

# Physical Activity, Bone Remodelling and Bone Metabolism Markers

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Received: April 03, 2018; Accepted: May 07, 2018; Published: May 16, 2018

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## Abstract

Sedentary lifestyle is associated with detrimental health effects on bone. Risk of fracture and lower bone mineral density (BMD) are increased among people with lower physical activity level. The onset of osteoporosis does not occur immediately. Instead, it slowly progresses throughout the years. The ideal approach and easier way to prevent or delay the onset of osteoporosis should focus on changing one's lifestyle by including higher amount of physical activity. Exercise or higher amount of physical activity helps to impose mechanical strain on the bone, and stimulate bone metabolism process. However, different exercise mode might impose different effect on bone metabolism. This review paper will focus on bone remodelling, bone formation and resorption markers, and effects of physical activity or exercise on bone metabolism markers.

**Keywords:** Bone Health; Bone Metabolism; Physical Activity, Exercise

## Bone Remodelling

Human bones are porous mineralized structure composed of 25% collagen fibres, 25% water and 50% crystallized salts which include calcium phosphate, calcium hydroxide, calcium carbonate, magnesium, fluoride and potassium[20]. During infancy, childhood and adolescence, long bones grow in length while all bones grow in thickness. Growth in length takes place in epiphyseal plate while growth in thickness takes place in periosteum. In adult, bone constantly undergoes remodelling which is the on-going replacement of old bones tissue by new one. Bone remodeling or turnover occurs via two main opposing processes, i.e. bone formation and bone resorption. Bone can increase in thickness even after longitudinal growth has stopped. During bone formation, collagen fibres and certain organic substances are synthesized by osteoblast cells and stored in bones along with minerals. However, during bone resorption, minerals and collagen fibres are degraded by osteoclast cells. Osteoclast cells attach to periosteum and release lysosomal enzyme and acids into the sealed pit to digest the collagen fibres and organic substances, while acids dissolve the bone minerals. The degraded bone matrix components are being transported out into the blood or excreted in the urine [2,3,19,20].

Normally, bone remodelling processes are tightly coupled and balanced. However, under certain condition, it could result imbalance in metabolism changes. For instances: aging (e.g.:

osteoporosis), metabolic bone diseases, states of mobility (e.g.: exercise), therapeutic interventions etc.. Normal bone metabolism is achieved by adequate dietary intake of minerals and vitamins such as calcium, Vitamin A and Vitamin D and regulated by various hormones and local mediators such as parathyroid hormone (PTH) and calcitonin[3,19,20]. To achieve optimal bone health, physical activity and/or adequate nutrition are vital [5].

## Bone Metabolism Markers

Bone mineral density can be measured directly using dual-energy X-ray absorptiometry (DXA) and quantitative computed tomography (CT) which is precise and accurate [5]. It is generally known that although bone density is not apparent following any intervention, however there might be a dynamic process of bone metabolism occurring. Bone metabolism changes or bone turnover can be accessed via biochemical markers which are bone formation markers and bone resorption markers. Bone formation markers include blood total alkaline phosphatase (ALP), bone-specific alkaline phosphatase (BALP), osteocalcin (OC) and procollagen type 1 N propeptide (P1NP). Meanwhile, bone resorption markers include C-telopeptide of type 1 collagen (CTX-1), N-terminal telopeptide of type 1 collagen (NTX), deoxypyridinoline (DPD) and pyridinoline (PYD) [2,3,5,9,19].

Bone metabolism markers are suitable to monitor the effect of any intervention on bone metabolism [6]. Bone turnover markers consist of enzymes such as BALP and proteins by-product such as OC and CTX-1. These markers either circulate in blood and/or are excreted in urine [3,9] Bone turnover reaches its peak in the early morning and lower significantly by lunchtime, and meals can suppress markers, mainly bone resorption, therefore, it is suggested that fasting blood should be collected in the early morning [3]. BALP and OC both are bone formation markers, which can be highly detected during bone formation activity, while CTX-1 is bone resorption marker which can be highly detected during bone resorption activity [2,3,9,19].

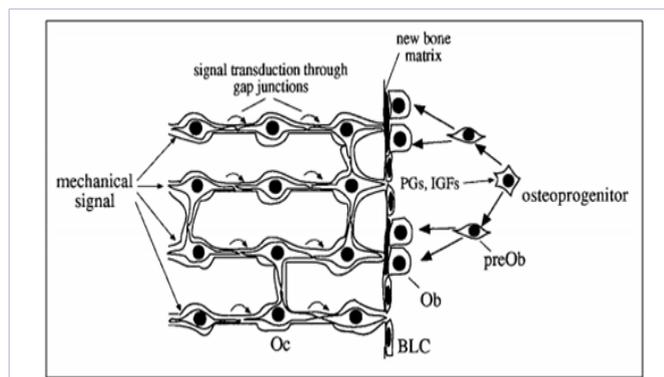
BALP is a membrane-bound osteoblast enzyme. Its function is to be involved with bone matrix mineralization. However, only about half of total blood circulating alkaline phosphatase (ALP)

is the bone isoform, whereas the other half is mostly the liver isoforms [3,9]. OC is the most abundant type of non-collagenous protein in bone. The majority of the OC synthesized by the osteoblasts is integrated into the matrix, while small amount of them enter blood circulation and cleared in the urine. Circulating OC is composed of the intact molecule (1-49 amino acid) and the large fragment (1-43 amino acid) [9].

The majority of bone resorption markers widely used are products of collagen degradation, such as CTX-1. This marker is released into the blood circulation during bone resorption. CTX-1 is a peptide compound made up of 8-amino-acid sequence, and it is highly susceptible to isomerization and racemization. CTX-1 is the product of cathepsin K digestion of type I collagen. Another marker, carboxyterminal cross-linked telopeptide of type I collagen (1CTP or CTX-MMP) is also used as a marker of bone resorption. 1CTP has longer peptide sequence than that of CTX. 1CTP is the product of matrix metalloproteinases digestion [9]. However, different bone pathological condition resulted in different response of 1CTP and CTX-1 markers, and it may be due to different enzymatic pathway [8,9].

### Effects of Physical Activity or Exercise on Bone Metabolism

Physical activity or exercises increase mechanical forces on bones, consequently initiates bone formation and increases bone mass [17,20]. Figure 1 shows how mechanical loading initiates bone formation. Theoretically, the mechanical signal transduction is transmitted through the osteocytic network via gap junctions to the bone lining cells (BLCs). The BLCs release paracrine factors such as prostaglandins, insulin-like growth factors that stimulate osteoprogenitor cells to divide and differentiate into osteoblasts. Subsequently, osteoblasts synthesize new bone matrix [4]. Physical activity or exercises exert mechanical loading on bones and thus stimulate bone formation.



**Figure 1:** Schematic presentation of mechanical impact mechanism on bone formation [4].

Regarding previous animal study on exercise and bone metabolism markers, it was reported that 8 weeks of jumping exercise elicited significantly higher tibial mass in exercised rat compared to sedentary rats [14]. However, there were no significant differences in serum OC, ALP and 1CTP concentrations between exercise and sedentary rats. When the rats were further trained for another 32 weeks, six out of nine groups with

increased training loads demonstrated significant increases in tibial mass compared to the respective sedentary control rats, however there was no significant difference in serum osteocalcin between the exercised rats and their respective sedentary control group. There were also no significant differences in serum alkaline phosphatase concentrations between the exercised rats and the respective sedentary control group except for rat with exercise loads of 40, 50 and 200J/week. Meanwhile, serum 1CTP concentrations were significantly lower in exercise groups with exercise load ranged from 40J/week to 200J/week when compared to the sedentary control. Hence, it was suggested that long term exercise up to 32 weeks has more beneficial effects on bone metabolism than short term exercise of only 8 weeks. Besides, these findings implying that the minimal weekly loads required to elicit beneficial effect on bone mass are 30J/week and above, while the minimum weekly load required to elicit reduction in 1CTP level is 40J/week. Nevertheless, this was an animal-based study and human studies are warranted to confirm these responses.

The members of the above research team have carried out a human study on effects of aerobic dance exercise on blood bone metabolism markers in young females with age ranged between 19 to 25 years old. The participants were required to attend aerobic dance classes for 3 sessions per week, one hour per session for 8 weeks. It was found that serum bone formation marker of ALP was significantly greater in post test as compared to pre test, and there was significantly lower post test serum resorption marker of 1CTP as compared to the pre test. This findings implied that aerobic dance exercise affect bone turnover of bone formation and resorption in young females [16].

As an extension of the of the above study, the effects aerobic dance on bone metabolism markers in women with age ranged from 25-40 years old was investigated [15]. It was observed in this previous study that serum bone resorption marker of 1CTP was significantly higher after 8 weeks of aerobic dance intervention compared to pre test. However, no significant change in serum bone formation of OC was observed. This study showed that aerobic dance exercise elicited greater effect on influencing bone resorption than formation in adult women.

Recently, the effects of a circuit training program with activities using dumbbells and elastic bands as resistance in 19 to 25 years old young males was investigated [13]. The training program was performed for one hour per session, 3 sessions per week for 6 weeks. It was found that after 6 weeks of study period, serum bone formation marker of ALP was significantly higher in the exercise group compared to the sedentary without exercise control group. This study finding reflects that circuit training has potential in increasing bone formation of young males.

The members of the above mentioned research team has also carried out a recent study to investigate the effect of jogging exercise on bone metabolism markers. It was found that moderate intensity of jogging exercise with 30 min per day, 3 days per week for 8 weeks could increase serum bone resorption marker of CTX-1 in 18 to 25 years old young males. This study finding implying

that jogging exercise could affect bone turnover by enhancing bone resorption in young males [18].

A study conducted on pre- and post-menopausal Korean women found that participants who performed more physical activity during leisure time showed a significant positive association with BMD at lumbar spine and femur [10]. In addition, dose-response relationships between duration of physical activity and BMD has been found in both pre and post-menopausal groups. Thus, it was suggested that the higher the amount of physical activity done, the higher the beneficial effect on bone health. Hence, higher amount of physical activity should be recommended as prevention of bone deterioration.

A study was carried out to investigate the effect of moderate walking exercise on bone metabolism in postmenopausal women with osteoporosis [21]. Throughout the 12 months of study period, it was observed that the percent reduction in a bone resorption marker, i.e. cross-linked N-terminal telopeptides of type I collagen (NTX) compared to baseline value became significant at month 3 and onwards. Percent reduction of serum BALP compared to baseline value was significant at month 12, while there was no significant percent change of serum osteocalcin compared to its baseline value. The post-lumbar BMD in both control and exercise group did not significantly increase from their respective baseline value. Instead, BMD in control group progressively decreased while BMD in exercise group progressively increased until month 12. Therefore, the changes of BMD in exercise group compared to control group was significant. In addition to BMD, there was significant negative correlation between the percent of urinary NTX level and lumbar bone mineral density. Hence, the authors concluded that NTX marker appears to be a more responsive and useful marker to predict the response of lumbar BMD to exercise, compared to OC and BALP.

The effect of resistance training on bone metabolism markers in young males for 4 months was investigated [7]. It was found that in training group, serum BALP and serum OC increased significantly at first month compared to baseline, and their levels remain consistent until the end. It was also found that there was no significant change of plasma procollagen type 1 C-terminal (PICP). Meanwhile, there were no significant changes in serum BALP and serum OC in the sedentary control group compared to baseline values, however plasma PICP concentration kept decreasing significantly until the end. Therefore, it was suggested that resistance training could highly stimulate bone formation, and it was also speculated that collagen synthesis at skin might contribute to the negative result of plasma PICP concentration in the training group.

Meanwhile, the effect of three different modes of exercise on biochemical markers of bone turnover in young inactive women, i.e., aerobic exercise, resistance exercise, and combined aerobic and resistance exercise was investigated [11]. After 8 weeks of exercise duration, it was observed that bone formation markers of BALP and OC significantly increased in resistance and combined group. Incorporation of resistance training did not cause substantial alterations in bone resorption markers. Meanwhile,

aerobic training marked no changes in both bone formation and resorption markers. Hence, resistance training appears to be more effective to stimulate bone formation compared to aerobic exercise. In another study, reported that it was reported 12 weeks of moderate aerobic training produced significant increases in serum BALP and serum OC, and significant decrease in DPD among middle-aged male and female subjects [1].

It was reported that the concentrations of biochemical markers of bone metabolism were different between controls, swimmers, cyclists and triathletes [12]. Serum ALP in cyclists was found significantly lower than other groups, there was no significant difference of ALP between triathletes, swimmers and controls. Meanwhile, OC in triathletes and swimmers was significantly higher than controls. However, urinary CTX-1 in swimmers was significantly higher than other groups. Highest urinary CTX-1 in swimmers might be due to the least mechanical strain effect from the training on the bone compared to other sports.

## Conclusion

It is generally known that exercise or higher amount of physical activity can impose certain amount of mechanical strain on the bone and subsequently stimulate bone metabolism processes. Nevertheless, different exercise mode can elicit different mechanical impact on bone physically and its metabolism. It is also known that bone response to physical activity or exercise is dependent on the age of an individual. In general, the previous studies mentioned in this review article observed that aerobic dance exercise, athletic training, resistance exercise, and circuit training with dumbbells and elastic bands could affect bone formation significantly in young population. Meanwhile, aerobic dance exercise could affect bone resorption significantly in population with older age. It is speculated that the forces generated by mechanical loading elicited by aerobic dance, athletic training, resistance and circuit training have contributed to the significant effects on bone metabolism. Thus, these few types of exercises can be recommended for enhancing bone health. Nevertheless, more future studies with different types of exercise and prescription are warranted to determine the relationship between physical activity or exercise and bone metabolism markers in different age categories.

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