

## THE IMPACT OF REGULAR FOOTBALL TRAINING ON BONE TURNOVER MARKERS

Wpływ regularnego treningu piłki nożnej na markery obrotu kostnego

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### ABSTRACT

#### Introduction

The condition of the skeleton is important not only in the perspective of osteoporosis prevention, but also as a factor affecting the frequency of injuries excluding physical activity. Monitoring the impact of specific sports on osteoclasts and osteoblasts activity allows optimization of programming of physical activity limiting the risk of bone mineralization disorders. The review analyzes available papers on the impact of regular football training on skeletal physiology changes analyzed by measuring bone turnover markers in the body.

#### Aim

Determining the impact of regular football training on bone mass regulation by analyzing bone turnover markers.

#### Material and methods

PubMed and SPORTDiscus with Full Text databases were searched using the keyword combination "*the name of team sport*" + *bone turnover*. There is no clinical trials about bone turnover markers among handball, hockey, basketball and volleyball players in the available literature that meet the inclusion criteria, so the topic of the review was narrowed down to football (soccer). After applying the exclusion criteria, five studies were qualified.

#### Results

In the analyzed papers, the concentration of osteocalcin, N-terminal procollagen type I extension propeptide and C-terminal telopeptide of type I collagen in blood increased as a result of regular football training. In 3 papers statistically significant ( $p < 0.05$ ) increases were noted.

#### Conclusions

Football training can stimulate bone metabolism, being an effective and attractive form of bone fracture prevention, regardless of your level of sport. Due to the limited availability of studies, there is a high need for further studies describing the impact of physical activity on bone metabolism.

**Keywords:** bone remodeling, football, osteoporosis, bone turnover markers

### STRESZCZENIE

#### Wstęp

Stan kośćca jest istotny nie tylko w perspektywie profilaktyki osteoporozy, ale też jako czynnik mający wpływ na częstość urazów wykluczających z aktywności fizycznej. Monitorowanie wpływu określonych aktywności na procesy kościotwórcze i kościogubne pozwala na optymalizację programowania aktywności fizycznej ograniczającej ryzyko zaburzeń mineralizacji kości. W pracy przeanalizowano dostępne prace na temat wpływu regularnego treningu piłki nożnej na zmiany fizjologii kośćca analizowane poprzez pomiary stężeń markerów obrotu kostnego w organizmie.

### **Cel**

Określenie wpływu regularnego treningu piłki nożnej na procesy regulacji masy kostnej poprzez analizę markerów obrotu kostnego.

### **Materiał i metody**

Bazy danych PubMed oraz SPORTDiscus with Full Text przeszukano z użyciem zestawienia słów kluczowych „nazwa danego sportu zespołowego” + *bone turnover*. W dostępnej literaturze nie znaleziono wyników spełniających kryteria włączenia na temat zmian markerów obrotu kostnego u zawodników uprawiających piłkę ręczną, hokej, koszykówkę oraz siatkówkę, dlatego temat przeglądu zawężono do piłki nożnej (frazy *football* lub *soccer*). Po zastosowaniu kryteriów wykluczenia, zakwalifikowano pięć prac.

### **Wyniki.**

W analizowanych pracach stężenia osteokalcyny, C-końcowego usieciowanego telopeptydu łańcucha alfa kolagenu typu I oraz N-końcowego propeptydu prokolagenu typu I w krwi zwiększyły się w następstwie regularnego treningu piłki nożnej. W 3 pracach odnotowane wzrosty były istotne statystycznie ( $p < 0,05$ ).

### **Wnioski**

Trening piłki nożnej może stymulować metabolizm kostny, będąc efektywną i atrakcyjną formą profilaktyki złamań kości, niezależnie od stopnia zaawansowania sportowego. Ze względu na ograniczoną dostępność badań, istnieje wysoka potrzeba dalszych badań z zakresu wpływu aktywności fizycznej na metabolizm kostny.

**Słowa kluczowe:** obrót kostny, piłka nożna, osteoporoza, markery obrotu kostnego

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### **Introduction**

Regular physical activity has a positive effect on the physiology of the human body on many levels. The beneficial effects of movement on health and body functionality have been proven many times, which led to placing activity as the basis of the health pyramid by WHO (Tuka et al., 2017). Among the numerous advantages attributed to movement, there are also indications of its beneficial effect on bone quality (Segev et al., 2018). Both through direct changes in bones subjected to sports loads, and as a result of induction of

hormonal changes by physical effort, bone mineralization may change (McArdle et al., 2010). Changes in skeletal composition and maintaining a balance between osteogenic and osteogenic processes are important in the prevention of osteoporosis, but are also important for high risk groups. Athletes are one of this group. With the increasing degree of bone mineralization, the risk of fractures decreases (Melton et al., 1998). Taking under consideration the great importance of injury prevention in professional sports, knowledge of mechanisms regulating bone mineralization and the impact of individual training elements are key to effective reduction of the risk of bone injuries. The most valuable tool we currently have that allows us to identify changes within the skeleton is the analysis of bone turnover markers. They allow to monitor bone formation processes, giving an insight into the current state of bone mineral management, which is why they are indicated as a better alternative to using densitometry for this purpose (Cefalu, 2004). Analysis of bone turnover mechanisms induced by specific forms of musculoskeletal loading can provide information that allows for more effective prevention of bone fractures.

#### *Bone turnover markers*

Among bone turnover markers there are two main groups, which are distinguished depending on biological activity towards bone tissue: bone formation markers and resorptive markers. Each of them reflects a specific pathway of anabolic or catabolic changes in bone tissue, thanks to which their analysis provides accurate information about the current state of the patient's skeleton.

*Osteocalcin (OC)* is a protein secreted by osteoblasts. It consists of 49 amino acids and is one of the most numerous non-collagenous proteins in the bones. It stimulates insulin production, increases energy expenditure and increases insulin sensitivity in specific organs. According to research, OC may be involved in regulating glycemia, prevention of glucose intolerance and obesity (Mizokami et al., 2017).

*N-terminal procollagen type I extension propeptide (P1NP)* is formed during the synthesis of type I collagen in bones. However, it can also be produced in other connective tissues, with particular emphasis on the skin. Considering the speed of metabolism and the fact that bone metabolism is faster than other connective tissues, it can be stated that the largest amounts of detected P1NP will come from bone. Circulating P1NP is received by the liver scavenger cells and then degraded.

*C-terminal telopeptide of type I collagen (CTX-1)* is a breakdown product of type I collagen, containing pyridinium cross-linking. Its serum level is associated with histomorphometric measurements of bone resorption. The kidneys are responsible for CTX-1 removal, and its amino acid sequence consists of lysine and the aspartate-glycine sequence (DG). This marker can transform into the mature form (beta-CTX-1) in the  $\beta$  isomerization process. It can be also racemized (Szulc et al., 2017).

In clinical practice, other markers, valued for their high specificity are also found. However, they are rarely found in scientific research. Pyridinoline (Pyr) and Deoxypyridinoline (D-Pyr) are considered to be one of the more specific bone markers. They are stable in stored urine, and the diet has no effect on it. Pyridinoline is mainly present in type I bone collagen type I collagen in cartilage and connective tissue. (Lawrentschuk et al., 2015) Bone alkaline phosphatase (BAP) is a glycoprotein and ectoenzyme. Unlike other bone turnover markers, it is accumulated in the urine, which makes it not clinically useful in kidney diseases. This organ does not directly affect BAP levels because it is not filtered or dialyzed in this area of the body. Studies report that bone alkaline phosphatase is a multifunctional enzyme because it is involved in the

binding of calcium and collagen (Sardiwal et al., 2013). Cross-linked N-telopeptide of type-I collagen (NTx) is a compound released during bone resorption, often used clinically to assess the effectiveness of osteoporosis drugs. It is valued for its high sensitivity, which allows quick capture of potential changes in bone mineral density (Greenspan et al., 1998). It can also be used in patients with cancer to assess the probability of bone metastases (Miura et al., 1997).

### **Aim**

To determine the impact of regular football training on bone mass regulation processes by analyzing bone turnover markers.

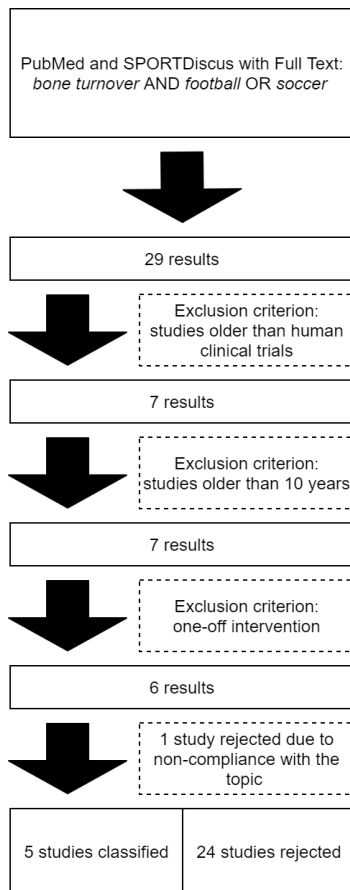
### **Material and methods**

Available PubMed and SportDISCUSS with Full Text databases were used to find articles. The entire article research team conducted the research process on 16/12/2019 - 30/12/2019 and on 13/10/2020-18/10/2020 using several methods to search for research results on individuals practicing selected teams of sport disciplines (Table 1).

**Table 1.** Number of results for individual phrases in the PubMed and SportDISCUSS with Full Text databases

<b>Phrase</b>	<b>Number of results</b>
bone turnover football / bone turnover soccer	29
bone turnover handball	0
bone turnover basketball	0
bone turnover volleyball	0
bone turnover hockey	1

In the available literature, no research about bone turnover markers in a group of players practicing handball, basketball and volleyball were found. One study conducted on athletes practicing ice hockey was excluded after consideration of the exclusion criterion from the analysis (it could not be older than 10 years). Considering the results, the review topic was finally narrowed to football (or soccer, how it's named in USA). After rejecting non-clinical and non-compliance with the topic trials, 6 articles remained. One study was rejected because of determining changes in one-off intervention, so 5 studies left. They were not older than 10 years and were carried out in the general population, what resulted in their qualification for review (Figure 1).



**Figure 1.** Flowchart.

The PEDro scale was used to evaluate selected studies (Physiotherapy Evidence Database, 1999). This particular scale examines methodological quality of researches with 11-criteria checklist (Figure 2).

1. Eligibility criteria were specified
2. Subjects were randomly allocated to groups (in a crossover study, subjects were randomly allocated an order in which treatments were received)
3. Allocation was concealed
4. The groups were similar at baseline regarding the most important prognostic indicators
5. There was blinding of all subjects
6. There was blinding of all therapists who administered the therapy
7. There was blinding of all assessors who measured at least one key outcome
8. Measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups
9. All subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analysed by "intention to treat"
10. The results of between-group statistical comparisons are reported for at least one key outcome
11. The study provides both point measures and measures of variability for at least one key outcome

**Figure 2.** PEDro scale criteria.

First criterion assess external validity of the articles and is not included within total score. The scoring system operates by awarding one point for an affirmative answer and zero points for a negative one (Bassett et al., 2010). The maximum score is ten points. In result, two articles were rated six points and other three articles were rated five points (Table 2). The average score of the analyzed studies was 5.4 points, which is higher than the average result of all the trial reports included in the PEDro database. It can be concluded that the classified studies belong to those of average methodological quality (Physiotherapy Evidence Database, 2020).

**Table 2.** PEDro score for analyzed studies.

Study	1	2	3	4	5	6	7	8	9	10	11	Total Score (1-10)
Helge, 2014	+	+	-	+	-	-	-	+	-	+	+	5
Uth, 2016	+	+	+	+	-	-	-	-	-	+	+	5
Skoradal, 2018	+	+	-	+	-	-	-	+	+	+	+	6
Uth,2016	+	+	-	+	-	-	-	+	-	+	+	5
Mohr, 2015	+	+	-	+	-	-	-	+	+	+	+	6

## Results

In the analyzed studies, the concentration of osteocalcin, CTX-1 and P1NP in the blood increased. In the studies of Helge et al., Skoradal et al. and Mohr et al., observed increases were statistically significant ( $p < 0.05$ ) (Table 3).

**Table 3.** Results.

Author, (Year)	G	N	M age	Group characteristics	D S	Training intensity	Findings in a football group		
							OC [ $\mu\text{g/L}$ ]	P1NP [ $\mu\text{g/L}$ ]	CTX-1 [ $\mu\text{g/L}$ ]
Helge, 2014	F	9	68.0 $\pm$ 4.0	No regular physical activity for the last 5 years	52	W 0-12 3x15mins 2m breaks 2-3/week	After 4 months		
							$\uparrow$ 45% $\pm$ 12% ( $p < 0,001$ )	$\uparrow$ 41% $\pm$ 16% ( $p < 0,001$ )	
	C	8	67.4 $\pm$ 2.7	Non-smoker Healthy		W 12-52 4x15mins 2m breaks 2-3/week	After 12 months		
							$\uparrow$ 46% $\pm$ 11% ( $p < 0,001$ )	$\uparrow$ 40% $\pm$ 17% ( $p < 0,001$ )	$\uparrow$ 43% $\pm$ 13% ( $p < 0,05$ )
Uth,	F	21	67.1 $\pm$ 7.1	Men with	32	WU:	23.89 $\pm$ (11.60)	59.43 $\pm$	1.01 $\pm$

2016	C	20	66.5±4.9	prostate cancer undergoing ADT for at least 6 months VO2Max≤35 ml/kg/min. <76 years Exclusion: cardiovascular disorders, osteoporosis, activity-limiting pain from bone metastases		15mins W 1-4 3x15mins 2/week  W 5-8 3x15mins 2/week  W 9-12 3x15mins 3/week  W 13-32 60mins (including warm-up) 2/week	) -> 25.70±(12.10) ) p=0,055	(34.53) -> 69.99±(37.83) p=0,148	(0.55)-> 0.91±(0.56) p=0,484
Skoradal, 2018	F	27	61±9	Sedentary lifestyle Prediabetes	16	WU: 10m W1-2 30mins 2/week  W3-4 40mins 2/week  W5-6 50mins 2/week  W7-16: 60mins 2/week	22.7 ± 1.8 -> ↑23 ± 8% P<0,05	48.9 ± 4.2 -> ↑52 ± 9% p<0,05	0.47 ± 0.05 -> ↑38 ± 7% p<0,05
	C	23							
Uth, 2016	F	26	67.1±7.1	Men with prostate cancer undergoing ADT for at least 6 months Exclusion: cardiovascular disorders, osteoporosis, activity-limiting pain from bone metastases	12	WU: 15m W1-4: 2x15mins 2/week  W5-8: 3x15mins 2/week  W 9-12: 3x15 mins 3/week	25.7±14.0 -> 34.4±19.1 p=0,002	66.1±44.8 -> 94.6±65.9 p=0,008	1.0±0.6 -> 1.0±0.6 p=0.591
	C	21	66.5±4.9						
Mohr, 2015	F	21	45±14	Premenopausal women Physically inactive Mildly hypertensive	15	3.0 ±0.5/week 60 mins	25.0 ± 12.4-> ↑37 ± 15% p<0.05	60.8 ± 25.3-> ↑52 ± 23% p<0.05	0.36 ± 0.27 -> ↑42 ± 18 % p<0.05
	C	20	45±9						

**Abbreviations:** G – Group Type, M – Mean, DS – Duration of study, F – Football Group, C- Control Group, WU – Warm-up, W - Week

## Discussion

When analyzing the results of collected research, attention should be paid to advanced age in the study groups. Only in one research project the average age did not exceed 60 years, it examined women in postmenopausal period. No studies have been found in the literature on the effect of football on bone marker levels in adolescents and young. Age was not a criterion for the selection of studies for review, and despite that, most studies were conducted on people of advanced age. A greater number of studies in the elderly people is understandable because they are particularly vulnerable to bone degenerative diseases. Knowledge of the physiology of bone changes in young people in the aspect of playing sports is also extremely important. Bone fractures are from 5 to 10% of all sports injuries (Robertson and Wood, 2015).

The analysis of bone turnover markers is a reliable indicator of the current state of bone tissue. They allow to determine the profile of bone changes. During childhood and growing-up period, their levels increase, while the levels of bone turnover markers decrease in the old age. During old age, bone resorption markers also increase with age. This corresponds to physiological changes in the body (Seibel, 2005). Changes in the concentration of bone turnover markers also depend on some metabolic diseases and environmental factors, such as the general level of physical activity causing an increase in the concentration of bone formation markers (Adami et al., 2008). Knowing the impact of specific stimuli on fluctuations in bone turnover markers allows to determine how they affect bone mineral density.

The collected research highlights the increase of bone turnover markers as a result of regular football training. This indicates the important role of this training methodology in relation to skeletal metabolism. Football in its specificity seems to be a discipline modulating the activity of both osteoclasts and osteoblasts. Comparing the results of the above review with other reports determining the impact of football training on bone mineral density (Hagman et al., 2018), it can be seen that football training causes a number of changes in bone metabolism. They lead to increase the level of bone mineralization. Despite the lack of direct elements of resistance training, which is considered as the most stimulating in relation to bone anabolism (Pasqualani et al., 2019), regular practicing football can also have a positive effect on the skeletal condition and be an element of osteoporosis prevention.

The problem of skeletal mineralization disorders affects 6-7% of men and 19-23.5% of women over 50 in European countries. It is a civilization disease leading to a large percentage of mortality as a result of osteoporotic fractures (Hernlund et al., 2013). One of the factors that contributes to the development of osteoporosis is the lack of physical activity. The beneficial effect on the mineral balance within the skeleton in football training encourages the promotion of this discipline among people at risk of osteoporosis. It can be an attractive form of preventing bone demineralization, while being a general developmental discipline favorably affecting cardiovascular parameters (Bangsbo et al., 2015).

Despite the lack of research in people before the age of 40, the benefits of regular football training on bone mineral density in these age groups should be emphasized. During adolescence, the prevalence of osteogenic processes may promote the development of a normal bone with a high degree of resistance to mechanical damage. In adulthood it can be an element of fracture prevention in professional sports. A noteworthy study was conducted by Bellver et al. in 2019 (Bellver et al., 2019). It compared the bone mineral density of people practicing water sports (swimming,



synchronized swimming and water polo) with professional football players. Significantly better results were shown in women training football. Based on them, a conclusion was drawn in which it is suggested to supplement the training plan in sports with a lower effect on the mineral balance of the skeleton with football training. This effect can have a positive effect on bone mineralization in training people.

The impact of football training on bone metabolism may be surprising in some measure, because sports with a high endurance component generally do not have a positive effect on the degree of skeletal mineralization (Suominen, 1993). An element of explosive research contained in the specifics of training and football itself can be responsible for this influence. There is study in which explosive training lowered sclerostin concentration and increased bone mineral density (Hinton et al., 2017). In another study, significant changes were noted in the concentration of osteocalcin and N-terminal procollagen type I extension propeptide after plyometric training (Prawiradilaga et al., 2020).

This review is not only a guide for all those interested in the prevention of fractures and bone degenerative diseases, but also an indication of new areas of research that can provide a lot of valuable information about the impact of specific components of physical activity on bone turnover. Only 5 papers which concerned older people have been found in the literature. Undoubtedly, there is a need to explore the topic of the impact of sport on bone turnover markers, taking into consideration individual sports disciplines, and even their individual motor components, as well as expanding the research to include younger age groups.

#### *Limitations*

The main limitation of this review is the small amount of available materials. The study also contains only research conducted on people which are over 40 years old.

#### **Conclusions**

Taking into account the results of previous studies, football training can stimulate bone metabolism, being an effective and attractive form of bone fracture prevention, regardless of the level of sport advancement. Due to the lack of studies on people under 40 age, there is a high need for further studies on the impact of physical activity on bone metabolism.

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