

Remodeling of the heel bone in athletes depending on genetic profile

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Abstract:

Balanced bone metabolism is vital for maintaining optimal bone health, which is crucial in sports. Both external and internal factors can affect bone remodeling, which determines bone integrity, recovery, and overall resilience to intense physical activity. The **aim** of the study was to analyze ultrasound densitometry of the heel bones in athletes in relation to laboratory parameters and the genetic profile of genes associated with bone remodeling.

Materials and methods. Ultrasound densitometry of the calcaneus and bioimpedance analysis assessing the body's mineral content, analysis of ionized calcium and 25-OH vitamin D levels, and analysis of the occurrence of gene polymorphisms (COL1A1 rs1800012; COL5A1 rs12722; VDR rs731236, IGF1 rs35767, PPARGC1A rs8192678) were performed in professional athletes (n = 111, males aged 18–45 years) from Central Kazakhstan who participated in team sports and martial arts. **Research results.** The athletes' mean densitometry values were consistent with osteopenia. The mean ionized calcium level was closer to the lower limit of normal, and the mean 25-OH vitamin D level in the studied athletes met the clinical threshold for deficiency. None of the athletes showed a mineral deficiency in bioimpedance measurements, but 17.51% had a body fat percentage deficit. Correlations were found between ionized calcium levels, mineral mass, and densitometry parameters, as well as between bioimpedance and densitometry parameters. Differences in laboratory parameters and densitometry parameters by genotype in athletes were identified for polymorphisms of genes regulating cell and tissue growth (IGF1 rs35767), metabolism (PPARGC1A rs8192678), and collagen structure (COL1A1 rs1800012).

Conclusion. Mineral deficiency, decreased adipose tissue content, and hypovitaminosis with associated bone remodeling should be taken into account when predicting the risk of injury in athletes and corrected to clinically acceptable levels achievement. When planning training loads, it is advisable to consider genetic polymorphisms of genes associated with bone remodeling.

Key Words: Densitometry, bioimpedancemetry, genetic polymorphism; injury risk; team sports, martial arts.

Introduction

Physical activity is widely known for its health benefits. One of the tissues particularly susceptible to the effects of physical activity is bone. A meta-analysis reviewing the literature by an international team of scientists (from France, Lebanon, India, Morocco, Iran, Canada) found that training in team sports (basketball, volleyball, rugby, handball, football) has a moderate effect on whole-body bone mineral density (1.07; 95% (0.77-1.37), $p < 0.00$) (Zouhal et al., 2024). According to current evidence, mechanical loading initiates bone remodeling by activating osteoblasts and regulating the balance between bone mineralization and resorption. This effect is particularly pronounced under multidirectional and impact loading (Hoenig et al., 2022). Measurements of SI (stiffness index), BUA (broadband ultrasound attenuation), SOS (speed of sound), T-score, and Z-score were significantly higher in Polish athletes with advanced, long-term practice (black belts) with long-term martial arts training ($p < 0.05$) (Glinkowski et al., 2023). These changes can be attributed to specific mechanical stimuli, such as impact loading and combined static and dynamic loading, which promote bone adaptation at the microarchitectural level and consequently enhance bone strength (Hoenig et al., 2025).

Former Japanese Olympians were noted to maintain high bone density long after retirement. Mean Z-scores for bone mineral density in the lumbar spine, pelvis, upper and lower extremities were greater than 0 in both men and women when monitored using dual-energy X-ray absorptiometry (Hoshikawa et al., 2024). This is associated with the formation of high peak bone mass, which is considered one of the most important aspects in the prevention of osteoporosis and in reducing fracture risk across the lifespan (Raiser et al., 2024). However,

excessive physical activity in professional sports increases the risk of musculoskeletal injuries due to bone remodeling. A significant proportion of Australian and British endurance athletes who experienced an energy deficit had low bone mass (Gowers et al., 2025). Relative energy deficiency in sport, accompanied by hormonal disturbances (including reduced levels of sex hormones and growth factors), negatively affects bone metabolism (Mountjoy et al., 2023). Researchers from Spain found that after one season at the professional level, bone mineral density of cyclists decreased significantly in the legs, ribs, and pelvic bones ($p \leq 0.05$) (Martínez-Noguera et al., 2023). These changes may be explained by the fact that cyclical (primarily aerobic) types of exercise do not provide sufficient stimulation of osteoblasts, unlike weight-bearing and impact-loading activities (Hoenig et al., 2022).

Numerous markers of bone formation and resorption have been identified. Vitamin D is known to play a significant role in bone metabolism, and vitamin D supplementation can modulate bone turnover in response to extreme exercise, potentially through effects on calcium homeostasis and parathyroid hormone (Stankiewicz et al., 2025). Athletes from the United States exhibited a seasonal decrease in 25(OH)D levels, with changes consistent across gender and sport. The overall fracture rate in athletes during one season with vitamin D supplementation was lower than the cumulative fracture rate over five seasons without supplementation (Williams et al., 2025).

The multifactorial etiology of injuries includes internal and external risk factors. Several studies indicate a hereditary component that influences bone tissue integrity, recovery, and overall susceptibility to stress. The integration of genetic profiling into the medical examination of athletes is becoming increasingly important (Ding et al., 2026). Several genes are associated with the regulation of bone remodeling and adaptation to mechanical stress. One of these is the COL1A1 gene, which encodes the alpha-1 chain of type I collagen, the main structural protein of connective tissues (bones and tendons). The COL5A1 gene encodes the alpha-1 chain of type V collagen, a key protein that is incorporated into type I collagen fibers, regulating their assembly and providing strength and elasticity to ligaments, tendons, skin, and bones. Analysis of polymorphisms of these genes is used to assess predisposition to bone diseases, as well as to identify risks associated with collagen structure disorders (Ryan-Moore et al., 2020).

The VDR (Vitamin D Receptor) gene is a nuclear protein that regulates genes involved in calcium metabolism. The VDR gene may influence blood vitamin D levels, receptor efficiency, and the risk of osteopenia and osteoporosis. Gene polymorphisms are studied in the context of calcium metabolism and bone metabolism (Varley et al., 2018). Differences in vitamin D receptor function may contribute to individual variability in response to vitamin D and, consequently, to variations in bone mineral density (Bouillon R. et al., 2019). Insulin-like growth factor-1 (IGF-1) plays an important role in regulating bone formation and mineralization. A study of the IGF1 rs35767 gene polymorphism in Chinese case-control groups (2807 people) showed that it is associated with the risk of osteoporosis in Chinese women and men (Chen et al., 2017). The PPARGC1A (Peroxisome proliferator-activated receptor gamma coactivator 1-alpha) gene encodes the PGC-1 α protein, a key regulator of mitochondrial biogenesis. It is highly versatile and capable to increase transcriptional activity of many nuclear receptors, including the vitamin D receptor. An experiment revealed that changes in PGC-1 α protein expression and serum 25(OH)D concentrations significantly correlated (Ra et al., 2022). Thus, the influence of genetic factors on the physiological and functional status of athletes is a complex process that requires further study.

Taking into account the above, the aim of the study was to analyze ultrasound densitometry of bone tissue in athletes from Central Kazakhstan in relation to laboratory parameters, bioimpedance analysis, and genetic profile of genes associated with bone remodeling.

Material & methods

Study design: prospective. The study involved 111 male athletes (team sports and martial arts) from Karaganda region of Central Kazakhstan. Participants signed informed consent to participate in the study and undergo clinical examination. The athlete study protocol complied with the ethical standards of the Declaration of Helsinki. The Bioethics Committee of Karaganda Medical University approved the study (Protocol No. 15, dated November 17, 2023). The average age of the studied athletes was 26.15 ± 0.90 years (CI 95% 24.58-27.73), with a median of 25.00 (Q1-19.00; Q3-32.00), a minimum of 18 years and a maximum of 45. 52.25% of the studied athletes were representatives of the Mongoloid race 47.75 were representatives of the Caucasian race. The examination was multidisciplinary and included a number of tests.

Densitometry was performed on the calcaneus of the right and left feet using a SONOST 3000 ultrasound densitometer (OsteoSys Co., Ltd., South Korea), with analysis of the following parameters: speed of sound (SOS), broadband ultrasound attenuation (BUA), bone quality index (BQI), T- and Z-score. A T- and Z-score greater than -1 indicates normal bone density, -1 to -2.5 indicates osteopenia, and less than -2.5 indicates osteoporosis. Bioimpedance analysis was performed using the InBody 770 device (Inbody Co. Ltd, South Korea) with segmental assessment of body composition (arms, legs, trunk) with analysis of mineral mass (mM) and

BMC (Bone Mineral Content) with individual ranking of the reference range and PBF (Percent Body Fat) analysis for assessment of deficiency states (with a reference range of 10-20%).

Blood tests were conducted at the OLIMP clinical diagnostic laboratory, one of the leading laboratory diagnostic companies in the Republic of Kazakhstan (RK), which meets international quality control criteria and is a leader in laboratory accreditation according to ISO 15189. Levels of ionized calcium and 25(OH) vitamin D were analyzed. Data triage was conducted by using established reference values. The reference interval for ionized calcium was in the range of 1.17-1.29 mmol/L. Reference values for 25(OH) vitamin D levels in persons up to 22 years of age were interpreted as follows: <15 ng/ml - deficiency, ≥15 to <20 - insufficiency, ≥20 to <100 - normal, and above 100 - risk of a toxic effect. For persons aged over 22 years: <20 ng/ml - deficiency, ≥20 to <30 - insufficiency, ≥30 to <100 - normal, more than 100 - risk of a toxic effect. Gene polymorphism analysis was performed by the TreeGene genetic laboratory during the collection of buccal epithelial samples by the INVIVO laboratory. Polymorphisms of genes associated with bone tissue remodeling were analyzed (COL1A1 rs1800012 (genotypes CC, CA, AA); COL5A1 rs12722 (CC, CT, TT); VDR rs731236 (AA, AG, GG), IGF1 rs35767 (AA, AG, GG), PPARGC1A rs8192678 (C/C, C/T, T/T)).

In cases where abnormalities in vitamin D levels were detected, athletes were referred for consultation with an endocrinologist and received corrective pharmacotherapy (cholecalciferol), in accordance with clinical protocol for the treatment of vitamin D deficiency in adults (ICD-10 code E55). All athletes with vitamin D deficiency or insufficiency were recommended 5,000 IU (10 drops) cholecalciferol daily or cholecalciferol 50,000 IU tablets once a week, administered with breakfast and a small amount of water for three month.

IBM SPSS Statistics was used for statistical analysis. For normally distributed data, as assessed by the Kolmogorov-Smirnov test, values were presented as the mean values with standard deviation error and confidence intervals using. Comparisons of results were considered statistically significant at $p \leq 0.05$, with a statistical trend present at $p \leq 0.1$. Descriptive statistics for the parameters included the percentage of feature occurrence, and relationships were assessed using the Pearson correlation coefficient with Chaddock's correlation scale (0.1-0.3 = weak, 0.3-0.5 = moderate, 0.5-0.7 = significant, 0.7-0.9 = high, 0.9-0.99 = very high).

Results

No significant differences were found between the average densitometry values for the calcaneus of the right and left legs in athletes. The average densitometry values corresponded to osteopenia, the minimum values - to osteoporosis, and the maximum - to normal bone density: SOS - 1496.83 ± 1.73 m / s (1493.70-1499.96), with a median of 1492.20 m / s (1480.90; 1512.60), a minimum value of 1456.40 1561.0 m / s; BUA - 121.36 ± 1.69 (118.30-124.41), with a median of 121.00 (107.70; 134.0), a minimum value of 53.70 and a maximum of 176.80; BQI - 82.63 ± 1.80 (79.37-85.89) with a median of 77.90 (66.40; 98.20), a minimum value of 42.80 and a maximum of 136.80; T-score - on average -1.17 ± 0.10 (from -1.35 to -1.00), with a median of -1.40 (-2.00; -0.30), a minimum value of -3.30 and a maximum of 1.80; Z-score - on average -1.30 ± 0.11 (from -1.50 to -1.10), with a median of -1.60 (-2.30; -0.30), a minimum value of -3.60 and a maximum of 2.70.

47.93% of athletes had calcaneal osteopenia, and 11.24% had osteoporosis. Z-score values had a weak direct correlation with age ($r=0.249$, $p=0.014$). Z-score values showed a difference between the groups of team sports athletes (with lower values) and martial athletes ($p=0.047$, Fig. 1a).

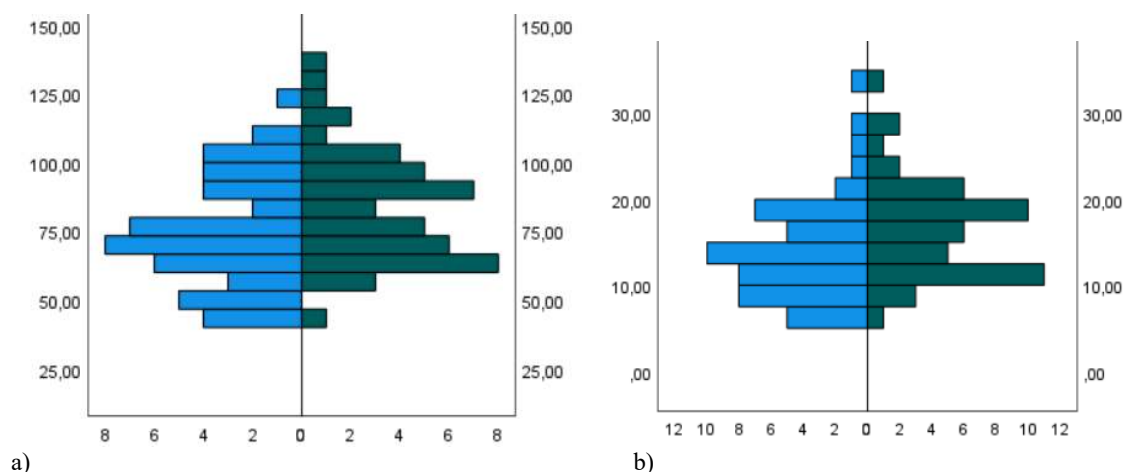
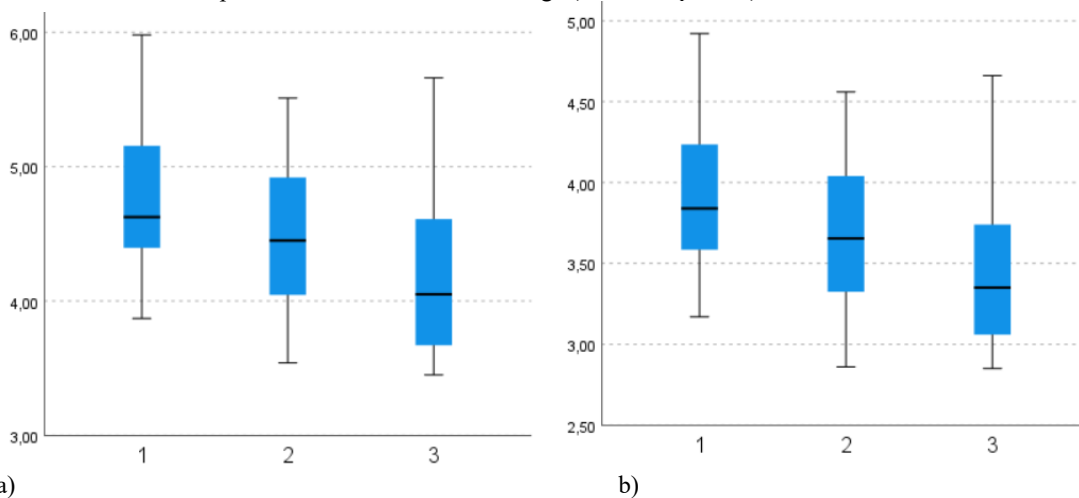


Figure 1: Comparison of Z-score (a) and PBF (b) between team sports athletes (1) and martial athletes (2) using the Mann-Whitney U test

None of the athletes showed a deficiency in mineral mass or BMC based on bioimpedance measurements. 55.67% of athletes exceeded the recommended individual mineral mass range by 0.03 to 0.93 kg. Similarly, 58.76% of athletes exceeded their BMC by 0.01 to 0.76 kg.

No significant differences in mean mineral mass and BMC were found between the team sport and martial athletes groups. A total of 17.53% of athletes had a fat mass deficit ranging from 5.1% to 9.6%, which may indicate a deficiency in energy reserves. PBF was above the reference range of 22.2% to 33.4% in 14.43% of athletes. PBF values differed between the team sport athletes (with lower values) and martial athletes groups ($p=0.030$, Fig. 1b). When comparing groups of athletes with established osteoporosis (3), osteopenia (2) and normal bone density (1), significant differences were found in the indicators of mineral content in the organism and bones (BMC) between the group with osteoporosis (with a lower content) and the group with normal bone density ($p=0.036$ and $p=0.044$, respectively, Fig. 2).

The average level of ionized calcium in athletes was closer to the lower limit of the norm (1.18 ± 0.01 mmol/l ($1.17-1.19$)) with a median of 1.18 (1.13; 1.21), a minimum of 1.06 and a maximum of 1.35 mmol/l). No significant differences in the average iCa level were found between the groups of team sports athletes and martial athletes. Calcium levels were below the norm in 41.96% of the subjects, and above it in 7.14%. There was a weak inverse dependence of calcium levels on age ($r=-0.222$, $p=0.03$).



a) b) Figure 2: Comparison of mineral content (a) and BMC (b) between athletes with normal bone density (1), osteopenia (2) and osteoporosis (3) using the Kruskal-Wallis test

The average 25(OH) vitamin D level in the studied athletes corresponded to the clinical deficiency threshold (20.80 ± 1.71 ng/ml; (95% CI 17.90-23.70), with a median of 17.70 (14.20; 23.45), a minimum value of 7.50 and a maximum of 54.60 ng/ml). No significant differences in the average 25(OH)D level were found in the group of team sports athletes and martial athletes. 54.55% of the studied athletes had 25(OH)D deficiency, and 27.27% had insufficiency.

An analysis of the correlations between the studied parameters revealed that ionized calcium levels had weak inverse relationships with bone mineral mass, bone mineral content, BQI, T- and Z-score, and densitometry results (Table 1). Thus, bone remodeling and calcium ion balance depends on bone formation and resorption processes. Bioimpedance parameters (mM, BMC) had a moderate direct relationship with densitometry parameters (BUA) and a weak direct relationship with BQI, T- and Z-score.

Table 1. Significant correlations between laboratory parameters, densitometry and bioimpedance data in athletes

Parameter	mM	BMC	BUA	BQI	T-score	Z-score
iCa	$r=-0.271$ $p=0.011$	$r=-0.266$ $p=0.012$	-	$r=-0.239$ $p=0.046$	$r=-0.249$ $p=0.037$	$r=-0.268$ $p=0.025$
mM	-	-	$r=0.348$ $p<0.001$	$r=0.224$ $p=0.027$	$r=0.221$ $p=0.030$	$r=0.211$ $p=0.038$
BMC	-	-	$r=0.345$ $p<0.001$	$r=0.223$ $p=0.028$	$r=0.219$ $p=0.031$	$r=0.206$ $p=0.042$

In a genetic study of the rs1800012 polymorphism of the COL1A1 gene in a group of athletes, the C/C genotype was dominant (Table 2). When studying the incidence of the COL5A1 rs12722 gene polymorphism in athletes, the heterozygous C/T variant was detected in more than half of the cases, with the C/C and T/T genotypes occurring in an average of a quarter of the cases. In a study of the VDR rs731236 and PPARGC1A

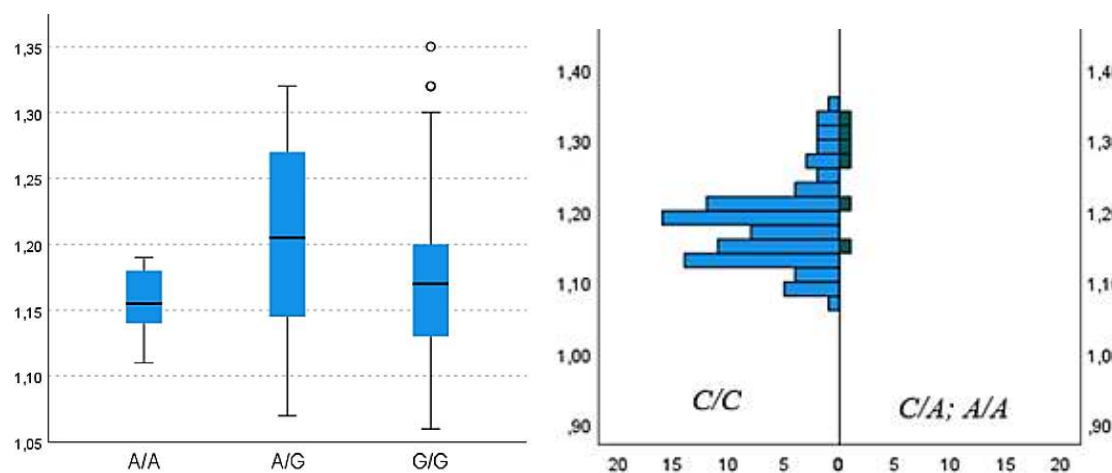
rs8192678 gene polymorphisms in athletes, homozygous A/A and C/C variants, respectively, accounted for approximately half of the cases, while the G/G and T/T genotypes were present in a minimal proportion of cases. The G/G genotype of the IGF1 rs35767 gene polymorphism was predominant.

Significant differences in genotype frequencies were identified for the groups of team sports and martial athletes for the COL5A1 rs12722 gene polymorphism (Mann-Whitney U test $p=0.028$), and for representatives of the Mongoloid and Caucasian races for the VDR rs731236 gene polymorphism (Mann-Whitney U test $p=0.004$).

Table 2. Genotype frequency (%) of gene polymorphisms associated with the functioning of the musculoskeletal system in athletes of the central region of Kazakhstan

Gene polymorphism	Allele	Team sports athletes, n=64	Martial athletes n=47	Representative s of the Mongoloid race, n=58	Representative s of the Caucasian race, n=53	Athletes, n=111
COL1A1 rs1800012	C/C	90,48	97,83	96,55	90,57	93,58
	C/A	6,35	2,17	3,45	5,66	4,59
	A/A	3,17	-	-	3,77	1,83
COL5A1 rs12722	C/T	63,49	43,48	55,17	60,38	55,05
	T/T	22,22	17,39	8,62	28,30	20,18
	C/C	14,29	39,13	36,21	11,32	24,77
VDR rs731236	A/A	46,03	65,22	68,97	37,74	54,13
	A/G	44,44	34,78	31,03	50,94	40,37
	G/G	9,52	-	-	11,32	5,50
IGF1 rs35767	G/G	71,88	73,33	62,07	83,02	72,48
	A/G	21,88	22,22	29,31	15,09	22,02
	A/A	6,25	4,44	8,62	1,89	5,5
PPARGC1A rs8192678	C/C	46,88	53,19	44,83	54,72	49,55
	C/T	46,88	38,30	43,10	43,40	43,24
	T/T	6,25	8,51	12,07	1,89	7,21

Differences in laboratory and densitometry parameters by genotype in athletes were identified for polymorphisms of genes regulating cell and tissue growth, metabolism, and collagen structure (Fig. 3). In the group with the A/G genotype, the level of ionized calcium in the blood was significantly higher than in the G/G group for the IGF1 rs35767 gene polymorphism. In athletes with the C/A and A/A genotypes, the level of ionized calcium in the blood was significantly higher than in the group with the C/C genotype for the COL1A1 gene polymorphism. Moreover, densitometry indices were, on the contrary, significantly lower in athletes with the C/A and A/A genotypes than in the group with the C/C genotype (BQI ($p=0.048$), T- and Z-score ($p=0.023$)). In athletes with the C/C genotypes, the blood 25(OH)D level was significantly higher than in the group with the C/T genotype according to the PPARGC1A gene polymorphism.



a) iCa, IGF1 rs35767 (A/G-G/G, $p=0,02$)

b) iCa, COL1A1 rs1800012 (C/C – C/A; A/A, $p=0,01$)

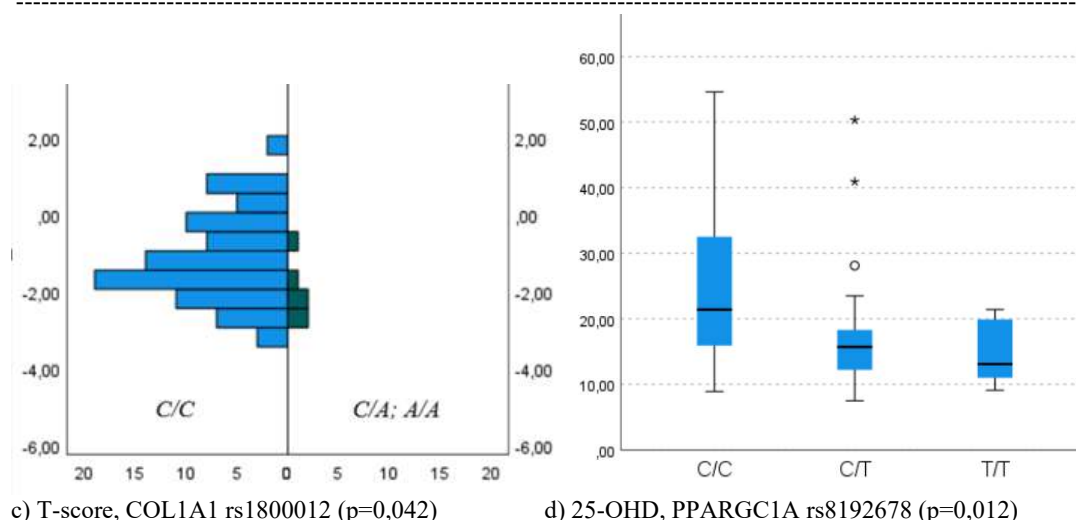


Figure 3: Comparison of laboratory parameters and densitometry parameters between gene polymorphism genotypes using the Kruskal-Wallis and Mann-Whitney U tests.

- a) Ionized calcium in IGF1 gene genotypes with the rs35767 polymorphism
- b) Ionized calcium in COL1A1 gene genotypes with the rs1800012 polymorphism
- c) T-score in COL1A1 gene genotypes with the rs1800012 polymorphism
- d) 25(OH)D in PPARGC1A gene genotypes with the rs8192678 polymorphism

When monitoring vitamin D levels in athletes diagnosed with hypovitaminosis in a month, its levels increased by an average of 1.51 ± 0.26 times (1.14-1.89), with a significant difference from the initial measurement ($p=0.018$). In 6.67% of athletes, vitamin D levels returned to normal, while in 40%, vitamin D levels transitioned from deficiency to insufficiency. When monitoring vitamin D levels one month after implementation of recommendations to improve its level, densitometry was also performed. There was no significant differences revealed between the initial and subsequent measurements, although the results tended to increase.

Dicussion

The results of the study confirm that bone remodeling in athletes is a multifactorial process influenced by both external and internal factors, including genetic predisposition, mineral and vitamin status, body composition, and nutrition. Average ultrasound densitometry values of the heel bones of athletes in Central Kazakhstan indicated osteopenia in 47.93% of participants and osteoporosis in 11.24%, which is consistent with previously published data on increased bone vulnerability during intense training and energy deficits (Gowers et al., 2025; Martínez-Noguera et al., 2023).

Literature data confirms a high risk of decreased bone mineral density in athletes with injuries in personal medical history. For example, USA athletes with previous injuries had a 4.6-fold higher risk of low bone mineral density (Tenforde et al., 2018). Significant physical activity during energy deficit leads to decreased bone mineral density in the spinal column and ribs. Decreased mineral density in the axial skeleton may reflect impaired calcium homeostasis. With predominant bone resorption, the calcium isotope composition in the blood and urine becomes lighter; homeostasis of calcium, as well as its entry into the bones and excretion, may be assessed by changes in $\delta^{44}/^{42}\text{Ca}$ in serum and urine (Coombs et al., 2025).

The widespread vitamin D deficiency among athletes may be due to depletion of vitamin D stores caused by its intense utilization during exercise. For example, a study of athletes from Hong Kong showed that 25(OH)D deficiency was more common among athletes engaged in strength sport compared to endurance athletes, due to higher vitamin D use and stores in skeletal muscle (Ip et al., 2022). Professional Italian football players had significantly lower 25(OH)D levels at the end of the season compared to its beginning (27.1 ± 5.9 vs. 36.6 ± 9.5 ng/mL, $p = 0.008$) and the prevalence of vitamin D deficiency increased from 25% to 73%. This led to the need for vitamin D supplementation to prevent hypovitaminosis and improve athletic performance (Filippella et al., 2020). In our study, mean ionized calcium levels were closer to the lower limit of normal (1.18 ± 0.01 mmol/L), and 25(OH) vitamin D levels corresponded to the threshold for clinical deficiency (20.80 ± 1.71 ng/mL). More than half of the participants had vitamin D deficiency. Correlation analysis revealed a weak inverse relationship between calcium levels, bone mineral mass and densitometry parameters, while bioimpedance data (mM, BMC) had a moderate to weak direct relationship with densitometry parameters (BUA, BQI, T- and Z-score), confirming the importance of energy status and body composition in maintaining bone mineral density.

Genetic analysis revealed a significant impact of gene polymorphisms involved in the regulation of bone remodeling to laboratory parameters and densitometry. Athletes with the C/A and A/A genotypes for COL1A1 rs1800012 had lower T- and Z-scores and BQI despite higher calcium levels. It confirms that collagen structure may determine bone quality independently of calcium homeostasis. The IGF1 rs35767 polymorphism was associated with variations in calcium levels, and the PPARGC1A rs8192678 polymorphism was associated with variations in 25(OH) vitamin D levels. These results are consistent with international data on the role of COL1A1, COL5A1, VDR, IGF1, and PPARGC1A in the predisposition to low bone density and musculoskeletal injuries (Jacob et al., 2022; Varley et al., 2018; Xu et al., 2024).

Numerous studies confirm the association of genetic variants with the risk of injury and impaired bone remodeling. Allelic ($p<0.001$), dominant ($p<0.001$), and heterozygous ($p=0.002$) models of COL1A1 rs1800012 are associated with an increased risk of osteoporosis and fractures in European population, while in North America significant association was found in the dominant ($p=0.035$) and heterozygous ($p=0.030$) models (Xu et al., 2024). The NOGGIN rs1372857-GG, COL5A1 rs12722-TT, IGF2 rs3213221-CC, and COL1A1 rs1800012-TT genotypes were associated with muscle, bone, tendon, and ligament injuries in Australian football players (Jacob et al., 2022). In British athletes with multiple stress fractures, homozygotes of the rare VDR rs731236 allele were associated with an increased risk of injury (Varley et al., 2018).

In addition to genetic factors, nutrition has a significant impact on bone mineral density. A study of Brazilian adolescent athletes showed that nutritional value, protein content, and total and fractional lipid intake, particularly mono- and polyunsaturated fatty acids, were predictors of bone mineral density in the ribs, lumbar spine, and femoral neck (Miranda et al., 2025). Therefore, a balanced diet rich in vitamins, minerals, and microelements, directed to prevention of bone mineral density decrease, is necessary for athletes throughout their professional career, sometimes in combination with vitamin D, calcium, magnesium, and phosphorus (Nikitina et al., 2025). In our study, all athletes with vitamin D deficiency or insufficient levels were recommended to receive cholecalciferol supplementation (5,000 IU daily or 50,000 IU weekly). A one-month follow-up showed a significant increase in 25(OH) vitamin D levels (an average increase of 1.51 ± 0.26 times, $p=0.018$), confirming the clinical effectiveness of this timely intervention. Post-treatment densitometry showed a trend toward improvement in mineral density, although the differences from baseline were insignificant.

Thus, integrating data on genotype, body composition, biochemical parameters, and nutrition allows us to predict the risk of decreased bone density and injury in athletes. These results highlight the need of personalized approach when planning training loads, developing nutritional support programs, and medical monitoring, including consideration of genetic polymorphisms, mineral and vitamin balance, and energy status. This comprehensive approach promotes optimal bone tissue adaptation to stress and reduces the risk of injury. Several limitations of this study should be noted. First, the sample size ($n=111$) limits the ability to detect weak genetic effects and conduct subgroup analyses by sport or age group. Second, cross-sectional measurements of densitometry and biochemical parameters do not allow to assess bone remodeling dynamics during the training season. Third, the genetic analysis was limited by selected polymorphisms of key genes, while other genes and variants influencing bone remodeling may have been overlooked. Finally, the influence of external factors — training load, sun exposure, nutrition, and physical activity level outside of training — was assessed indirectly and could have introduced additional variability into the results.

Conclusion

Average calcaneal densitometry values in athletes were consistent with osteopenia, more expressed in the team sports group, indicating bone remodeling associated with professional activity. Average ionized calcium levels in athletes were closer to the lower limit of normal, and average 25(OH) vitamin D levels in the studied athletes corresponded to the clinical threshold for deficiency. 17.53% of athletes had a deficient percentage of body fat, which may be associated with high physical activity, energy deficit, and overtraining.

Genotype-specific differences in ionized calcium levels and densitometry parameters among athletes were identified for polymorphisms of genes regulating cell and tissue growth (IGF1 rs35767), metabolism (PPARGC1A rs8192678), and collagen structure (COL1A1 rs1800012). These differences should be considered when planning training for professional athletes to reduce the risk of injury. The identified genotypes help in understanding the body's capabilities and minimizing the risk of complications associated with physical activity in professional athletes, as well as in developing individualized lifestyle and nutrition strategies tailored to these characteristics. For example, lower calcium levels were observed in athletes with the G/G and C/C genotypes of the rs35767 and rs1800012 polymorphisms, respectively. Furthermore, bone mineral density values were significantly lower in athletes with the C/A and A/A genotypes of the rs1800012 polymorphism, which may indicate different mechanisms of bone remodeling. Athletes with the C/T genotype of the rs8192678 polymorphism had lower blood 25-OHD levels, which may explain different vitamin D supplementation requirements. The identified clinical risk factors for injury in athletes (osteopenia, osteoporosis, hypovitaminosis and low calcium levels) should be monitored to ensure timely and effective correction.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors didn't use of AI in the writing of the article.

Conflicts of interest The authors declare no conflicts of interest.

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References

- Bouillon, R., Lips, P., Bilezikian, J.P. (2019). Vitamin D supplementation and musculoskeletal health. *Lancet Diabetes Endocrinol*, 7(2), 85-86. [https://doi.org/10.1016/S2213-8587\(18\)30348-6](https://doi.org/10.1016/S2213-8587(18)30348-6)
- Chen, Y.C., Zhang, L., Li, E.N., Ding, L.X., Zhang, G.A., Hou, Y., Yuan, W. (2017). Association of the insulin-like growth factor-1 single nucleotide polymorphisms rs35767, rs2288377, and rs5742612 with osteoporosis risk: A meta-analysis. *Medicine (Baltimore)*, 96(51), e9231. <https://doi.org/10.1097/MD.00000000000009231>
- Coombs, C.V., Capella, S., Taylor, N., Gifford, R.M., Eisenhauer, A., Kolevica, A., Heuser, A., Koivula, F., Greeves, J.P., O'Leary, T.J. (2025). Bone calcium balance following an Antarctic expedition. *J Appl Physiol.*, 139(6), 1687-1693. <https://doi.org/10.1152/jappphysiol.00849.2025>
- Ding, H., Deng, Q., Guo, Z. (2026). Genetic and epigenetic determinants of injury risk and recovery in elite athletes: toward precision sports medicine. *Gene*, 980, 149957. <https://doi.org/10.1016/j.gene.2025.149957>
- Filippella, M., Altieri, B., Falchetti, A., Cosso, R., Cena, H., Musso, C., Geronutti, E., Rassat, L., Cipriani, G., Colao, A., Di Somma, C., Faggiano, A. (2020). Bone metabolism, bone mass and structural integrity profile in professional male football players. *J Sports Med Phys Fitness.*, 60(6), 912-918. <https://doi.org/10.23736/S0022-4707.20.09913-2>
- Glinkowski, W.M., Żukowska, A., Glinkowska, B. (2023). Quantitative Ultrasound Examination (QUS) of the Calcaneus in Long-Term Martial Arts Training on the Example of Long-Time Practitioners of Okinawa Kobudo/Karate Shorin-Ryu. *Int J Environ Res Public Health*, 20(3), 2708. <https://doi.org/10.3390/ijerph20032708>
- Gowers, C.R., McManus, C.J., Chung, H.C., Jones, B., Tallent, J., Waterworth, S.P. (2025). Assessing the risk of low energy availability, bone mineral density and psychological strain in endurance athletes. *J Int Soc Sports Nutr*, 22(1), 2496448. <https://doi.org/10.1080/15502783.2025.2496448>
- Hoening, T., Ackerman, K.E., Beck, B.R., Boussein, M.L., Burr, D.B., Hollander, K., Popp, K.L., Rolvien, T., Tenforde, A.S., Warden, S.J. (2022). Bone stress injuries. *Nat Rev Dis Primers.*, 8(1), 26. <https://doi.org/10.1038/s41572-022-00352-y>
- Hoening, T., Hollander, K., Popp, K.L., Fredericson, M., Kraus, E.A., Warden, S.J., Tenforde, A.S.; Bone Stress Injury Authorship Group. International Delphi consensus on bone stress injuries in athletes. (2025) *Br J Sports Med.*, 59(2), 78-90. <https://doi.org/10.1136/bjsports-2024-108616>
- Hoshikawa, A., Nakajima, K., Okuwaki, T., Hangai, M., Aono, H., Ishizuka, S., Morioka, Y., Itou, S., Kawahara, T. (2024). Former Olympians had remained on high bone mineral density for a long period: Consecutive checkup of the 1964 Tokyo Olympic Japanese contestants for over 50 years. *Bone*, 187, 117203. <https://doi.org/10.1016/j.bone.2024.117203>
- Ip, T.S., Fu, S.C., Ong, M.T., Yung, P.S. (2022). Vitamin D deficiency in athletes: Laboratory, clinical and field integration. *Asia Pac J Sports Med Arthrosc Rehabil Technol.*, 29, 22-29. <https://doi.org/10.1016/j.asmart.2022.06.001>
- Jacob, Y., Anderton, R.S., Cochrane Wilkie, J.L., Rogalski, B., Laws, S.M., Jones, A., Spiteri, T., Hince, D., Hart, N.H. (2022). Genetic Variants within NOGGIN, COL1A1, COL5A1, and IGF2 are Associated with Musculoskeletal Injuries in Elite Male Australian Football League Players: A Preliminary Study. *Sports Med Open*, 8(1), 126. <https://doi.org/10.1186/s40798-022-00522-y>
- Martínez-Noguera, F.J., Alcaraz, P.E., Ortolano-Ríos, R., Marín-Pagán, C. (2023). One Season in Professional Cycling Is Enough to Negatively Affect Bone Health. *Nutrients*, 15(16), 3632. <https://doi.org/10.3390/nu15163632>
- Miranda, C.C., de Araújo Pinto, A., de Lima, T.R., Bim, M.A., Fernandes, R.A., Pelegrini, A. (2025). Association of Energy, Macronutrients, and Fiber Intakes with Bone Health in Adolescent Athletes. *Calcif Tissue Int.* 116(1), 118. <https://doi.org/10.1007/s00223-025-01430-5>
- Mountjoy, M., Ackerman, K.E., Bailey, D.M., Burke, L.M., Constantini, N., Hackney, A.C., Heikura, I.A., Melin, A., Pensgaard, A.M., Stellingwerff, T., Sundgot-Borgen, J.K., Torstveit, M.K., Jacobsen, A.U., Verhagen, E., Budgett, R., Engebretsen, L., Erdener, U. (2023). 2023 International Olympic Committee's (IOC) consensus statement on Relative Energy Deficiency in Sport (REDs). *Br J Sports Med.*, 57(17), 1073-1097. <https://doi.org/10.1136/bjsports-2023-106994>
- Nikitina, .K.I., Strelnikova, T.V., Vykhodets, I.T., Abramova, T.F., Nikitina, T.M. (2025). [The role of nutrition in the prevention of bone metabolism disturbances in high performance sports]. *Vopr Pitan.*, 94(1), 21-36. Russian. <https://doi.org/10.33029/0042-8833-2025-94-1-21-36>

- Raiser, S.N., Schroeder, A.N., Lawley, R.J., Tenforde, A.S. (2024). Bone health and the masters runner. *PM R.*, 16(4), 363-373. <https://doi.org/10.1002/pmrj.13175>
- Ra, S.G., Nakagawa, H., Tomiga, Y., Iizawa, H., Nakashima, S., Higaki, Y., Kawanaka, K. (2022). Effects of Dietary Vitamin D Deficiency on Markers of Skeletal Muscle Mitochondrial Biogenesis and Dynamics. *J Nutr Sci Vitaminol (Tokyo)*, 68(4), 243-249. <https://doi.org/10.3177/jnsv.68.243>
- Ryan-Moore, E., Mavrommatis, Y., Waldron, M. (2020). Systematic Review and Meta-Analysis of Candidate Gene Association Studies With Fracture Risk in Physically Active Participants. *Front Genet*, 11, 551. <https://doi.org/10.3389/fgene.2020.00551>
- Stankiewicz, B., Kochanowicz, A., Brzezińska, P., Niespodziński, B., Reczkowicz, J., Waldziński, T., Kowalik, T., Piskorska, E., Wędrowska, E., Antosiewicz, J., Mieszkowski, J. (2025). Single high-dose vitamin D supplementation impacts ultramarathon-induced changes in serum levels of bone turnover markers: a double-blind randomized controlled trial. *J Int Soc Sports Nutr*, 22(1), 2561661. <https://doi.org/10.1080/15502783.2025.2561661>
- Tenforde, A.S., Parziale, A.L., Popp, K.L., Ackerman, K.E. (2018). Low Bone Mineral Density in Male Athletes Is Associated With Bone Stress Injuries at Anatomic Sites With Greater Trabecular Composition. *Am J Sports Med*, 46(1), 30-36. <https://doi.org/10.1177/0363546517730584>
- Varley, I., Hughes, D.C., Greeves, J.P., Stellingwerff, T., Ranson, C., Fraser, W.D., Sale, C. (2018). The association of novel polymorphisms with stress fracture injury in Elite Athletes: Further insights from the SFEA cohort. *J Sci Med Sport*, 21(6), 564-568. <https://doi.org/10.1016/j.jsams.2017.10.038>
- Williams, K., Askew, C., Hughes, D., Guy, J.A., Jackson, Iii, J.B., Gauthier, C. (2025). Supplemental Vitamin D3 for the Prevention of Bone Stress Injuries in Collegiate Athletes. *Cureus*, 17(5), e83320. <https://doi.org/10.7759/cureus.83320>
- Xu, P., Wang, Y., Wu, X., Wang, W., Wang, Q., Lin, W., Zhang, Z., Li, M. (2024). The COL1A1 rs1800012 polymorphism is associated with osteoporosis or fracture risk: a meta-analysis of 30 studies. *Int J Burns Trauma*, 14(6), 148-159. <https://doi.org/10.62347/KKAM3344>
- Zouhal, H., Berro, A.J., Maliha, E., Khalil, N., El Khoury, G., Jayavel, A., Laziri, F., Saeidi, A., Laher, I., El Hage, R. (2024). Team Sports Practice and Bone Health: A Systematic Review and Meta- Analysis. *J Clin Densitom*, 27(4), 101508. <https://doi.org/10.1016/j.jocd.2024.101508>