Increased Vertebral Bone Mineral in Response to Reduced Exercise in Amenorrheic Runners

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Seven female runners found to have exercise-induced amenorrhea and decreased bone mineral were reevaluated after 15 months. During the 15-month period, four runners took supplemental calcium and reduced their weekly running distance by 43%, resulting in an average 5% increase in body weight, increased estradiol levels and eumenorrhea. Bone mineral content increased from 1.003 ± 0.097 to 1.070 ± 0.089 grams per cm.[2] Three runners continued to have amenorrhea, with no change in running distance or body weight. Estradiol levels remained abnormally low and there was no significant change in the bone mineral content, although all three took supplemental calcium. We found that early osteopenia associated with exercise-induced menstrual dysfunction improved when runners reduced their running distance, gained weight and became eumenorrheic.

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Exercise-induced amenorrhea has recently received much attention following reports that bone mineral content in the young women with this disorder is reduced to levels seen in postmenopausal women with osteoporosis.[1-3] Suggested causes of exercise-induced osteopenia include distance running, reduced body fat, decreased estradiol levels and increased prolactin levels.[2-6] In a recent study, we postulated that reducing running distance and increasing calcium intake would improve bone density in amenorrheic runners.[1] After 15 months, we reevaluated 7 of the 11 amenorrheic runners in our original study. We present the results of our follow-up.

Subjects and Methods

Seven of the eleven original runners identified as having secondary amenorrhea with osteopenia were available for reevaluation after 15 months. Only seven of the eleven original runners could be found and would agree to restudy. The eleven originally studied were runners who volunteered on the basis that they were running at least 20 miles per week and had amenorrhea for at least one year. Reevaluation consisted of repeat vertebral bone mineral analysis, weight measurements and measurement of estradiol levels. The patients were interviewed twice, at 15 months and at 17 months, regarding changes in calcium intake, weekly running distance and gynecologic history to verify their information.

Random plasma estradiol levels from each runner were measured in frozen specimens obtained on initial evaluation during amenorrhea and at 15 months' follow-up either during continuous amenorrhea or during the normal cycle. An estradiol level was determined by a radioimmunoassay (Diagnostic Products, Los Angeles) with a sensitivity of 7 pg per ml and a within-assay coefficient of variability of 10%. Spinal bone mineral measurements were made using a dual photon absorptiometer (Model DP 3, Lunar Radiation Corporation, Madison, Wis) and a gadolinium 153 radiation source with a better than 2% short-term measurement precision (reproducibility). Short-term precision has been measured on the same instrument used for this study as between 1.3% and 1.9% in three persons with normal, low normal and reduced spine mineral content. High-precision measurement is accomplished by carefully positioning subjects, remeasuring the same lumbar segments, using a computer-based edge finder

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for automatic determination of bone edges and by measuring several segments, the first through the fourth lumbar segments in this instance. Our precision data are supported by published reports on the method using a variety of instruments.[7-9]

Subject 1

This 33-year-old woman had amenorrhea for ten years, five years after beginning a program of running 160 km per week. On reevaluation, she has been eumenorrheic for six months, starting two months after decreasing her running distance by 48 km per week. She had a 4.5-kg weight gain and a 6.5% increase in vertebral bone mineral (Figure 1).

Subject 2

This 31-year-old woman had amenorrhea for 3 years, 1½ years after beginning a program of running 32 km per week and aerobic dancing four times per week. On reevaluation, she has been eumenorrheic for four months after discontinuing her running program but continuing aerobic dancing. During this period, she has had no stress fractures, compared with two per year previously. She has had a 3-kg weight gain and an 11% increase in vertebral bone mineral content.

Subject 3

This 26-year-old woman had amenorrhea for three years after beginning a program of running 64 km per week, swimming 8 km per week and cycling 67 km per week. On reevaluation, she has been eumenorrheic for six months, beginning two months after discontinuing her running but continuing her swimming and cycling. She has had no stress fractures, compared with two per year previously. She has had a 2-kg weight gain and a 5.5% increase in vertebral bone mineral content.

Subject 4

This 32-year-old woman had amenorrhea for eight years after beginning a program of running 72 km per week. On reevaluation, she has been eumenorrheic for six months, starting five months after she decreased her running distance by 24 km per week. She has had no stress fractures, compared with two per year previously. She has had a 1.5-kg weight gain and a 3.3% increase in vertebral bone mineral content.

Subject 5

This 38-year-old woman has had amenorrhea for four years, two years after starting a program of running 40 km per week. On reevaluation, she has continued the same exercise program and continues to have amenorrhea. A repeat measurement of her vertebral bone mineral content shows a 2% increase, and her weight has further decreased by 0.3 kg.

Subject 6

This 28-year-old woman had oligomenorrhea for 8 years and amenorrhea for 1½ years, 1 year after beginning a program of running 72 km per week and sustaining a 5-kg weight loss. She has no change in body weight, and she continues to have amenorrhea. A repeat vertebral bone mineral measurement showed a 2.3% decrease.

Subject 7

This 32-year-old woman has had amenorrhea for four years, two years after beginning a program of running 38 km per week. On reevaluation, she continues to run 38 km per week. Her weight has further decreased by 3 kg, and she continues to have amenorrhea. A repeat vertebral bone mineral determination showed a 3.5% decrease.

Results

All seven runners are white women who, on initial evaluation 15 months previously, had amenorrhea and were found by vertebral bone mineral analysis to have L-1 to L-4 bone mineral content below the normal range. During the interim period, all seven runners remained physically active and all were taking calcium supplementation (Table 1). The four runners (subjects 1 to 4) who reduced their weekly running distance increased their body weight by at least 3%, became eumenorrheic, had increased estradiol levels to within the normal range (45 to 400 pg per ml) and showed increased bone mineral content, changing as a group from 1.003 ± 0.097 to 1.070 ± 0.089 grams per cm^2 ($\overline{X} \pm$ standard deviation). In these four runners, the frequency of stress fractures was reduced. The three runners (5 to 7) who did not reduce their weekly running distance had no increase in body weight, continued to have amenorrhea with abnormally low estradiol levels and showed no significant improvement in bone mineral content.

The overall change in bone mineral in both groups, as determined by vertebral bone mineral analysis, was positively correlated with the change in body weight ($N = 7$, $r = +0.88$, $P < .005$) (Figure 2). The increase in bone density in the runners who reduced their running distances was significantly greater by *t* test ($P < .02$) compared with the runners who did not reduce exercise.

Exercise has been believed to be important in preventing bone mineral loss.[10,11] The total body calcium level is re-

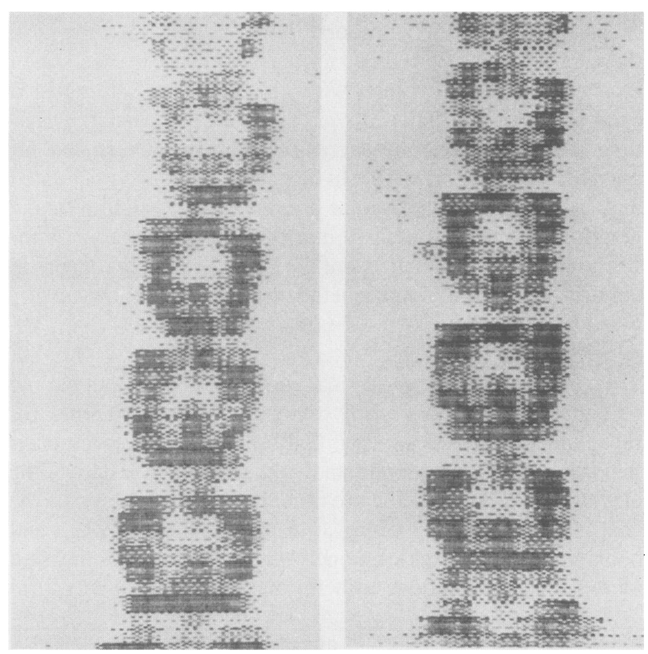

Figure 1.—Transmission gadolinium 153 scans of subject 1, before (on the left) and 15 months after (on the right) exercise modification showing a 6.5% increase in bone density in the lumbar spine. (These transmission scans were printed at the same time from the original data sets and then were photographed on the same negative for optimum comparability.)

TABLE 1.—*Changes in Female Runners During a 15-Month Follow-up*

Subject	Current Menstrual Status*	Height, cm	Weight, kg, Pre/Post	Bone Density, grams/cm², Pre/Post	Weekly Distance Run, km Pre/Post	Other Sports Pre/Post	Estradiol Level, pg/ml Pre/Post†	Calcium Supplement, mg/day
1	E	167.0	60.0/64.5	1.084/1.155	160/112	0/0	17/50	750
2	E	170.2	54.0/57.0	0.879/0.975	32/0	Aerobics/Aerobics	18/349	1,500
3	E	174.0	60.0/62.0	1.076/1.135	64/0	Swim/Swim Cycling/Cycling	48/67	500
4	E	152.4	45.5/47.0	0.976/1.014	72/48	0/0	UD/80	350
5	A	165.1	47.3/47.0	0.900/0.925	40/40	0/0	UD/UD	1,500
6	A	162.6	51.0/51.0	0.915/0.894	72/72	0/0	10/42	900
7	A	165.1	53.0/50.0	0.868/0.838	38/38	0/0	45/9	1,500

*E=eumenorrheic, A=amenorrheic.
†UD=undetectable, less than 7 pg/ml.

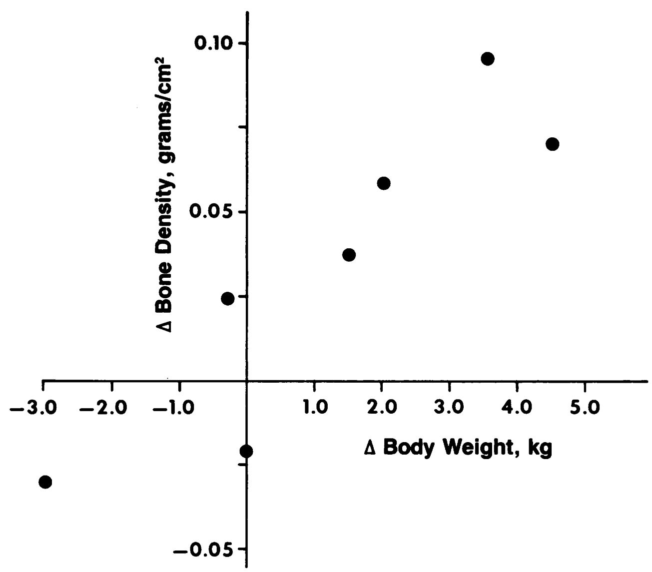

Figure 2.—Relationship of change in body weight to change in bone density over a 15-month period in 7 women with a diagnosis of osteopenia due to exercise-induced amenorrhea.

ported to be 11% higher in male marathon runners than in nonrunners.[12] Physically active women have been noted to have bone mineral values higher than sedentary controls as determined by cortical bone measurements in the radius.[13] Recent work, however, suggests that runners with amenorrhea may show a mineral loss in trabecular bone in the absence of a significant change in cortical bone mineral levels.[1,2]

A variety of factors are suggested to be involved in the loss of bone mineral with exercise-induced amenorrhea. Cann and Genant found spinal trabecular mass determined by quantitative computed tomography to be reduced by 25% to 30% in physically active, amenorrheic women and postulated that this condition was caused by the low plasma estradiol levels observed in ten patients.[3] Linnell and co-workers in their study of ten amenorrheic runners found reduced body fat to be the most important factor in reducing bone mineral.[4] Drinkwater and associates found the distance run and low estradiol levels to be the significant factors associated with decreased bone mineral content in runners with amenorrhea.[2] Dietary factors, specifically a calcium intake of less than 1,000 mg per day, may also contribute to the development of osteopenia in these athletes.[14]

Though the suggested causes of reduced bone mineral content appear interrelated, a single factor has yet to be identified. In light of these findings, we advised the amenorrheic runners in the present study to take calcium supplementation of 1,500 mg per day and to reduce their weekly running distance by 16 to 32 km. Similar recommendations have since been proposed by Marcus and colleagues[15] and supported by Heath.[16]

Fifteen months later, four runners had reduced their running distance, yet remained physically active. These runners took 350 to 1,500 mg of calcium supplement per day. When they were reevaluated, their bone density had increased by 6.6% (range 3.3% to 11.0%), an average increase of more than three times the precision of the measurement.

The alterations in bone density in the present study correlate with the changes in body weight. The runners whose body weights increased by more than 3% also had increased bone densities. The relationship between these two variables is not clear, but both may be associated with changes in running distance or menstrual function. Though not conclusive as to the cause of decreased bone mineral, our findings show that an increase in body weight in amenorrheic runners with osteopenia correlated with an increase in mineral content.

Many healthy-appearing female athletes present to physicians with histories of long periods of amenorrhea. In the past, this amenorrhea has been thought to be benign, its main complication being infertility. It is now apparent that the consequences of long-term exercise-induced amenorrhea may also include early osteopenia and an increased frequency of stress fractures. We found that our patients who decreased their running distance subsequently increased body weight, reestablished a normal menstrual cycle, reduced the frequency of stress fractures and had increased bone mineral content.

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Medical Practice Question

EDITOR'S NOTE: *From time to time medical practice questions from organizations with a legitimate interest in the information are referred to the Scientific Board by the Quality Care Review Commission of the California Medical Association. The opinions offered are based on training, experience and literature reviewed by specialists. These opinions are, however, informational only and should not be interpreted as directives, instructions or policy statements.*

Hospital Admission Following Rigid Esophagoscopy

QUESTIONS:

When should rigid esophagoscopy be used?

When is it medically necessary for patients who undergo rigid esophagoscopy to remain in hospital overnight?

If it is not necessary for all such patients to stay in hospital overnight, are there criteria that would identify patients who should receive this level of observation?

OPINION:

In the opinion of the Scientific Advisory Panel on Otolaryngology/Head and Neck Surgery, rigid esophagoscopy is considered established practice for the diagnosis of esophageal neoplasms, strictures and burns as well as inflammatory, metabolic, congenital, traumatic and neoplastic diseases. It is preferred by clinicians for the removal of foreign bodies, dilatation of esophageal strictures and retrieval of biopsy specimens from esophageal lesions. Rigid esophagoscopy is also standard practice for the evaluation of patients with cancer in the upper respiratory tract.

Hospital admission to observe a patient overnight following this procedure should be determined by the endoscopist based on the patient's physical condition and the likelihood of postoperative complications. Among the indications that support the medical necessity of hospital admission are the following: actual or suspected perforation of the esophagus, any unexplained tachycardia, fever, throat or chest pain, the presence of air in the soft tissues of the neck or mediastinum, evidence of general medical instability and when there is no responsible person to assist the patient should it be necessary to return to the hospital. Because the risk of perforating a patient's esophagus is high in first-time dilatation of strictures, after the removal of any foreign body and with any deep biopsy or manipulation of an esophageal tumor, it is established practice to admit these patients to hospital for 24 hours observation. For some patients who have had an uncomplicated diagnostic esophagoscopy that showed no lesions, caused no bleeding, collected no biopsy specimens or involved no other uses of the instrument, some physicians feel it is reasonable to discharge them the day of the procedure following several hours of observation.