Original Articles

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Characteristics of Bone Metabolism in Middle-Aged and Older Mountaineers

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Objective: This study aims to elucidate the characteristics of bone metabolism in middle-aged and older mountaineers and compare them with those who walk regularly and those who do not exercise regularly.

Materials: We enrolled 17 middle-aged and older mountaineers [Mountaineer Group; 8 males (age: 65.9 ± 4.5 years) and 9 females (age: 60.4 ± 5.5 years)], 20 people who walked regularly [Walker Group; 10 males (age: 67.5 ± 5.2 years) and 10 females (age: 63.2 ± 5.7 years)], and 17 people with sedentary lifestyle [Control Group; 9 males (age: 67.3 ± 5.2 years) and 8 females (age: 62.7 ± 4.9 years)] in this study.

Methods: All assessments in this study were based on the osteo sono-assessment index (OSI) and bone metabolism markers. We used bone alkaline phosphatase (BAP) and procollagen type 1 aminoterminal propeptide (P1NP) as bone formation markers. In addition, we used tartrate-resistant acid phosphatase 5b (TRACP 5b) and type I collagen cross-linked N-telopeptide in serum (sNTX) as bone resorption markers.

Results: There was no significant difference in OSI among the three groups in males and females. In addition, there was no significant difference between BAP and P1NP in males. The TRACP-5b level was significantly higher in the Mountaineer Group $(459.5 \text{ mU/d}l)$ than in the Control Group $(333.0 \text{ mU/d}l; \text{p} < 0.05)$ in males. In addition, there was no significant difference in the bone formation/resorption ratio among the three groups in males. In females, there was no significant difference in each bone metabolism marker among the three groups.

Conclusions: Middle-aged and older males who mountaineer regularly had higher resorption than those who do not exercise regularly, but there was no difference in coupling. Furthermore, there were no prominent traits in the bone metabolism of middle-aged and older females who mountaineer regularly.

Key words: exercise, mountain climbing, bone metabolism, bone quality

Introduction

Besides other diseases, such as cerebrovascular disease and ischemic heart disease, one of the leading health-related concerns in a super-aging society is osteoporosis. After menopause, females are typically susceptible to osteoporosis because reduced estrogen secretion curtails bone resorption, resulting in a sudden decline in bone mass¹. However, males should also be aware of decreased bone mass because of aging. In fact, a recent study²⁾ has reported that increased mortality risk after

bone fractures and degree of life-impairing disorders are more severe in males than in females. Thus, osteoporosis is one of the current diseases that should be prevented in both males and females.

Osteoporosis can be efficiently prevented through exercise, and several intervention studies have been conducted on various exercise types. Anaerobic exercise training, such as resistance exercises^{3) 4)} and jumping exercises^{5) 6)}, are reportedly useful in maintaining and increasing bone density and bone mineral content. However, results of studies investigating aerobic exercise training,

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such as walking, are inconclusive $(7)-11$). During changes in bone mass, both bone formation and resorption (bone metabolism) are considered to match the mechanical stress applied to the bone, and the formation and resorption adjust 12 according to the form and mass that are appropriate to maintain bone strength. In fact, differences in the mechanical stress on the bone from aerobic exercise are considered accountable for no consensus on the effects of aerobic exercise on bone mass.

Regarding bone strength assessment, quantitative element such as bone mass (bone density) is assessed and qualitative elements such as bone turnover, microstructures, microfracture, and degree of calcification are assessed¹³⁾. Typically, both quantitative and qualitative elements are used for assessing bone strength. Bone metabolism markers can be used for assessing the dynamic state of systemic bone metabolism as one of the elements of bone quality assessment. Conventionally, changes in these indicators are often used to determine bone condition, diagnose bone disease, and assess treatment effects $14)$ -16). However, some ongoing studies are investigating the dynamic state of bone metabolism in long-distance runners for preventing stress fractures or determining the correlation between menstruation and bone metabolism in female athletes $17)$ 18). In addition, some studies have reviewed the physiological changes occurring in middle-aged and older people $19)$ and changes in bone metabolism because of training²⁰⁾. Bone density is attributed to both past and present bone metabolism. In contrast, bone metabolism markers signify the present state of bone metabolism dynamics and function as an indicator that predicts future changes in bone strength. Thus, evaluating bone density and elucidating bone metabolism dynamics through metabolism markers are necessary to assess bone strength.

Mountaineering has become a booming practice in middle-aged and older Japanese people. Mountaineering is a type of aerobic exercise, similar to walking, and can be an effective exercise for maintaining and improving health. Reportedly, 4-h hiking once a week has a 1.7-fold higher metabolic rate per week than walking for 30 min every day on a level surface²¹⁾. Hence, hiking not only is more enjoyable than walking but also ensures an effective metabolic rate. In addition, when exercising on a treadmill that simulates hiking, the muscle activity of the erector spinae, gluteus maximus, tibialis anterior, and gastrocnemius muscles is relatively higher when walking on an upward slope than on a level surface. Reportedly, the muscle activity level for the rectus abdominis and rectus femoris muscles is high when walking on a downward slope²²⁾. However, high-strength, highimpact exercises are not recommended for middleaged and older people to prevent injuries. Thus, we hypothesized that hiking was an ideal intermediate form of exercise for middle-aged and older people because the muscle activity level increases more by climbing and walking down hills in hiking compared with walking on level surfaces. Hence, we can anticipate an increase in the mechanical stress on the bone and subsequent positive effect on the bone strength.

This study aims to elucidate the characteristics of bone metabolism in middle-aged and older mountaineers by comparing them with people who walk regularly and those who do not exercise regularly.

Materials and Methods

This study was approved by the Ethical Committee of Juntendo University (Tokyo, Japan) $(27-16)$, and we obtained informed consent from all participants after providing oral and written explanations about the study before written consent was obtained.

1. Subjects

In our study, we included 17 subjects (8 males and 9 females; Mountaineer Group) who hiked mountains more than once a month on an average, 20 people (10 males and 10 females; Walker Group) who walked regularly more than once a week, and 17 people with sedentary lifestyle (9 males and 8 females; Control Group) who did not exercise regularly. The exclusion criteria of the study were as follows: smoking > 20 cigarettes a day²³; consumption of three or more units (equivalent to 60 g) of pure alcohol) of alcohol a day²⁴⁾; diseases (osteoporosis, diabetes mellitus, and hyperthyroidism) that might result in decreased bone mass; and taking medication that impacts bone metabolism²⁵⁾. Among the indices demonstrating the impact on bones according to subjects' history of exercising [Bone-Specific Physical Activity Questionnaire $(BPAQ)^{26}$, we used the index that reveals the impact on subjects' bones from regular exercise

patterns in the last 12 months [current BPAQ (cBPAQ)]. The Mountaineer and Walker Groups were defined as people who regularly hike and walk, respectively, and the Control Group was defined as people who do not regularly exercise or those who perform extremely light exercise (walking once a week or less; cBPAQ score ≤ 0.4).

2. Measurement items and methods

1) Osteo sono-assessment index (OSI)

We used the quantitative ultrasound measurement system (AOS-100; Hitachi-Aloka Medical, Ltd., Tokyo, Japan) to assess OSI of the right calcaneus as an indicator of bone strength. To evaluate OSI, we transmitted a low-frequency pulse at the center frequency of 0.5 MHz after fixing the oscillator and calculated the operation [speed of sound squared $(SOS^2) \times$ transmit index (TI) from the ultrasonic propagation velocity [SOS after passing through the calcaneus and the ultrasonic eattenuation (transmission) coefficient (TI)].

2) Bone metabolism

We collected blood samples of participants to assess bone metabolism markers. All samples were collected between 9 am and 11 am, and subjects were restricted from eating or drinking 3 h before blood collection. For bone formation markers, we measured bone alkaline phosphatase (BAP; in μ g/L) and procollagen type 1 aminoterminal propeptide (P1NP; in ng/ml) levels. In addition, we measured tartrate-resistant acid phosphatase 5b $(TRACP-5b;$ in mU/dl and type I collagen cross-linked N-telopeptide in serum [sNTX; in nmol bone collagen equivalents (BCE)/L] as bone resorption markers. Note that all measurements were outsourced to SRL Inc. (Tokyo, Japan).

3) Body composition (weight and body fat percentage)

We used InBody430 (Biospace Japan Inc., Tokyo, Japan) to measure the body weight and body fat percentage. All subjects stepped onto the machine; entered their age, height, and gender; assumed the posture for measurement; and recorded measurements.

4) BPAQ

BPAQ is a questionnaire associated with sports and physical activities that specifically affect bone formation. The questionnaire comprises items such as sports and physical exercises performed regularly, duration (years) for which these have been practiced [past BPAQ (pBPAQ)], and current sports and physical exercises practiced regularly over the last 12 months and the average number of times per week (cBPAQ). All subjects were asked to complete the questionnaires. We calculated the BPAQ score using the following formulas:

$pBPAQ = R \times y \times a$

where R is the effective load stimulus, y is years of participation, and α is the age weighting factor (age weightings: $\langle 15 \text{ years} = 0.25; \rangle 15 \text{ years}$: 0.10).

$cBPAQ = [R + 0.2 R (n-1)] \times a$

where R is the effective load stimulus, ν is the frequency of participation (per week), and α is the age weighting factor (age weightings: < 10 years= 1.2; 10-15 years=1.5, 15-35 years=1.1, and \geq 35 years: 1.0).

5) International Physical Activity Questionnaire (IPAQ)

We used the highly versatile IPAQ to assess the amount of daily physical activity of subjects. IPAQ assesses the average number of days and the length of time for high-intensity and moderate physical activity in 1 week. While we used the long version to determine the lifestyle perspective, such as during work or at home, the short version (SV) was used to determine the amount of activity in terms of activity intensity, regardless of the lifestyle. In this study, we used the Japanese version of SV IPAQ, which was translated into Japanese by Murase et $al.^{27}$.

To calculate energy consumption, amount of time (min) was multiplied by the intensity (METs) of each physical activity, which was calculated by assessing the amount of physical activity (METs/min) per week, and then divided by 7 to convert the figure into a daily mean. In addition, the amount of energy per $1 L$ for maximal oxygen consumption was 0.005 kcal. As 1 METs = 3.5 ml/kg/min, we calculated energy consumption according to the following formula:

Energy consumption $(kcal)$ = Amount of physical activity $(METs/min) \times 3.5$ $(ml/kg/min) \times 0.005$ $(kcal/ml) \times weight (kg)$

3. Statistical analysis

In this study, statistical analysis was performed

using a nonparametric model based on small sample size. We used the Kruskal-Wallis test to compare the variance among the three groups for each measurement item and conducted a multiple comparison test for items with a significant difference. We considered p< 5% as statistically significant. Of note, SPSS statistics ver. 23 (IBM Corp., Armonk, NY) was used for statistical analysis in this study.

Results

Tables-1〜4 summarize the physical characteristics of subjects and provide information on mountain climbing in the Mountaineer and Walker Groups. We observed no significant difference in physical characteristics among the three groups in both males and females. In this study, as the grouping was selected using cBPAQ, the cBPAQ

*: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$

Table-**2** Physical characteristics (females)

	Mountaineer Group (M) $(n=9)$	Walker Group (W) Control Group (C) $(n=10)$	$(n=8)$	Significant difference	Multiple comparison
Age (years)	60.4 ± 5.5	63.2 ± 5.7	62.7 ± 4.9	n.s.	n.s.
Age of menopause (years)	49.1 ± 5.1	48.9 ± 5.7	53.3 ± 3.3	n.s.	n.s.
Years passed since menopause (years)	11.1 ± 7.8	14.3 ± 9.2	10.0 ± 5.9	n.s.	n.s.
Height (cm)	156.4 ± 4.7	155.1 ± 3.7	156.9 ± 6.5	n.s.	n.s.
Weight (kg)	53.6 ± 5.5	52.8 ± 9.9	55.4 ± 11.5	n.s.	n.s.
Body fat $(\%)$	27.7 ± 4.9	27.2 ± 7.9	29.9 ± 8.6	n.s.	n.s.
cBPAO	0.6 ± 0.3	0.6 ± 0.3	0.1 ± 0.2	***	M vs. C: $**$ W vs. C: $*$
pBPAQ	2.7 ± 3.0	23.0 ± 30.2	13.9 ± 14.4	n.s.	n.s.
Amount of physical activity according to IPAQ $(kcal/day)$	171.4 ± 155.6	107.2 ± 57.7	202.5 ± 371.8	n.s.	n.s.

*: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$

value was significantly lower in the Control Group than in the Mountaineer and Walker Groups in both males and females. In this study, as groups were created using the cBPAQ value, it was significantly lower in the Control Group than in the Mountaineer and Walker Groups in both males and females.

No significant difference was observed among the three groups in terms of OSI of males and females $(Table-5)$. In terms of comparison of bone metabolism markers among the three groups, BAP bone formation marker for males (Table-6) was the highest in the Mountaineer Group, followed by the Walker and Control Groups $(13.1 \pm 3.2, 11.2 \pm 1)$ 3.2, and 10.6 ± 1.7 μ g/L, respectively); however, the difference was not significant. P1NP exhibited the same pattern, with the highest level in the Mountaineer Group, followed by the Walker and Control Groups $(40.5 \pm 11.3, 37.4 \pm 12.1,$ and 35.0

 \pm 7.0 ng/ml, respectively); however, the difference was not significant. Regarding the bone resorption marker sNTX, the levels in the Mountaineer, Walker, and Control Groups were $15.2 \pm$ 3.7, 14.7 \pm 4.2, and 15.3 \pm 2.5 nmol BCE/L, respectively, exhibiting no significant difference among the three groups. Regarding TRACP-5b, the levels were the highest in the Mountaineer Group, followed by the Walker and Control Groups (459.5 \pm 100.6, 372.1 \pm 104.3, and 333.0 \pm 47.7 mU/dl, respectively). Compared with the Control Group, the Mountaineer Group exhibited significantly higher values $(p<0.05)$ in TRACP-5b. In addition, the bone formation/resorption ratio calculated for assessing the balance between bone formation and bone resorption exhibited no significant difference among the three groups for any item. In females (Table-7), both BAP and P1NP levels in the

Table⁻⁵ Comparison of OSI among the three groups

	Mountaineer $Group(M)$ $(n=8)$	Walker Group (W) $(n=10)$	Control Group (C) $(n=9)$	Significant difference	Multiple comparison
OSI (males)	2.861 ± 0.301	2.968 ± 0.321	2.960 ± 0.335	n.s.	n.s.
OSI (females)	2.516 ± 0.245	2.441 ± 0.202	2.340 ± 0.098	n.s.	n.s.

Table-6 Comparison of bone metabolism markers among the three groups (males)

 $*: p < 0.05$

Table-7 Comparison of bone metabolism markers among the three groups (females)

	Mountaineer Group (M) $(n=8)$	Walker Group (W) $(n=10)$	Control Group (C) $(n=9)$	Significant difference	Multiple comparison
BAP (μ g/L)	13.0 ± 4.3	12.9 ± 3.5	13.9 ± 4.5	n.s.	n.s.
$P1NP$ (ng/ml)	49.3 ± 14.5	43.3 ± 5.3	51.6 \pm 21.8	n.s.	n.s.
$sNTX$ (nmol BCE/L)	19.3 ± 6.4	16.1 ± 2.3	14.7 ± 3.3	n.s.	n.s.
$TRACP-5b$ (mU/dl)	497.4 ± 180.5	412.3 ± 75.0	484.6 ± 171.4	n.s.	n.s.
BAP/sNTX	0.699 ± 0.203	0.806 ± 0.191	0.953 ± 0.291	n.s.	n.s.
BAP/TRACP-5b	0.027 ± 0.008	0.032 ± 0.008	0.030 ± 0.009	n.s.	n.s.
PINP/sNTX	2.637 ± 0.662	2.760 ± 0.580	3.522 ± 1.339	n.s.	n.s.
PINP/TRACP-5b	0.104 ± 0.026	0.107 ± 0.016	0.107 ± 0.024	n.s.	n.s.

Mountaineer, Walker, and Control Groups were 13.0 ± 4.3 , 12.9 ± 3.5 , and 13.9 ± 4.5 mg/L and 49.3 ± 14.5 , 43.3 ± 5.3 , and 51.6 ± 21.8 ng/ml, respectively, with no significant difference among the three groups for any item. Regarding bone resorption markers, sNTX and TRACP-5b levels were 19.3 ± 6.4 , 16.1 ± 2.3 , and 14.7 ± 3.3 nmol BCE/L and 497.4 ± 180.5 , 412.3 ± 75.0 , and 484.6 \pm 171.4 mU/dl, respectively, with no significant difference among the three groups for any item. In addition, even for the bone formation/resorption ratio, we observed no significant difference among the three groups for any item.

Discussion

1. Comparison of OSI among the Mountaineer, Walker, and Control Groups

Both past and present bone metabolism are accountable for bone density. OSI determines bone strength by indirectly measuring with ultrasound waves. Although a margin of error occurs because ofindirect measurement, a positive correlation has been reported between OSI and bone density 28 . which is why OSI is considered a rough reflection of subjects' bone metabolism to date. In this study, we observed no significant difference in OSI for males and females in the Mountaineer, Walker, or Control Groups $(Table-5)$. Regarding the impact of regular exercise on the bone (pBPAQ), no significant difference was observed among the three groups (Tables-1 and 2). Hence, OSI does not reflect the impact of exercises that the subjects are currently performing, but reflects the impact of exercises performed regularly in the past.

2. Comparison of bone metabolism among the Mountaineer, Walker, and Control Groups

The effects of exercise on bones vary depending on the subject's age, sex, conditions of exercise (intensity, type, and duration), and bone evaluated $(typ$ e and location of bone); therefore, the reports of various studies do not match. In general, small exercise loads do not affect bone dynamics and may even reduce bone mass in cases in which overtraining causes marked decrease in body fat or dysfunction of the ovaries 29 . In terms of sports activities in young individuals, athletes who train in muscle strength and jumping strength exercises have high bone mineral content and density, but

these are low in long-distance runners or swimmers 30 . The results of this study demonstrated that in males, TRACP-5b was the only parameter that was significantly higher in the Mountaineer Group than in the Control Group, and resorption was also increased (Table-6). Mountaineering simulations, both climbing up and down, on a treadmill have been reported to have higher activity levels compared with walking on a level surface²²⁾. Furthermore, when climbing down, eccentric contraction occurs in the leg extension muscle groups such as the quadriceps muscle, but the level of the resorption marker (TRACP-5b) has been reported to increase as well 31 ²¹. Based on these findings, we can assume that the Mountaineer Group had higher muscle activity levels than the other groups and apply higher mechanical stress to the bone to promote resorption. On the other hand, the effects of high resorption on bone mineral density can be expected, but the decrease in bone mineral density is known to occur not by a simple increase in resorption but by a bone formationresorption balance characterized by resorptiondominant uncoupling. In this study, no intergroup difference was observed in terms of the bone formation/resorption ratio, which is an indicator of bone metabolism balance, but the level of bone formation marker was the highest in the Mountaineer Group, although the difference was not significant (Table-6). Furthermore, the levels of bone density markers in males were within the normal range for all three groups²⁵⁾, with no levels representing pathological states. These suggest that it is unlikely that bone metabolism of the Mountaineer Group was in a resorption-dominant uncoupling state. It is known that senile osteoporosis exhibits no changes in resorption levels but lowers bone formation levels, causing resorptiondominant low-turnover bone metabolism. However, the Mountaineer Group likely maintained the bone metabolism they had when they were young. A previous study indicating the normal range of TRACP-5b stated that the mean level for males of the same age group, similar to those of our study (60-69 years), was approximately 350 ± 130 mU/dl^{32} , which is clearly lower compared with that of the Mountaineer Group. Thus, we speculate that mountaineering for males prevented bone metabolism dynamics from decreasing as a result of low

turnover caused by aging.

In females, there were no significant differences in the bone formation or resorption markers among the three groups (Table-7). Their bone metabolism markers were also within the normal range for all three groups, similarly to the males. It is known that menopause in females impacts bone metabolism dynamics. In the 10 years following menopause, decreased secretion of estrogen promotes resorption to cause a resorption-dominant uncoupling, thereby causing a sudden decrease in bone mass 33) 34). There were some subjects in this study with <10 years since menopause (Mountaineer Group: 11.1 ± 7.8 years, Walker Group: 14.3 ± 9.2 years, Control Group: 10.0 ± 5.9 years), suggesting that menopause had a greater impact on their bone metabolism than exercise. Previous studies have reported that high-impact exercises such as resistance exercises and jump training are necessary for maintaining bone density in post-menopausal females $^{35)}$, and it is possible that the levels of exercise load by mountaineering investigated in this study were not intense enough to affect bone metabolism dynamics of post-menopausal females. However, these are only hypotheses at this time, and warrants further investigation.

Mountaineering is a form of exercise that applies higher mechanical stress on the bones compared to walking on a level surface. In this study as well, the effects seemed potentially positive in the Mountaineer Group for both males and females, but the exercise was not sufficient to have great change on bone turnover. One of the primary factors of exercise on bone metabolism is not only the intensity of the mechanical stress on the bones but also hormone secretion associated with intensity in endurance exercises. The growth hormone, which is involved with bone metabolism 37 , increases by endurance exercise 38), particularly at intensities equal to or higher than the anaerobic threshold (AT) ³⁹⁾. Walking for training conducted at intensities corresponding to 90% AT and 110% AT resulted in the suppression of spine bone mineral density reduction at 110% AT only⁹⁾. As such, intensity of \geq AT is optimal to affect bone metabolism by endurance exercises. However, in order to ensure safety while avoiding fatigue during mountaineering, it is important to do it at an intensity below AT. The lactic acid levels of male

members of the university hiking club, who are experts of mountaineering, during mountaineering is around 2.0 mmol, which indicates that they walk at levels that do not exceed AT^{40} . The subjects in the Mountaineer Group of this study were members of a community hiking club, and the males and females had 21.1 ± 18.5 and 11.9 ± 7.1 years of mountaineering experience, respectively. Because they are believed to be practicing at a pace that does not exceed AT, it is possible that the intensity of mountaineering was not enough to have any major effect on bone metabolism.

While dividing the subjects for this study, we established the exclusion criteria based on current exercise habits and factors in daily living that may have an effect on bone metabolism. In this study, we could not completely restrict meals for the blood test; therefore, we cannot rule out the effects of diet, but the bone metabolism markers used in this study are known to be less susceptible to the effects of diet. Because the subjects were restricted from eating or drinking for 3 h before the blood collection time, the effects of the diet must be minimal. There are many factors that affect the bone metabolism of middle-aged and older individuals. In addition to exercise, these include amount of activity in daily living, nutritional intake, and menopause for females. Further detailed investigations are required to validate the effects of mountaineering on bone metabolism.

Conclusion

Middle-aged and older males who mountaineer regularly had higher resorption than those who do not exercise regularly, but there was no difference in coupling. Furthermore, there were no prominent traits in the bone metabolism of middle-aged and older females who mountaineer regularly.

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