[Primary Care]

Bone Health: Part 2, Physical Activity

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Mechanical loading is a crucial factor for maintaining skeletal health. Physical activities, exercise, and sports provide a wealth and variety of mechanical loads to bones, through muscle forces, ground reaction forces, and other contact or impact forces. Weightbearing activities can be effective exercises to enhance bone health—particularly, those that involve jumping and impact loads (with greater strain magnitudes, rates, and frequencies). Physical activity appears to be acutely beneficial for enhancing bone health in the early pubertal period and in older age, such as in postmenopausal women. In preparing this article, PubMed, Web of Science, and relevant edited books (English language) were reviewed from 1961 to present.

Keywords: bone health; physical activity; mechanical loading

Bone is dynamic, and it is influenced by genetic, intrinsic, and environmental factors. In particular, mechanical loading—as generated during physical activity and exercise or diminished because of inactivity or weightlessness—can have a potent effect on bone homeostasis. Physical activity transmits mechanical loads to the skeleton that are vital for maintaining or enhancing bone strength. The skeleton's sensitivity to mechanical loads depends on multiple factors, including age, sex, and menarcheal status.[4,6,32] The mode of physical activity determines the mechanical environment, and mechanical parameters such as strain rate,[33,66] strain magnitude,[12,56] and strain frequency[50,52,55] have been associated with increases in bone formation that lead to changes in bone structure and so influence bone strength.

The structural and metabolic demands on bone are linked to the ability of bone to functionally adapt to its surrounding physical environment. Cortical and trabecular tissues are strategically arranged to accommodate stress demands (ie, force/area) and strain demands (ie, deformation with respect to original shape) imposed on the skeleton by muscular and ground reaction forces during weightbearing activities. Microscopically, bone cells—and the signaling pathways that control these cells—initiate adaptation in response to physical stimuli, promoting a structure that minimizes metabolic demand while maximizing bone strength.[12] This implies that increases in bone strength attributed to mechanical stimuli are not solely due to an increase in the amount of bone added but to improvements in the quality of the tissue and its architecture.

This review focuses on the role of physical activity on skeletal tissue in athletic and physically active populations. We include human and animal studies to emphasize mechanical factors, activities, and sports and how they promote healthy bone growth and prevent bone loss.

Here, we review key mechanical parameters associated with adaptation of the skeleton to exercise: strain magnitude, strain rate, and strain frequency. A majority of the earlier studies in this area were conducted using animal models in which one mechanical parameter was manipulated to determine the effects of physical loading on the skeleton. Loading regimes applied in animal models differ from loading patterns experienced by humans while exercising; that is, loads are often applied to the animals exogenously while the animal is under anesthetic, and they may be applied at supraphysiological strain magnitudes. In addition, many studies use rodents. Unlike humans, rodents do not normally experience secondary remodeling in cortical bone[2]; they experience longitudinal growth for a greater proportion of their lifespan than that of humans.[40] Human studies have corroborated many of the findings from animal studies, however, and have applied this knowledge to develop physical (ie, exercise) interventions to accumulate and maintain bone mass. We describe the effects of these mechanical factors and exercise on bone health, which is collectively determined by bone mass, structure, quality, and rate of turnover. Bone mass, or bone mineral content (BMC), is typically assessed in humans using dual-energy X-ray absorptiometry. Bone mineral density (BMD), when assessed by the same technology, is reported as

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No potential conflict of interest declared.
DOI: 10.1177/1941738109338823
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a 2-dimensional quantity termed *areal bone mineral density* (aBMD), and measured in g/cm^2. Areal BMD represents a combination of properties, including bone mass and material properties. Volumetric BMD, measured in g/cm^3, is assessed with quantitative computed tomography.

STRAIN MAGNITUDE

Peak strain magnitudes measured in diverse vertebrates are remarkably similar, ranging in amplitude from 2000 to 3500 με (0.20% to 0.35% strain), suggesting that skeletal morphology is adjusted such that functional load-bearing elicits a specific and potentially beneficial level of strain to the bone tissue.[53,54] Rubin and Lanyon[56] found that in functionally isolated turkey ulnae, as strain magnitude was increased from 1000 to 4000 με, change in bone mass increased in a linear fashion (r = 0.83), suggesting that bone adaptation was roughly proportional to the magnitude of strain induced during loading. Furthermore, strain magnitudes below 500 με were associated with 10% to 15% bone loss after 8 weeks, increased remodeling activity, increased endosteal resorption, and increased intracortical porosity.[56] Whereas more complex models have been proposed to explain bone adaptation—and have been validated to some extent[5,59]—bone is similar to other musculoskeletal tissues where reasonable increases in function lead to tissue hypertrophy and where decreases in function lead to tissue atrophy.[65]

For humans, tennis players provide a useful model to understand the effects of mechanical loading on bone, because the nondominant (ie, nonplaying) arm can be used as an internal control. Large side-to-side differences have been reported in BMC and aBMD between the dominant and nondominant humerus and radius of high-caliber tennis players (eg, 17% greater BMC in the dominant humeral shaft of experienced tennis players).[17,24] Similar trends have been reported between dominant and nondominant arms of nontennis players, although the differences were smaller in magnitude. Such differences are attributed to site-specific geometric adaptations rather than increases in volumetric BMD.[18]

Similarly, a 3-year longitudinal study showed that female gymnasts, compared with normally active controls, had consistently greater total body BMC, from prepubertal to postpubertal stages.[48] The large increases in BMC and aBMD observed in gymnasts have been attributed to the substantial strain magnitudes and rates experienced by these athletes during training.[63] Likewise, nonelite ballet dancers had significantly greater prepubertal BMC than that of controls.[43] Similar results have been reported for other sports involving large strain magnitudes—for example, competitive rope skippers had significantly higher total body aBMD versus athletes who experienced smaller strain magnitudes, such as soccer players.[49]

Most evidence suggests that repetitive nonweightbearing activities have minimal benefit to bone.[8,45] Bone has a lazy zone in which certain modes of exercise or loading, such as cycling or swimming, may not elicit strain effects large enough to promote adaptive osteogenesis.[8] A recent study comparing the aBMD of runners, swimmers, cyclists, and triathletes found that long-distance runners had the greatest aBMD of all 4 groups and that swimmers, despite extensive training (about 15 hours per week) in nonweightbearing environments (ie, pool), had aBMD no different from that of nonathletic controls in upper body and lower body sites.[8] In contrast, a recent peripheral quantitative computed tomography study compared several types of sports and found that the polar section modulus (a geometric factor associated with bone strength) of the humeral midshaft was similar between swimmers and athletes of impact-loading sports such as volleyball and racquet sports.[46] This finding suggested that in addition to large ground reaction forces produced from weightbearing activities, large magnitude forces can be produced via muscular contraction that can significantly alter bone geometry and quality.

STRAIN RATE

To discern the effects of strain rate on adaptive osteogenesis, Turner and colleagues applied bending loads, equal in peak strain magnitude and frequency but varying in strain rate, to adult rat tibiae for 2 weeks.[66] Bone formation was significantly increased in the 2 experimental groups with the highest strain rates, and the amount of new bone formation was directly proportional to the rate of strain in the bone tissue.[66] LaMothe and colleagues[33] substantiated those results using skeletally mature female mice exposed to cantilever bending, with similar peak magnitude and frequency but varied strain rate. After 4 weeks of loading, periosteal mineral apposition rate, mineralizing surface, and bone formation rate were increased in all 3 strain rate groups relative to control tibiae. A monotonic, dose-response relation was observed between applied strain rate and periosteal bone formation rate.

Higher strain rates occurred in jumping activities, rather than running activities, despite similar strain magnitudes.[22,23] In immature male roosters, drop jumps were more effective than treadmill locomotion at stimulating bone formation.[22,23] This finding has been supported by several randomized controlled trials of young and elderly humans.[11,20,68]

Supporting the theory that strain rate, in addition to strain magnitude, is an important osteogenic stimulus, power lifting—using fast, explosive concentric contraction exercises and slow eccentric contraction exercises—was more effective than strength training at improving lumbar spine and hip aBMD of postmenopausal women.[62] However, the participants in this study were involved in a 3-year resistance training program before commencing the power training; thus, the authors were hesitant to generally recommend power loading to the postmenopausal population.

Jumping interventions have also been employed for children.[30] A 16-month randomized controlled trial using a school-based daily jumping program, in addition to 15 minutes of daily classroom physical activity, increased the bone strength index at the distal tibia of prepubertal boys, as assessed with peripheral quantitative computed tomography (775-mg^2/mm^4 increase in intervention, compared with 651-mg^2/mm^4 increase for controls).[36] This jumping intervention took less than

3 minutes of classroom time and used various jumping styles (eg, countermovement jumps and side-to-side jumps) to create unique strain environments.

More extensive interventions have been effective. For example, a 12-minute program, 3 days per week, of diverse weightbearing activities implemented into regular physical education classes resulted in a 4% to 5% greater increase in lumbar spine and femoral neck BMC of prepubertal and early pubertal girls, compared with controls after 2 years.[38] Similarly, prepubertal boys had 4% greater gains in femoral neck BMC.[39] Another school-based exercise program for prepubertal children—requiring 20 minutes per day, 3 days per week for 7 months—elicited significantly greater gains in lumbar spine aBMD (3%) and femoral neck aBMD (5%), compared to controls.[13] These results suggested that less-time-consuming exercise interventions can be employed to increase peak aBMD in children and perhaps maintain aBMD in adult populations.

STRAIN FREQUENCY

Skeletal adaptation is generally considered to be proportional to loading frequency. In cortical bone, Rubin and Lanyon found that a mechanical signal induced at 2000 με and 0.5 Hz maintained bone mass with just 4 cycles per day.[55] By increasing the loading frequency to 3 Hz, bone mass was maintained with 1800 cycles with a peak strain magnitude of 800 με.[50] Only 200 με was necessary to maintain cortical bone mass if applied at 30 Hz,[57] suggesting that the sensitivity of cortical bone to mechanical loads increased quickly with increasing frequency. Possibly more influential to the skeleton than high-magnitude events that occur at low frequencies were extremely small strains (2 orders of magnitude below peak strains) induced at sufficiently high frequencies, such as those generated from muscle activity. As such, the loss of the 20- to 50-Hz spectral content of muscle contraction—subsequent to the loss of fast-twitch muscle fibers with sarcopenia—was suggested as a potential factor in bone loss with age.[21]

Gilsanz and colleagues[14] investigated the application of extremely low-magnitude mechanical signals applied at high frequencies (30 Hz), daily for 12 months, on young women with low trabecular BMD—specifically, its effect on skeletal growth of the axial skeleton (spine) and appendicular skeleton (femur), as well as on the musculature of the spine. After 1 year, as little as 2 minutes per day of this physical intervention incurred significant benefits: 3.9% increase in cancellous bone in the spine, 2.9% increase in cortical bone of the femur, and 7.2% increase in musculature of the spine.[14] Similar results were found in 70 postmenopausal women exposed to low-magnitude, high-frequency signals. After 1 year of treatment, the control group lost 3.3% aBMD in the lumbar spine, compared to an attenuated loss of 0.8% in the experimental group (2.5% benefit of treatment). In addition, the controls lost 2.9% aBMD in the trochanteric region of the femur, whereas the experimental group exhibited a gain of 0.4% (3.5% benefit of treatment).[52]

REST INSERTION

Adaptive osteogenesis saturates quickly in response to mechanical strain.[34] Rubin and Lanyon[55] found that osteogenesis in avian ulnae did not increase as the number of loading cycles per day increased from 36 to 1800 (a 50-fold increase). Similarly, Umemura and colleagues[67] observed that rats trained to jump 100 times per day did not significantly increase their hind limb adaptive responses over rats trained to jump 40 times per day. Consequently, methods to attenuate that saturation response have been investigated. Researchers have found the insertion of rest periods within loading regimes can circumvent adaptive response saturation. Robling et al[51] found a significant increase in osteogenesis with the division of a 360-cycle loading regime into discrete bouts. Increases in osteogenesis were positively correlated with the number of discrete bouts introduced. For example, 6 bouts of 60 cycles of loading per day were more osteogenic than 2 bouts of 180 cycles.[51]

Srinivasan and Gross[61] found that the insertion of 10-second rest periods between 1-Hz loading cycles transformed an otherwise mild low-frequency regime into a potent anabolic stimulus for bone growth. LaMothe and Zernicke[34] substantiated those results using skeletally mature female mice randomly assigned to a continuous-loading group or a rest insertion group. Both cohorts received mechanical loading signals of equal strain magnitude (800 με) and frequency (1 Hz) for 100 seconds. The rest-inserted group had loads applied in 1-second pulses, followed by 10-second periods of rest. After 3 weeks, bone formation rate relative to control (ie, contralateral) tibiae was significantly increased in the continuous-loading group (> 88%) and rest-inserted group (> 126%). Loaded tibiae in the rest-inserted group had significantly greater mean periosteal bone formation rate relative to loaded tibiae in the continuous group (>72%), despite a 10-fold decrease in loading cycles.

These results and others support the premise that bone fluid flow affects skeletal adaptation. Studies revealed that bone pore fluid pressure relaxation occurred at approximately 1.5 seconds, suggesting that at high frequencies, not enough time existed for fluid relaxation to take place between loading cycles.[58,60] As such, load-induced fluid flow near osteocytes would be substantially decreased in subsequent cycles beyond the first few load cycles. Periods of rest would diminish that effect, essentially resensitizing bone cells to mechanical stimuli.[34]

To our knowledge, exercise interventions using defined rest periods have not been systematically tested against continuous exercise in humans. However, results from these animal studies have been used to design human trials. For example, Macdonald and colleagues,[36] whose exercise intervention had positive effects on bone strength, asked their human participants to perform 3 bouts of jumping per day, rather than a single continuous jumping session, to prevent the desensitization that has been reported in animal studies.[eg,61]

IMPLICATIONS FOR TYPE OF EXERCISE

The most osteogenic exercise activities appear to be those that have high-strain magnitudes and/or high-strain rates, such as jumping (for the lower body) and racquet sports (for the upper body). Repetitive activities, such as running, may be more osteogenic if continuous movement is separated by short rest bouts (eg, interval training). Although high-frequency, low-magnitude loading appears osteogenic when applied through force platforms, it is unknown whether any specific exercise activities would mimic this pathway. Nevertheless, physical activities incorporating increased muscle activity can be positive and more beneficial to bone health than inactivity.

EXERCISE AND BONE GAIN ACROSS THE LIFESPAN

Not only do different types of exercise have differential effects on the skeleton, but the skeleton appears to be more responsive to exercise at different times across the lifespan.[24] There is also evidence for sex-specific bone responses to exercise.[18,31]

Adolescence

Adolescence is a critical time for bone development. Boys and girls gain approximately 40% of their peak bone mass between the ages of 12 and 16 years.[19,64] In addition, 35% of total body BMC is laid down in the 2 years around peak height velocity.[1] Early puberty may provide a window of opportunity to enhance bone mass and strength.[37] Kannus and colleagues found a significant benefit to BMC in the dominant arms of female racquet sport players who began playing before or at the age of menarche.[24] The researchers have also shown that side-to-side differences of female tennis players become significant only around the age of menarche.[17]

A review of exercise interventions aimed at enhancing bone health found that the majority of trials showed increased improvements in BMC at the conclusion of the study.[20] The type of exercise used varied among studies, but all were weightbearing activities, including aerobics, football, plyometrics, and jumping activities. All studies intervening with early pubertal children showed significant improvements in BMC,[20] and the magnitude of the improvements of early pubertal children, as extrapolated over a 6-month period, was greater than that of prepubertal and pubertal children, ranging from 1.1%[38] to 5.5%,[7] depending on the intervention and site measured. Children in the study with the greatest effect were not randomly assigned to receive an exercise intervention but had been recruited from local sports clubs.[7] Unfortunately, there are few studies of older children (pubertal or postpubertal), and those that have been performed were poorly designed[20]; thus, it is difficult to draw conclusions about the effectiveness of exercise interventions in this maturity group.

Premenopausal Women

Far fewer controlled studies have been conducted with premenopausal women as compared with postmenopausal women. One of 4 meta-analyses of controlled trials conducting exercise interventions with premenopausal women reported a significant treatment effect,[70] whereas the other meta-analyses found no treatment effect.[26,29,69] The smaller magnitude effect in this age group is likely associated with the attainment of peak bone mass around age 20.[16]

Postmenopausal Women

Because of the high prevalence of osteoporosis in postmenopausal women, most exercise interventions have focused on improving aBMD in postmenopausal women. Although there has not been an overwhelming number of studies performed, several meta-analyses of controlled clinical trials have been performed showing varying degrees of exercise effectiveness. In general, aerobic, weightbearing, and resistive exercises can all have positive effects on lumbar spine aBMD.[3,41]

Regarding postmenopausal women, a meta-analysis of controlled clinical trials using exercise to enhance aBMD found that a trend toward increased aBMD in the femoral neck,[27] although it was not significant. Previous meta-analyses, which did not use individual patient data, found that site-specific aerobic exercise and progressive resistive training increased hip aBMD by approximately 2% in pre- and postmenopausal women.[25,29] Because these previous analyses included the aBMD measurement throughout the proximal femur, these analyses suggested that the effects of exercise were likely site-specific and did not always affect the femoral neck.

Martyn-St James and Carroll[42] found that walking exercises alone were insufficient to maintain lumbar spine aBMD. Effects on femoral neck or total hip aBMD were less consistently reported, with varying results.[41,42] However, the way that the exercises were delivered would have a large influence on the bone structural outcomes.

Observational studies have indicated that involvement in leisure-time physical activity or walking reduces the risk of hip fracture in older women.[10,15] However, to our knowledge, fracture has not been used as an outcome in any exercise interventions.

Men

Comparatively far less research has been conducted on the effects of exercise interventions on men. A meta-analysis of available randomized controlled trials found positive effects of exercise for elderly men but not younger men.[28] However, many cross-sectional studies have demonstrated that participation in physical activity has a benefit to bone mass and/or aBMD, compared with nonathletic controls.[eg,35,44,47] As with premenopausal women, more studies are needed to fully understand the effects of exercise on bone health in men.

Clinical Recommendations

SORT: Strength of Recommendation Taxonomy
A: consistent, good-quality patient-oriented evidence
B: inconsistent or limited-quality patient-oriented evidence
C: consensus, disease-oriented evidence, usual practice, expert opinion, or case series

Clinical Recommendations	SORT Evidence Rating
Activities with larger strain magnitudes (eg, gymnastics, dance, power sports), higher strain rates (eg, jumping activities), and higher strain frequencies (eg, running) appear to be more beneficial than nonweightbearing activities. These recommendations are assigned a C because evidence to date is limited to disease-oriented outcomes, such as bone mineral density, rather than fracture risk.	C
Considerable evidence suggests that the early pubertal period provides an unparalleled opportunity to enhance bone health through various types of exercise.	C
The capacity of typical physical activities such as walking to enhance skeletal health may be limited to elderly men and postmenopausal populations. In younger adult populations, such activities may be sufficient to maintain skeletal health, whereas activities with atypical strain patterns may be required to enhance skeletal health. Although these findings are consistent throughout the literature, the recommendations can achieve only a B-C because the evidence from clinical trials is limited to intermediate outcomes. Only observational studies have used fracture as an outcome. There is a need for randomized controlled trials, with fracture as an outcome.	B-C

For more information about the SORT evidence rating system, see www.aafp.org/afpsort.xml and Ebell MH, Siwek J, Weiss BD, et al. Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. *Am Fam Physician.* 2004;69:549-557.

CLINICAL RECOMMENDATIONS

Many factors interact to maintain bone health, including genetic, intrinsic, and environmental factors. Physical activity is one of the strongest nonpharmacological means to develop and maintain healthy bone mass; moreover, it represents a modifiable risk factor to achieving skeletal health. Although the blend of mechanical parameters that best enhance bone growth and prevent loss has not been identified, the skeleton responds to a combination of ground reaction forces from weightbearing activities, as well as muscular forces incurred through locomotion and movement, to create a mechanical profile suited to augment skeletal growth. The effectiveness of physical activity in enhancing skeletal health appears to depend on the timing within the lifespan. Recommendations for physical activity to maintain and/or enhance bone health are being made based on the current evidence and the SORT guidelines.

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