloric restriction–induced weight loss or exercise-induced weight loss: A randomized controlled trial. *Arch. Intern. Med.* **2006**, *166*, 2502–2510. [CrossRef]
62. Nuti, R.; Martini, G.; Merlotti, D.; Valleggi, F.; De Paola, V.; Gennari, L. Professional sport activity and micronutrients: Effects on bone mass. *J. Endocrinol. Investig.* **2005**, *28*, 52–60.
63. Kohrt, W.M. American College of Sports Medicine position stand on physical activity and bone health. *Med. Sci. Sports Exer.* **2004**, *36*, 1985–1996. [CrossRef] [PubMed]
64. Taaffe, D.R.; Marcus, R. The muscle strength and bone density relationship in young women: Dependence on exercise status. *J. Sport. Med. Phys. Fit.* **2004**, *44*, 98–103.
65. Bemben, D.A.; Buchanan, T.D.; Bemben, M.G.; Knehans, A.W. Influence of type of mechanical loading, menstrual status, and training season on bone density in young women athletes. *J. Strength Cond. Res.* **2004**, *18*, 220–226. [CrossRef]
66. Kirchner, E.M.; Lewis, R.D.; O'Connor, P.J. Bone mineral density and dietary intake of female college gymnasts. *Med. Sci. Sport. Exerc.* **1995**, *27*, 543–549. [CrossRef]
67. Marques, E.A.; Mota, J.; Viana, J.L.; Tuna, D.; Figueiredo, P.; Guimarães, J.T.; Carvalho, J. Response of bone mineral density, inflammatory cytokines, and biochemical bone markers to a 32-week combined loading exercise programme in older men and women. *Arch. Gerontol. Geriatr.* **2013**, *57*, 226–233. [CrossRef]
68. Harridge, S.D.; Lazarus, N.R. Physical activity, aging, and physiological function. *Physiology* **2017**, *32*, 152–161. [CrossRef]
69. Brach, J.S.; FitzGerald, S.; Newman, A.B.; Kelsey, S.; Kuller, L.; VanSwearingen, J.M.; Kriska, A.M. Physical activity and functional status in community-dwelling older women: A 14-year prospective study. *Arch. Intern. Med.* **2003**, *163*, 2565–2571. [CrossRef] [PubMed]