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Original Article

Thyroid Function Decline and Diet in Female High School Long-distance Runners

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We aimed to clarify the state of thyroid function in female high school long-distance runners. We evaluated the associations between thyroid function and menstrual condition, bone mineral density (BMD), nutritious status, and body composition. The subjects' height and weight were measured, along with fat percentage, fat mass, muscle mass, and BMD with dual-energy X-ray absorptiometry. A nutrition and dietary survey measured the subjects' intake of energy and nutrients based on meals provided at the subjects' dorm for 3 days in July of 2016 and 2017. Blood parameters including thyroid hormone and estradiol were measured. Most of the subjects (81.3%) were underweight (body mass index <18.5). The thyroid hormone free T3 value was decreased, but TSH was not increased and was similar to that observed in individuals with anorexia nervosa. In our subjects, thyroid hormone was associated with BMD and nutritional intake. To improve the menstruation abnormality of female athletes and to increase their bone density, the athletes' weight should be managed by proper nutrient intake and the maintenance of their thyroid function.

Key words: thyroid function, nutritious status, female high school long-distance runners, bone mineral density, menstrual condition

Female long-distance runners may encounter problems with their health, including low energy availability, amenorrhea (low levels of estrogen), and low bone mineral density (BMD). Low energy availability caused by an increase in physical exercise (such as the exercise in long-distance running) without a proper diet may result in menstrual disorders [1]. Secondary amenorrhea is a state in which menstruation is paused for ≥3 months, and when this state is triggered by exercise, it is called 'exercise-associated amenorrhea,' in which estrogen levels remain low. Because estrogen is also involved in bone metabolism, a reduction in estrogen leads to a decrease in BMD. The bone mass of humans peaks around 20 years of age, and thus individuals in their late teen years with menstrual disorders may not experience the necessary increase in bone mass. A sub-optimal bone mass may result in an increased likelihood of fatigue fractures, particularly in female athletes. Indeed, among female athletes who develop fatigue fractures, menstrual disorders such as secondary amenorrhea are frequently observed [2]. These problems are likely to occur in high school students and may affect the students' future bone health [3-5].

Thyroid hormones activate metabolism and coordinate activities of the body. Hypothyroidism can thus lead to a decrease in female athletes' performance;

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moreover, hypothyroidism is also involved in amenorrhea (low levels of estrogen) and decreased BMD [6-8]. Only a few studies have focused on the thyroid function of female athletes. The synthesis of thyroid hormones requires nutrients such as fat, proteins, B Vitamins, iron, iodine, selenium, and n-3-based fatty acids [9]. Research on the thyroid function of female athletes is thus nutritionally important.

We conducted the present study to clarify the state of thyroid function in female high school long-distance runners, and we evaluated the associations between thyroid function and nutritious status, menstrual condition, body composition, and BMD.

Subjects and methods

Study design. A case series study of female high school long-distance runners was conducted. We revealed their states of thyroid function and evaluated the associations among nutritious status, menstrual condition, body composition, and BMD.

Subjects. The subjects were female long-distance runners belonging to the top class long-distance relay team of a high school in Japan.

We conducted physical measurements and collected fasting blood samples and urine samples from 16 female high school long-distance runners between July 2016 and July 2017. All subjects were eating a similar diet at a boarding school, and a survey of their diet was conducted for 3 consecutive days during training.

Measurement items/methods. The physical measurements included body height, body weight, abdominal circumference, and hip circumference, after which each subject's body mass index (BMI = weight (kg)/height $(m)^2$) was calculated. We used the dual-energy X-ray absorptiometry method for the calculations of the subjects' body fat percentage, amount of fat, muscle mass, and BMD.

The self-reported nutrition and dietary survey calculated the energy and nutrients according to the Japan's National Health and Nutrition Survey, based on the menu provided at the subjects' dorm for the 3 consecutive days. By taking digital photographs of the front and back of each subject's nutrition and dietary survey, we obtained the exact amount of supplementary food and meal intake of one person. From results of the dietary survey, the subjects were divided into a group that ingested nutritionally enriched foods and supplements and a group that did not ingest them.

In order to calculate the amount of energy required for the subject, physical activity level, which is an indicator of the amount of activity, was measured. Physical activity level was calculated from the amount of activity calculated using during the day. It complies with the Ministry of Health, Labor and Welfare's "Physical Activity Standards for Promotion of Health".

The bone metabolism markers, type I collagen cross-linked N-telopeptide (NTx) levels, in serum and urine (with creatinine correction) were measured.

The blood sample examination measured the complete blood count (CBC), aspartate transaminase (AST), alanine aminotransferase (ALT), γ-glutamyl transpeptidase (γ-GTP), cholinesterase (CHE).

Thyroid function was evaluated by measurement of thyroid stimulating hormone (TSH), thyroid hormone free triiodothyronine (T3), free thyroxine (T4) <http://www.japanthyroid.jp/doctor/guideline/japanese.html> (accessed Dec, 2018).

Regarding menstrual conditions, we measured serum estradiol and interviewed about menstruation.

Ethical consideration. We explained the purpose of this study, the protection of personal information, the method of preserving data, the burden of study cooperation, *etc.* to the responsible person, subjects and their parents orally and by a document. We obtained the written consent from each subject and her parent. This study was conducted after the approval of Ethic Committee, Department of Nursing, Okayama University Graduate School of Health Sciences (Ethics Committee Approval Number T15-01).

Statistical analyses. The statistical analyses were performed using SPSS ver. 25 software (IBM, Tokyo), with the significance level set to $p < 0.05$. Statistical significance was determined by the Mann-Whitney *U*-test. Pearson's correlation coefficient was used to measure the associations between parameters.

Results

Physical condition. The subjects were 15.7 ± 0.8 years old (mean ± standard deviation [SD]; range 15-17 years old), with body height 156.6 ± 6.3 cm (148.8-166.2) cm, body weight 43.4 ± 5.0 kg (range 35.9-52.1) kg. Their BMI values were 17.7 ± 1.5 (range 15.0-20.8), and 81.3% of the subjects were underweight (*i.e.*, a BMI < 18.5). The subjects' body weight was positively correlated with both their BMD values and the muscle mass of the entire body ($r = 0.691$, $r = 0.885$, respectively, $p < 0.05$).

Diet survey. The subjects' energy intake was 2,340 ± 454 kcal (range 1,553-3,176 kcal). Nutrients other than vitamin D (5.6 ± 2.4 μg) and B1 (1.1 ± 0.8 mg) were above the standard values (Dietary Reference Intakes for Japanese, 2015) when viewed as averages (Table 1). The intake of iodine, a nutrient related to thyroid function, was 2,955 ± 1,514 μg (range 1,253-4,266 μg), with all 16 subjects ingesting more than the recommended amount (mean, 21.1-fold higher). The main sources of iodine were kelp and seaweed.

The subjects' intake of vitamin A was 2,325 ± 688 μgRAE (Retinol activity equivalents) (range 1,696-3,810 μgRAE), and all of the subjects ingested more than the recommended amount (mean, 3.6-fold higher). All of the subjects whose iodine levels exceeded the tolerable upper limit were taking nutrition-enhanced foods and supplements. There was no significant difference in the physical measurements or body composition between the group with the intake of nutrition-enhanced foods and supplements ('intake group,' $n = 7$) and the non-intake group ($n = 9$). The levels of energy, protein, fat, carbohydrate, calcium, iron, vitamin D, vitamin B2, vitamin C, dietary fiber, sodium chloride equivalent, iodine, and n-3 based fatty acids were significantly higher in the intake group than in the non-intake group (Table 1). There was also a negative correlation between vitamin D intake and the general body fat percentage ($r = -0.517$, $p < 0.05$).

Physical activity level. The runners' average physical activity level was as high as 2.57, assuming a basal metabolic rate of 1. The required amount of energy calculated from the physical activity level was 2,865 ± 357 kcal, but the amount of energy actually ingested was 2,340 ± 454 kcal, indicating a significantly lower intake ($p < 0.01$).

Examination of the subjects' bones. The BMD of the subjects' lumbar vertebra was 0.89 ± 0.09 g/cm^2, which was 88.2 ± 8.9% (range 77.3-101.0%) of the young adult mean (Table 2). A marker for bone destruction, serum NT_X, was ≥ 16.5 (indicating a high risk of fracture) in 10 (62.5%) of the subjects, and the urinary NT_X (with creatinine correction) was ≥ 54.3 in 13 (81.3%) of the subjects (Table 2). The urinary NT_X value negatively correlated with both the systemic bone mass and the systemic muscle mass ($r = -0.713$, $r = -0.566$, respectively, $p < 0.05$). Serum NT_X was negatively correlated with both the intake of selenium and the intake of n-3-based fatty acids, ($r = -0.506$, $r = -0.569$, respectively, $p < 0.05$).

Blood results. Abnormal values were observed in 2 (12.5%) of the subjects for hemoglobin (≤ 12.0), 9 subjects (56.3%) for AST (≥ 30), 4 subjects (25.0%) for ALT (≥ 30), 1 subject (6.3%) for γ-GTP (≥ 50), 1 sub-

Table 1 Ingestion of energy and nutrients

		Overall		Dietary Reference Intakes for Japanese (2015)			Intake group (n = 7)	Non-intake group (n = 9)	*P* value
Energy	(kcal)	2,340 ± 454	[1,553–3,176]	2,550		EER	2,734 ± 299	2,033 ± 278	0.001
Protein	(g)	100.8 ± 23	[69.9–141.7]	55		RDA	120.6 ± 16.3	85.4 ± 13.6	0.001
Fat	(g)	72.3 ± 18.8	[44.7–106.6]	20–30		DG	89.1 ± 10.8	59.3 ± 11.7	0.001
Carbohydrates	(g)	318.4 ± 65.8	[192.6–419.1]	50–65		DG	362.5 ± 52.1	284.1 ± 55.2	0.012
Calcium	(mg)	917 ± 217	[594–1,382]	650		DG (2,500 : UL)	1,058 ± 236	807.6 ± 124.7	0.033
Iron	(mg)	12.6 ± 4.2	[5.2–20.4]	10.5		RDA (40 : UL)	15.1 ± 4.3	10.7 ± 3.1	0.030
Vitamin A	(μgRAE)	2,325 ± 688	[1,696–3,810]	650		RDA (2,600 : UL)	2,444 ± 612	2,232 ± 764	ns
Vitamin D	(μg)	5.6 ± 2.4	[1.6–12.5]	6.0		RDA (90 : UL)	7.1 ± 2.6	4.4 ± 1.5	0.024
Vitamin B1	(mg)	1.1 ± 0.8	[0.6–4]	1.2		RDA	1.6 ± 1.1	0.8 ± 0.2	ns
Vitamin B2	(mg)	1.8 ± 0.8	[0.9–4.3]	1.4		RDA	2.4 ± 1	1.3 ± 0.3	0.028
Vitamin C	(mg)	126 ± 53	[58.3–299.3]	100		RDA	157.6 ± 62.9	101.3 ± 27.1	0.029
Dietary fiber	(g)	22.6 ± 8.7	[10.5–43.1]	17	<	DG	30.4 ± 6.9	16.6 ± 3.5	0.001
Salt	(g)	10.4 ± 2.7	[6.2–16.8]	7	>	DG	12.1 ± 2.6	9.1 ± 2	0.021
Iodine	(μg)	2,955 ± 1,514	[1,253–4,266]	140		RDA (2,000 : UL)	3,796 ± 1,007	2,301 ± 1,562	0.046
Selenium	(μg)	91.4 ± 28	[43–142]	25		RDA (350 : UL)	107 ± 22	79 ± 27	ns
N-3 based fatty acids	(g)	2.9 ± 1.2	[0–4.7]				3.7 ± 0.6	2.3 ± 1.2	0.012

mean ± S.D. [range] RAE, Retinol activity equivalents; *, Dietary reference intakes for Japanese (2015 edition) were used.
EER, estimated energy requirement; RDA, recommended dietary allowance; AI, adequate intake; DG, tentative dietary goal for preventing life-style related diseases; UL, tolerable upper intake level.

Table 2 Bone density and bone markers

Bone density		
Right arm (g/cm^2)	0.6 ± 0	[0.6–0.7]
Left arm (g/cm^2)	0.6 ± 0	[0.5–0.7]
Right leg (g/cm^2)	1.1 ± 0.1	[0.9–1.2]
Left leg (g/cm^2)	1.1 ± 0.1	[0.9–1.2]
Right ribs (g/cm^2)	0.6 ± 0.1	[0.5–0.6]
Left ribs (g/cm^2)	0.6 ± 0	[0.5–0.6]
Upper vertebral column (g/cm^2)	0.7 ± 0.1	[0.5–0.8]
Lower vertebral column (g/cm^2)	0.9 ± 0.1	[0.7–1.1]
Pelvis (g/cm^2)	1 ± 0.1	[0.8–1.2]
Body trunk (g/cm^2)	0.8 ± 0.1	[0.6–0.8]
Head (g/cm^2)	1.8 ± 0.2	[1.3–2.0]
Whole body (g/cm^2)	1 ± 0.1	[0.8–1.1]
Lumbar vertebra (g/cm^2)	0.9 ± 0.1	[0.7–1.0]
Serum NT_X (nmolBCE/L)		
Fracture risk 16.5 62.5%	20.8 ± 10.9	[9.3–30.8]
Reduction in bone mass 13.6 45.5%		
Urinary NTx concentration (nmolBCE/L)	1,601.8 ± 2,057	[325–3350]
Urinary NT_X (with creatinine correction) (ng/mL)		
Fracture risk 54.3 81.3%	106.6 ± 88.7	[27.715–378]
Reduction in bone mass 35.3		

mean±S.D. [range]

Table 3 Biochemical examination

				Reference value※1	Rate of abnormal data
Red blood cells	count/μL	416.1 ± 32.2	[31.4–363]	474	
Hemoglobin	g/dL	12.8 ± 0.8	[10.8–13.7]	12.1 or more	12.50%
Hematocrit	%	38.4 ± 2.0	[35.7–41.3]	35.5 to 43.9	
AST	IU/L	32.1 ± 7.2	[23–47]	30 or less	56.30%
ALT	IU/L	26.7 ± 11.4	[11–50]	30 or less	25%
γ-GTP	IU/L	23.6 ± 15.6	[12–75]	50 or less	6.30%
ChE	IU/L	248.3 ± 40.9	[172–316]	173 to 432	6.30%
Albumin	g/dL	4.8 ± 0.3	[4.5–5.3]	4 or more	
CRE	mg/dL	0.7 ± 0.1	[0.55–0.83]	0.7 or less	43.80%
Uric acid	mg/dL	4.4 ± 0.7	[2.9–5.9]	2.1 to 7.0	
T-CHO	mg/dL	187.2 ± 33.2	[143–276]	140 to 219	12.50%
TG	mg/dL	69.3 ± 20.3	[41–110]	30 to 149	
HDL-C	mg/dL	77.1 ± 12.9	[61–114]	40 to 119	
Blood glucose	mg/dL	88.9 ± 7.8	[75–108]	99 or less	6.30%
TSH	(μIU/mL)	1.4 ± 0.7	[0.19–2.57]	0.3 to 4.0	6.30%
FT3	(pg/mL)	2.4 ± 0.4	[1.74–3.31]	2.2 to 4.3	31.30%
FT4	(ng/mL)	0.9 ± 0.1	[0.62–1.17]	0.75 to 1.75	6.30%

mean±S.D. [range] ※1 Health Promotion Center in the South of Okayama Prefecture.

ject (6.3%) for ChE (≥ 173), 7 subjects (43.8%) for creatinine (≥ 0.7), 2 subjects (12.5%) for total cholesterol (≥ 219), and 1 subject (6.3%) for fasting blood sugar ≥ 99 (Table 3). AST and ALT were negatively correlated with both the body fat percentage and the amount of fat of the entire body (AST: $r = -0.737$, $r = -0.646$; ALT: $r = -0.729$, $r = -0.622$, respectively, $p < 0.05$).

Thyroid function. The thyroid examinations showed no abnormally high values, but abnormally low values were observed in one of the 16 subjects (6.3%) for TSH (≤ 0.3), five subjects (31.3%) for free T3 (≤ 2.2), and one subject (6.3%) for free T4 (≤ 0.75) (Table 3).

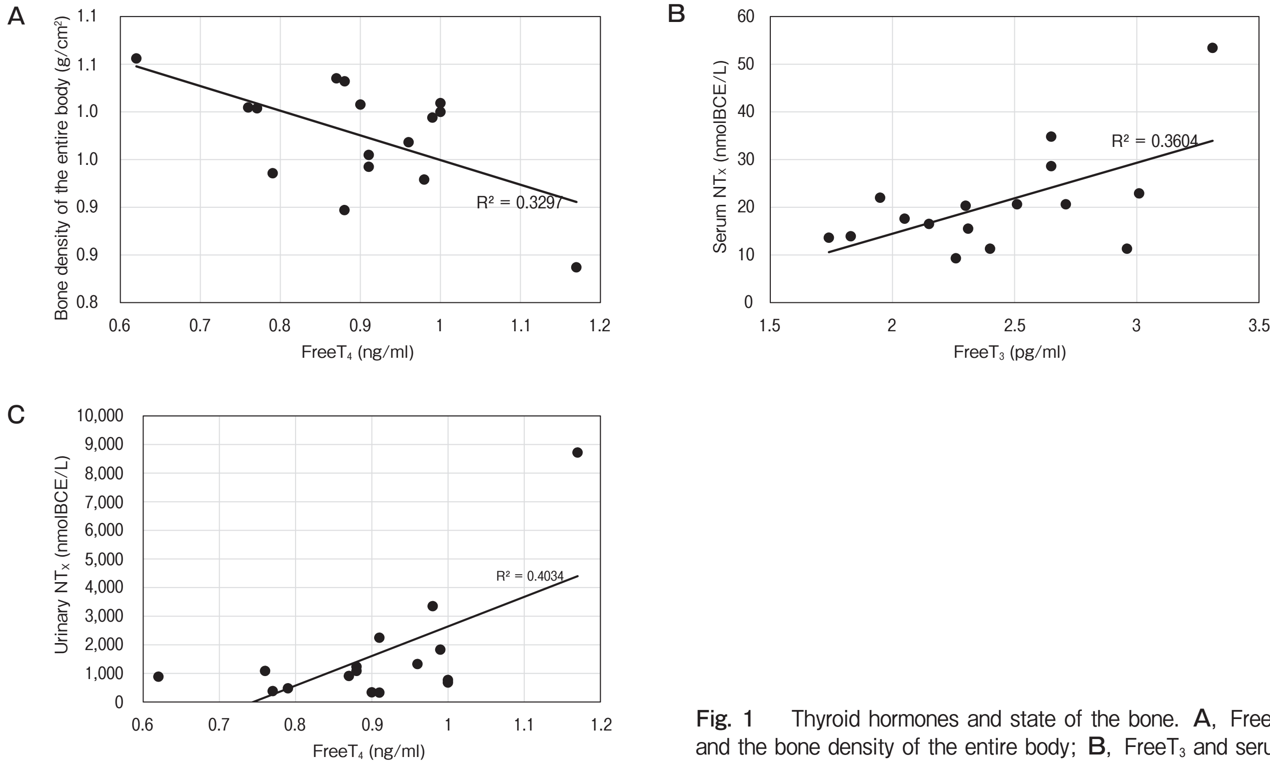

Fig. 1 Thyroid hormones and state of the bone. **A**, $FreeT_4$ and the bone density of the entire body; **B**, $FreeT_3$ and serum NT_X; **C**, $FreeT_4$ and urinary NT_X.

There was no correlation between the subjects' thyroid function and physical activity level. Free T4 was negatively correlated with bone density of the whole body (Fig. 1A). Free T3 showed a positive correlation with serum NT_X (Fig. 1B). Free T4 showed a positive correlation with urinary NT_X (Fig. 1C). Free T3 was negatively correlated with the intakes of protein ($r = -0.511$), lipids ($r = -0.516$), vitamin D ($r = -0.601$), dietary fiber ($r = -0.557$), iodine ($r = -0.563$), and n-3 based fatty acids ($r = -0.719$), all $p < 0.05$.

Menses and estradiol values. All 16 of the high school long-distance runner subjects suffered from secondary amenorrhea. The estradiol value was low at 18.6 ± 34.4 pg/mL (range 1-143.6 pg/mL), with 87.5% subjects at < 21 pg/mL. Estradiol was negatively correlated with both the intake of fat and the intake of n-3 based fatty acids ($r = -0.520$, $r = -0.549$, respectively, $p < 0.05$).

Discussion

The results of our analyses demonstrated that a large proportion of the female high-school long-distance runners in this study were thin, amenorrheic and had low bone density, which is consistent with the findings of a past study [10].

In our study, female high-school long-distance runners were able to intake the necessary nutrients other than energy by ingesting three meals a day. Although young female athletes may believe that they need more nutrients than normal, only a few of them understand proper nutrition [11] and they tend to rely on supplements [12]. Some athletes ingest nutrition-enhanced foods and supplements, leading to excessive intakes of vitamin A, iodine, *etc*., which are nutrients related to thyroid function.

It has been suggested that an excessive accumulation of vitamin A can result in complications such as liver damage [13, 14]. Since our subjects consciously ingested kelp (which is a common food product in Japan, in the form of dried seaweed and other forms), their iodine intake exceeded that of the general Japanese population. There was a negative correlation between our subjects' iodine intake and fT3 ($r = -0.563$). There was no correlation between their iodine intake and fT4 ($r = 0.095$) and TSH ($r = 0.354$) levels. The relationship between an excessive intake of iodine and hypothyroidism is not clear. A continuous overdose of iodine from nutritionally enriched foods and supplements may cause a suppression of thyroid function, but this effect is transient [16]. It is thus likely that effect of an excess intake of iodine on thyroid function is small. Because we observed correlations between some nutrients and thyroid hormone, further investigation is necessary.

In our subjects, the free T3 value was decreased, but the TSH level was not increased. In anorexia nervosa, the TSH value is normal even if free T3 is low, and it is clear that these female long-distance athletes were in the same state as anorexia nervosa. The peripheral transformation to free T3 is known to be impaired at the time of chronic hunger [16, 17]. A female long-distance runners who is slender may similarly have a decline in thyroid function. It was reported that endocrine abnormalities in women with anorexia nervosa decrease their thyroid hormones and cause severe bone loss [18]. Similar endocrine abnormalities and bone loss were observed in the present female high school long-distance runners. However, the physical load and dietary intake of nutrients can be completely different between female high school long-distance runners and adult women with anorexia nervosa. Particularly when the decline in endocrine function is remarkable, it may adversely affect the athlete's competitive performance; its measurement is thus advisable.

In order to properly increase the body's muscle mass, it is necessary to increase the body's energy intake [19]. We observed that the energy intake of female high school long-distance runners was lower than the required amount calculated based on their physical activity level. Among female long-distance runners and gymnasts, it is believed that limited energy intake tends to increase menstrual disorders [20]. All 16 of our present subjects had menstrual disorders. Their BMD values were also reduced, and their NT_X (serum, urine) values corresponded to the levels observed in postmenopausal women, suggesting a high risk of fracture. The bone mineral density was low in our subjects with low vitamin D intake. It has been suggested that the intake of vitamin D, a nutrient involved in calcium absorption to the bone, is related to body composition, particularly the amount of body fat [21]. The intake of vitamin D increases the body's muscle mass and lowers the body fat percentage [22], and a similar tendency was observed in the present study. Several clinical trials have reported that the ingestion of vitamin D ($\geq$17.5 μg) resulted in the prevention of fractures in the vicinity of the femur [23, 24]. Thus, the ingestion of vitamin D may be effective in increasing bone density in female long-distance runners as well.

Our analyses revealed that the subjects' thyroid hormone free T4 was negatively correlated with their systemic BMD. Their free T3 was positively correlated with their serum NTx, and free T4 was positively correlated with urinary NTx. These data indicated that thyroid function is related to bone metabolism and mineral density. In order to maintain thyroid function and prevent fractures, nutritionists should recommend the proper intake of nutrients such as energy, protein, lipids, vitamin D, *etc.* while paying attention to the potential iodine overdose provided by nutrient-strengthened foods and supplements.

The relationship between thyroid hormones and bone density in female high school long-distance athletes has been elucidated herein. Thyroid function is related to estradiol and physique [25]. Although we assume that maintaining proper weight is essential for proper thyroid function and preventing bone fractures, further studies of the thyroid function of female high school long-distance athletes are merited.

In conclusion, in female high school long-distance runners, thyroid hormone was associated with bone mineral density and nutritional intake. In order to improve the menstruation abnormalities that frequently occur in female athletes, and to increase these athletes' bone density, and to maintain their thyroid function, the athletes' optimal body weight should be maintained by proper nutrient intake.

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