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Therapeutic and Prophylactic Effects of Sports and Exercise on Osteoporosis and Fracture Risk

Therapeutische und prophylaktische Effekte von Sport und Training bei Osteoporose und Fraktur Risiko

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ZUSAMMENFASSUNG

Osteoporose kann entweder durch reduzierten Knochenaufbau oder erhöhten altersbedingten Knochenabbau verursacht werden. Im Gegensatz zu den Ursachen des Knochenabbaus, die seit längerer Zeit untersucht werden, hat die Forschung nach Mechanismen des Knochenaufbaus erst in den vergangenen zehn Jahren begonnen. Die gängige Lehrmeinung derzeit besagt, dass die Kindheits- und Jugendjahre entscheidend für den Aufbau der Knochendichte sind. Desweiteren haben Lebensgewohnheiten, wie z.B. körperliche Aktivität einen entscheidenden Einfluss auf die Knochendichte. Mechanische Beanspruchungen haben sich als effektive Reize für den Erhalt und Aufbau der Knochendichte und Knochenstärke erwiesen. Knochendichte sowie Knochenstärke können entscheidend in der späten prä-pubertären Phase sowie auch in der frühen peri-pubertären Phase durch körperliches Training verbessert werden. Es gibt Studien die belegen, dass eine Erhöhung der Knochendichte durch mechanische Belastungen während der Wachstumsphasen bei Kindern und Jugendlichen im Alter weitgehend erhalten bleiben, auch bei einem geringeren Umfang körperlicher Aktivität. Untersuchungen zeigen, dass frühere männliche Leistungssportler ein geringeres Frakturrisiko aufweisen im Vergleich zu nicht-Leistungssportlern der gleichen Altersgruppen. Diese Befunde sprechen dafür, dass körperliche Aktivität bei Kindern und Jugendlichen während der Wachstumsphasen empfohlen werden sollte, unter anderem um das Frakturrisiko im Alter zu reduzieren.

Schlüsselwörter: Sportliches Training, Knochendichte, BMD, Knochenaufbau, Fraktur.

SUMMARY

Osteoporosis and low bone strength in older people may be due to low bone mass accrual or elevated age-related loss of bone mass. The mechanisms underlying loss of bone mass have long been subjected to research. However, research has only started in the last decade to focus on strategies to increase bone mass. The current opinion is that childhood and adolescence are critical periods for building up bone mineral density. It is also known that life style factors, such as physical activity, may influence the accrual of bone mineral density. Mechanical loading has been shown to be one of the best stimuli to enhance not only bone mass but also structural skeletal adaptations, both independently contributing to bone strength. Exercise prescription also includes a window of opportunity to improve bone strength in the late pre- and early peri-pubertal period. There is some evidence supporting the notion that gains in bone mass obtained by mechanical loading during growth are maintained at older age despite reduction of physical activity in adulthood. The notion that former male athletes have a lower fracture risk compared to non-athletes of the same age suggests that physical activity during growth and adolescence should be recommended as a feasible strategy to reduce the future incidence of fragility fractures.

Key words: Physical activity, bone mass, BMD, bone structure, fractures.

ADAPTIVE RESPONSE OF BONE TO LOADING

Key features for osteogenic stimuli include load that is dynamic, have a high magnitude, a high frequency and unusually distributed strains, where the required mechanical loading necessary to stimulate osteogenesis decreases as the strain magnitude and frequency increases (30). However, the osteogenic response to high magnitude loading becomes saturated after a few loading cycles (28) where after additional loading confers limited benefit (32). But, bone cell mechanosensitivity seems to recover following rest so that separating loading into short bouts with periods of rest in between optimises the osteogenic response (26). That is, the loading characteristics associated with an improvement in bone strength are very specific, making the general prescription of exercise for cardiovascular health or weight management unsuitable for skeletal health. Stu-

dies have also shown that the osteogenic response is maturity and gender dependent (8, 15) so that a stronger response to mechanical stimuli, predominantly occur during growth especially in the pre- or early pubertal period (8, 9, 15, 20). In adulthood, prospective studies have shown that physical activity can reduce age related bone loss or at best produce increments in bone mineral density (BMD) of a few percentage points (4, 12). These benefits are much lower than the ones obtained by physical activity during growth and of questionable biological significance. The reported lower fracture incidence

accepted: November 2011

published online: February 2012

DOI: 10.5960/dzsm.2012.007

Karlsson MK, Rosengren BE: Therapeutic and Prophylactic Effects of Sports and Exercise on Osteoporosis and Fracture Risk. Dtsch Z Sportmed 63 (2012) 9-12.

in physically active elderly is therefore probably the result of non-skeletal effects such as increased muscle strength and improved neuromuscular function. As the aim of this review was to evaluate exercise as prophylaxis and treatment of osteoporosis and fragility fractures, it focuses on effects of physical activity during growth and if exercise induced skeletal effects are retained at older ages.

PHYSICAL ACTIVITY AND THE SKELETON AT GROWTH

Physical activity enhances bone mineral accrual especially during the first two decades in life and a variety of reports have inferred practice of high impact sports such as tennis, squash, gymnastics and soccer to be associated with higher BMD than expected while practice of endurance sports such as running, cycling and swimming show less promising results (17). For example, young female gymnasts have a 30 to 85% more rapidly increase in BMD than sedentary children (2) and young tennis players display 10-15% arms side-to-side difference in BMD in comparison with lower than 5% difference in age-matched controls (3,15). Studies in children have also shown that exercise intervention provided as education classes or exercise additional to regular physical education classes with up to 5 years of follow-up is associated with skeletal benefits but of a lower magnitude than in athletes (6,9,20). The interventions have in these studies in general resulted in up to 5% greater increase in BMD at mechanically loaded sites. Such benefits should however not be underestimated as small increase in bone mass can generate a more than two-fold increase in bone strength (27). In addition, today we know that these interventions can be initiated without an increased rate of childhood fractures (9,20), an adverse effect that have been reported to follow high level of physical activity, as a result of a higher exposure to trauma (7,31).

The prepubertal skeleton seems to have the capacity to respond to loading by adding more bone on the periosteal surface than would normally occur through growth-induced periosteal apposition (10,21). But studies also infer that there is an endosteal apposition in pre-pubertal boys as a response to mechanical loading (7,21). Such a response is less obvious in pre-pubertal girls (3,34). Exercise in late puberty is therefore associated with bone apposition on the endosteal surface, as shown in female tennis players (3) and the enlargement of bone size in response to loading has been reported to increase from pre- to peri-puberty in male but not in female tennis players (3,21). The effects of physical activity on periosteal apposition (bone size) are also translated to a greater increases in bone strength than an increase in bone mass alone (3,11,19). Bone size is for example 10% larger in upper limbs of young pre-pubertal gymnasts than in normo active children (10,34) as is the arms side-to-side difference in young pre-pubertal tennis players (3,21). But bone may also be laid down on the endosteal surface so that cortical thickness increases and there are reports that infer cortical cross-sectional area to be 5 to 12% greater in the lower limbs of young runners and young gymnasts compared to controls in spite of having the same bone size (34). The endosteal apposition is however less beneficial than a periosteal apposition since the bone resistance to bending increases by the forth power of the radius (29).

The osteogenic response in the upper and lower limbs are site-specific (13,34) and endosteal apposition has been found at the 60-70% distal humerus but not at the 40-50% mid humerus in

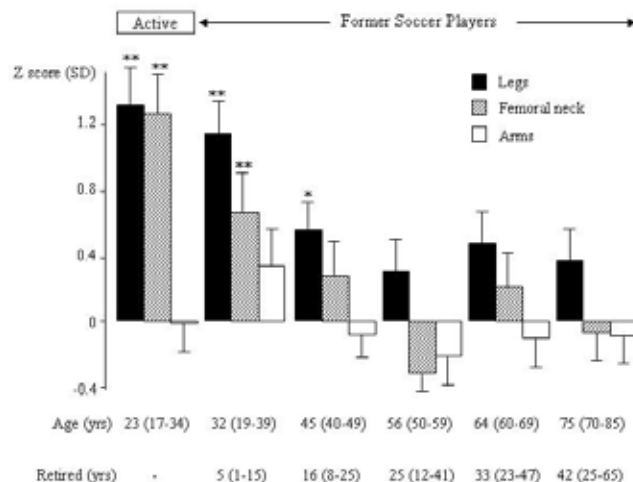


Figure 1: Bone mineral density (BMD) of the legs, femoral neck and arms in active and formerly active male soccer players and controls in relation to age. BMD in the active and former athletes is presented as Z-scores (number of standard deviations (SD) difference compared to age- and gender-matched controls) in groups with advancing age and increased time since retirement from active exercise career. Bars represent SD, * $p < 0.05$, ** $p < 0.01$. Adapted from Karlsson et al. 2000.

young tennis players (3,8,14). There is also a different response to mechanical loading in anterior-posterior compared to the medial-lateral direction and in the proximal, mid-diaphysis or distal part of a long bones (3,8,11,13,14,27,34). But increased bone strength could also be derived by redistribution of bone mass to areas submitted to high mechanical strains. Bone strength could thus be increased by changing the shape of the bone without an associated increase in bone mass or bone size, an adaptive model that have been reported in several human studies (14,22). That is, the effects of mechanical stimuli must be evaluated in a region specific and gender specific fashion in relation to the applied loading histories and loading magnitudes.

ARE BONE MASS BENEFITS GAINED DURING GROWTH PRESERVED WITH CESSATION OF EXERCISE?

Hypothetically it seems less likely that exercise-induced skeletal benefits obtained during growth are maintained into late adulthood as the mechanostat-theory indicates a decrease in bone strength as a response to reduced level of physical activity. Prospective studies infer that there is a larger BMD loss with retirement from exercise so that a BMD benefit of 1.0-1.5 SD during active career is transferred to a benefit of 0.5-1.0 SD after 5-10 years after reduced activity level (2,23,33) and a non significant 0.3 standard deviation (SD) lower leg BMD 4-5 decades after retirement (16) (Figure 1). However, there is now also prospective, controlled study data that infer exercise induced benefits in BMD to be retained also after long term retirement. Male athletes aged 53-79 years and retired from sports for a mean 30 years still had higher BMD than expected by age (31) (Figure 2). If so, this would hypothetically be transferred to a reduced incidence of fragility fractures.

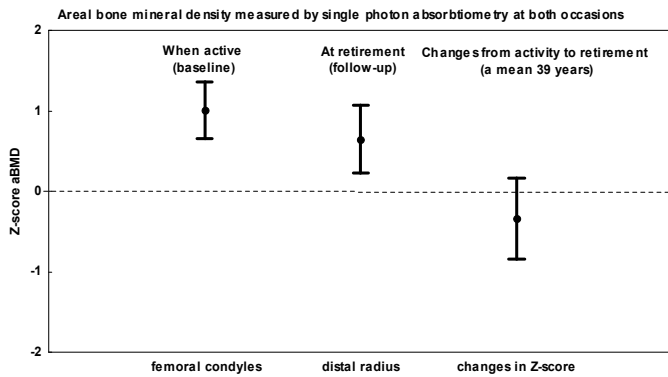


Figure 2: Bone mineral density (BMD) in 46 prospectively followed former male athletes and 24 age and gender matched controls now aged 53-79 years measured at active career and mean 39 years later when they had been retired for mean 29 years. Bone mineral density (BMD) was estimated by single photon absorptiometry (SPA). Data are presented as Z-scores (number of standard deviations (SD) difference compared to age- and gender-matched controls) with 95% confidence intervals (95% CI). Adapted from Tveit et al. 2010.

ARE BONE STRUCTURAL BENEFITS GAINED DURING GROWTH PRESERVED WITH CESSATION OF EXERCISE?

As the mature skeleton is thought to lose bone mass essentially through remodelling on the endosteal envelope, and to a much lower extent on the periosteal envelope (25), the structural adaptations obtained by physical activity during growth (8,9,20) may be better preserved (16) than bone mass. This would be of clinical importance as bone structure contributes to the skeletal resistance to fractures independently of bone mass (1). Haapasalo et al. reported an exercise-associated enlargement in bone size that was maintained after retirement in former racket players (11), children aged 3 to 5 years that had reached structural benefits of the skeleton by training retained these benefits with cessation of the training program (5) and old retired athletes still had structural benefits (18). These structural benefits could also hypothetically be transferred to a lower fracture incidence than expected by age.

IS EXERCISE DURING YOUNGER YEARS FOLLOWED BY REDUCED FRACTURE INCIDENCE AT OLD AGES?

Reduced fracture risk has been reported in retired athletes. The prevalence of fractures in 663 former athletes above age 50 years, and retired from sports for up to 65 years were lower than in 943 age- and gender matched controls, 8.9% in the former athletes versus 12.1% in the controls (24). Additionally, the proportion of subjects with low energy fragility fractures sustained after age 50 years was lower in the former athletes in comparison with the controls, 2.3% versus 4.2%, as well as the proportion of individuals with a distal radius fracture, 0.8% versus 2.3% (Figure 3). Similar conclusions have been reported in 400 former male soccer players and 800 controls (18) and there are now also data published that infer among 2075 former male athletes and controls aged 50-91 years, a lower incidence of both all type of fractures as well as fragility fractures in the former sportsmen (31). But other studies refute the view. One often cited study includes 2622 former female college athletes and

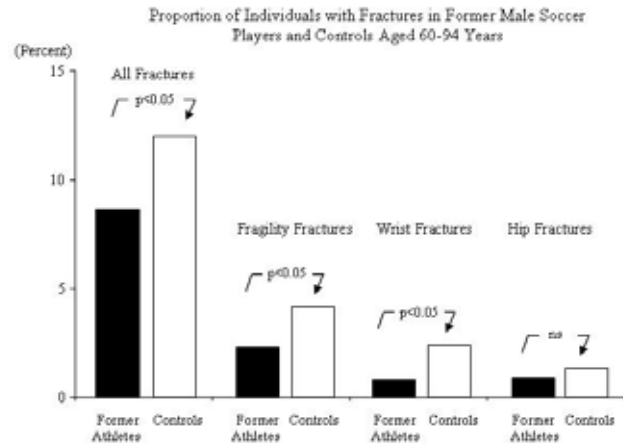


Figure 3: Proportion of individuals with fractures among 663 former male athletes now aged 50 to 94 years and in 943 age- and gender-matched controls. The figure includes the risk of sustaining a fracture after age 35 (after retirement) and the risk of sustaining a fragility fracture, a wrist fracture and a hip fracture after age 50 due to a low-energy trauma. Adapted from Nordstrom et al. 2005.

2776 controls now aged 20-80 years, a trial that reported a similar fraction of former athletes with fractures than controls after retirement, 29% versus 32% (35). However, as this study includes individuals from age 20 years with an extremely short retirement period and former recreational athletes, there could have been too few elderly individuals and too few highly active athletes in the cohort to give a true risk evaluation of osteoporosis related fractures after training during growth.

CONCLUSIONS AND PERSPECTIVE

Childhood and adolescence are critical periods for the skeleton. Mechanical loading has then been shown to be one of the best stimuli to enhance not only bone mass but also the structural skeletal adaptations, both contributing to bone strength. Exercise prescription also includes a window of opportunity to improve bone strength in the late pre- and early peri-pubertal period. There are some evidence supporting the notion that skeletal gains obtained by mechanical loading during growth are maintained at older age despite reduction of physical activity in adulthood in the notion that former male athletes have a lower fracture risk than expected by age at least do not oppose the view that physical activity during growth and adolescence should be supported as one feasible strategy to reduce the future incidence of fragility fractures.

The future research should now determine: (i) the minimum threshold of exercise during growth that is necessary to obtain a clinically significant increase in bone strength and (ii) the minimum threshold of exercise during adulthood that is required to maintain the skeletal benefits (gained during growth) and prevent osteoporosis and (iii) in prospective long term studies evaluate if exercise induced benefits in the skeleton with accompanied fracture reduction are retained after cessation of exercise. This is a pivotal area of research that underpins future decisions regarding the role of exercise during growth for improved bone health in the aged individual.

Angaben zu finanziellen Interessen und Beziehungen, wie Patente, Honorare oder Unterstützung durch Firmen: Keine.

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