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The importance of *NFκB1* rs4648068 and *RUNX2* rs7771980 polymorphisms in bone metabolism of postmenopausal Polish women

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ABSTRACT

Objectives: Osteoporosis is a multifactorial disease that causes a loss of bone density. However, genetic factors play an increasingly important role in its development. To thoroughly understand the molecular mechanisms, polymorphic variants of genes candidate for osteoporosis are still being sought. The aim of our study was to investigate the influence of *NFκB1* gene rs4648068 (A>G) and *RUNX2* gene rs7771980 (-1025T>C) polymorphisms on the risk of osteoporosis.

Material and methods: A group of 675 postmenopausal Caucasian women (109 women with osteopenia, 333 with osteoporosis and 233 with normal T-score) were examined. The bone mineral density (BMD) at the lumbar spine (L1-L4) was measured by dual energy x-ray absorptiometry (DXA). The analysis of *NFκB1* and *RUNX2* polymorphisms was performed using real-time PCR method.

Results: Analysis of *NFκB1* gene rs4648068 polymorphism showed that the GG genotype was slightly more frequent in the study groups compared to the control group. In the osteoporosis group, patients with the G allele in the genotype have lower bone mineral density values. For the *RUNX2* rs7771980 polymorphism, in women with osteopenia we observed an increased incidence of TC heterozygotes compared to the control group (29.40% vs 24.90%, $p > 0.05$), and in women with osteoporosis, the TT genotype was more common (78.70% vs 73.80%, $p > 0.05$). No correlation was observed between the genotypes and the clinical parameters.

Conclusions: The analysis showed no significant relationship between the genotypic distribution and the individual clinical parameters. However, it is suggested an association between the rs4648068 polymorphism of the *NFκB1* gene and an increased risk of developing osteoporosis.

Key words: osteoporosis; polymorphism; *NFκB1*; *RUNX2*; postmenopausal women

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INTRODUCTION

Osteoporosis is a multifactorial, chronic metabolic disease of the skeletal system. It is characterized by a progressive decrease in bone density (BMD), which leads to an increased risk of fractures [1]. Initially, it develops asymptomatically, there is a painless deterioration of the state of the skeletal system and destruction of bone mass. Osteoporotic fractures, caused as a result of light injuries, are usually the first noticeable symptom, indicating the very advanced disease [2]. The occurrence of osteoporosis depends on age,

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race, sex and ethnicity. The incidence increases with age; however, most cases are observed in patients over 70 years of age. Osteoporosis is more common in women, especially in postmenopausal women (postmenopausal osteoporosis). The greatest risk of developing osteoporosis was observed in Caucasian and Asian women [2, 3].

In order to determine the genetic basis for the development of osteoporosis, the single nucleotide polymorphisms involved in bone tissue metabolism, such as receptor activator for nuclear factor κ B (RANK), receptor activator for nuclear factor κ B ligand (RANKL) or other genes affecting ossification, are analyzed [4]. RANKL is a protein found on the surface of osteoblasts that participates in the formation of mature osteoclasts.

It binds RANK, located on the surface of osteoclasts, as a result of which these cells differentiate into mature multinucleated forms. Blocking RANKL prevents its attachment to a receptor that inhibits osteoclast maturation and bone resorption. The effect of the RANK and RANKL interaction is the activation of nuclear factor of activated T cells transcription complex 1 (NFATc1), nuclear factor κB (NFκB) i cellular Finkel-Biskis-Jinkins murine osteosarcoma (cFos/Fra-1) transcription factors. The NF-κB protein family regulates the expression of many genes involved in various immune and inflammatory response processes. It includes five transcription factors NF-κB1 (also named p50), NF-κB2 (or p52), RelA (or p65), RelB and c-Rel [5–7]. It is not known exactly how NFκB affects mature osteoclasts. It has been found in mice that the deletion of the gene encoding the NFκB transcription factor, more specifically the p50 and p52 subunits, is responsible for osteoclast-independent, rare, hereditary disease marbled bone called Albers and Schönberg disease or osteopetrosis [8, 9].

Another gene involved in bone formation is runt-related transcription factor 2 (RUNX2), located at the 6p21 locus. It contains two promoters P1 and P2 and seven exons and encodes two protein isoforms: RUNX2-I and RUNX2-II. It is a key transcription factor associated with osteoblast differentiation, RUNX2-I involved in the early stages of osteoclastgenesis, and RUNX2-II in the process of osteoblast maturation. Studies have shown that mice deficient of the transcription factor RUNX2 did not show complete bone formation, and craniofacial dysplasia (CCD) was observed in knockout heterozygous.

The aim of our study was to check whether selected polymorphisms *NFκB1* rs4648068 (A>G) and *RUNX2* rs7771980 (-1025T>C) are more common in postmenopausal women and whether they may predispose to the development of osteoporosis.

MATERIAL AND METHODS

A group of 675 postmenopausal Caucasian women with Polish origin was examined. The patients were divided into three groups: 109 women with osteopenia (mean age 53.24 ± 0.74 years), 333 with osteoporosis (mean age 56.06 ± 0.75 years) and 233 control group with normal T-score (mean age 53.38 ± 1.01 years). During the interview, information was obtained on illnesses, medications taken, patient's age, reproduction age, number of pregnancies and birth weight, and age of first and last menstruation. Women with ovariectomy and taking medicines which might influence the bone metabolism (hormone therapy, selective modulators of estrogen receptors) as well as women with diseases affecting the density and loss of bone mass were excluded from the study.

Bone mineral density (BMD) measurements were performed at the Densitometry Laboratory, Clinical Hospital No. 1, Pomeranian Medical University in Szczecin, using a densitometric apparatus — LUNAR DPX 100 (Lunar Corp., Madison, USA). Each woman was examined in the lumbar spine from L2 to L4 using DEXA (Dual Energy X-ray Absorptiometry). The study determined BMD, T-score and Z-score parameters, as well as the average BMD YA and AM for young-adult and age-matched. Based on the value of the T-score, women were classified into the group with osteopenia (–2.5 < T-score < –1), osteoporosis (T-score < –2.5) and with the correct T-score – control group (T-score > –1). The study was approved by Local Bioethical Committee of Pomeranian Medical University in Szczecin.

The genetic analysis was performed at the Department of Stem Cell and Regenerative Medicine, Institute of Natural Fibers and Medicinal Plants, Poznan. Genomic DNA was isolated from the blood using a commercial QIAamp Blood Kit (Qiagen GmbH, Hilden, Germany) according to the protocol. The LightCycler FastStart DNA Master HybProbe (Roche Diagnostics) and LightCycler®96 instruments were used for *NFκB1* and *RUNX2* genotyping. Determination of the *NFκB1* rs464806 polymorphism and the *RUNX2* rs7771980 polymorphism was performed using LightSNiP *NFκB1* and *RUNX2* (TIBMolbiol, Germany). PCR was carried out according to the manufacturer's protocol.

Data analysis was performed using SPSS Statistics 17.0 using one-way ANOVA test. The value of $p < 0.05$ was considered as statistically significant.

RESULTS

The characteristics of clinical parameters of the study groups and the control group in postmenopausal women was showed in Table 1. The differences in the T-score and Z-score values between the groups (osteoporosis T-score: –3.16 ± 0.06, Z-score: –3.57 ± 1.95, osteopenia: T-score: 1.83 ± 0.04, Z-score: 0.84 ± 0.08, control group: T-score: 0.08 ± 0.11, Z-score: 0.64 ± 0.20) were observed. Studies have shown a correlation between the patients' BMI and individual groups (osteoporosis: 23.79 ± 0.32, osteope-

Table 1. Characteristics of the study population (postmenopausal women with osteopenia, osteoporosis and normal T-score)

		Mean ± SEM	95% CI	
			Min	Max
T-score	Osteopenia*	–1.83 ± 0.04	–1.91	–1.75
	Osteoporosis	–3.16 ± 0.06	–3.28	–3.05
	Controls	0.08 ± 0.11	–0.15	0.30
Z-score	Osteopenia	–0.84 ± 0.08	–1.01	–0.68
	Osteoporosis	–3.57 ± 1.95	–7.46	0.32
	Controls	0.64 ± 0.20	0.24	1.04
Body mass [kg]	Osteopenia*	65.17 ± 1.00	63.20	67.14
	Osteoporosis	61.21 ± 0.94	59.35	63.07
	Controls	68.73 ± 1.49	65.75	71.71
Height [cm]	Osteopenia*	162.63 ± 0.45	161.74	163.52
	Osteoporosis	160.25 ± 0.53	159.20	161.30
	Controls	163.08 ± 0.74	161.61	164.55
BMI [kg/m^2]	Osteopenia*	24.64 ± 0.36	23.94	25.35
	Osteoporosis	23.79 ± 0.32	23.16	24.42
	Controls	25.88 ± 0.56	24.77	26.99
Age [years]	Osteopenia*	53.24 ± 0.74	51.78	54.69
	Osteoporosis	56.06 ± 0.75	54.59	57.54
	Controls	53.38 ± 1.01	51.36	55.40
Birth weight [g]	Osteopenia*	3226.79 ± 77.68	3067.39	3386.18
	Osteoporosis	3141.25 ± 134.08	2855.47	3427.03
	Controls	3628.95 ± 110.29	3397.23	3860.66
Years of reproduction	Osteopenia	36.20 ± 0.64	34.93	37.47
	Osteoporosis	35.62 ± 0.62	34.37	36.86
	Controls	36.38 ± 0.95	34.45	38.30
Age of first menstruation	Osteopenia	13.12 ± 0.31	12.50	13.74
	Osteoporosis	12.94 ± 0.27	12.40	13.47
	Controls	13.38 ± 0.33	12.70	14.05
Age of last menstruation	Osteopenia	49.21 ± 0.50	48.22	50.20
	Osteoporosis	48.16 ± 0.55	47.07	49.25
	Controls	50.17 ± 0.69	48.79	51.56
Number of pregnancies	Osteopenia	1.89 ± 0.10	1.69	2.08
	Osteoporosis	1.96 ± 0.14	1.69	2.22
	Controls	1.94 ± 0.04	1.64	2.24
Years after menopause	Osteopenia*	7.18 ± 0.11	5.63	8.74
	Osteoporosis	10.63 ± 0.08	9.21	12.06
	Controls	7.03 ± 0.08	5.02	9.05
BMD L2-L4 [g/cm^2]	Osteopenia	0.97 ± 0.20	0.93	1.01
	Osteoporosis	0.98 ± 0.81	0.95	1.00
	Controls	0.97 ± 1.00	0.93	1.01
BMD L2-L4 YA [%]	Osteopenia	80.90 ± 1.49	77.49	84.32
	Osteoporosis	81.28 ± 0.66	78.82	83.74
	Controls	81.02 ± 0.45	77.46	84.59
BMD L2-L4 AM [%]	Osteopenia	89.13 ± 0.74	85.50	92.76
	Osteoporosis	89.50 ± 0.32	87.07	91.94
	Controls	89.78 ± 0.36	85.88	93.67

*$p < 0.05$ — comparison between the groups with osteopenia/osteoporosis and normal T-score (one-way ANOVA); BMI — body mass index; BMD — bone mineral density

nia: 24.64 ± 0.36 vs control group: 25.88 ± 0.56, p < 0.05). A similar relationship was observed for birth weight (osteoporosis: 3141.25 ± 134.08 g, osteopenia: 3226.78 ± 77.68 g vs control group: 3628.95 ± 110.29 g, p < 0.05). Other clinical parameters do not differ significantly between the study groups and the control group.

The genotype distribution of the *NFκB1* (rs4648068) and *RUNX2* (rs7771980) polymorphisms between the groups was analyzed (Tab. 2 and 3). For the *NFκB1* rs4648068 polymorphism, no significant differences were observed between the genotypes in the individual groups. The GG genotype was slightly more frequent in the study groups than in the control group (osteoporosis 11.40%, osteopenia 10.10% vs control group 8.20%, p > 0.05). In the case of rs7771980 polymorphism of the *RUNX2* gene in women with osteopenia, a higher frequency of TC heterozygotes was observed compared to the control group (29.40% vs 24.90%, p > 0.05), and in the group with osteoporosis the most common was the TT genotype (78.70% vs 73.80%, p > 0.05). There was no statistically significant difference between the distribution of genotypes of the studied polymorphism in the control and tested groups. No correlation was observed between genotype occurrence and osteoporosis development.

In addition, an analysis of the correlation between the *NFκB1* rs464806 and *RUNX2* rs7771980 polymorphisms with clinical parameters was performed (Tab. 4 and 5). The analysis did not show any statistical significance between the genotypic distribution and the individual clinical parameters analyzed. In the case of the *NFκB1* polymorphism, lower BMI values were observed for patients with the G allele in the genotype in both osteopenia and osteoporosis. Patients with the GG genotype had a higher birth weight compared to the other genetic variants tested. It has been shown that women with the G allele in the osteoporosis group have lower bone mineral density values. It is suggested that the G allele in the genotype is associ-

Table 2. The frequency of alleles and genotypes of *NFκB1* polymorphism (rs4648068) in the group of women with osteopenia, osteoporosis and in the control group

	Osteopenia		Osteoporosis		Control	
	Observed value n (%)	Expected value (%)	Observed value n (%)	Expected value (%)	Observed value n (%)	Expected value (%)
Genotype						
AA	46 (42.20)	43.70	145 (43.50)	43.70	106 (45.50)	47.20
AG	52 (47.70)	44.80	150 (45.00)	44.80	108 (46.40)	43.00
GG	11 (10.10)	11.50	38 (11.40)	11.50	19 (8.20)	9.80
Total	109 (100%)	100.00	333 (100%)	100.00	233 (100%)	100.00
Allele						
A	144 (66.10)	–	440 (66.10)	–	320 (68.70)	–
G	74 (33.90)	–	226 (33.90)	–	146 (31.30)	–
Total	218 (100.00)	–	666 (100.00)	–	466 (100.00)	–

Table 3. The frequency of alleles and genotypes of *RUNX2* polymorphism (rs7771980) in the group of women with osteopenia, osteoporosis and in the control group

	Osteopenia		Osteoporosis		Control	
	Observed value n (%)	Expected value (%)	Observed value n (%)	Expected value (%)	Observed value n (%)	Expected value (%)
Genotype						
TT	77 (70.60)	72.76	262 (78.70)	78.15	172 (73.80)	74.50
TC	32 (29.40)	25.08	65 (19.50)	20.51	58 (24.90)	23.60
CC	0	2.16	6 (1.80)	1.35	3 (1.30)	1.90
Total	109 (100%)	100.00	333 (100%)	100.00	233 (100%)	100.00
Allele						
T	186 (85.30)	–	589 (88.40)	–	402 (86.30)	–
C	32 (14.70)	–	77 (11.60)	–	64 (13.70)	–
Total	218 (100.00)	–	666 (100.00)	–	466 (100.00)	–

Table 4. Characteristics of the postmenopausal women with normal T-score, osteopenia and osteoporosis taking part in the study of the rs4648068 polymorphism of *NFκB1* gene

Genotype	Mean ± SEM	Mean ± SEM	Mean ± SEM
	AA	AG	GG
Controls			
T-score	–0.11 ± 0.13	0.13 ± 0.19	0.83 ± 0.55
Z-score	0.51 ± 0.28	0.65 ± 0.30	1.17 ± 0.76
Body mass [kg]	66.44 ± 2.46	69.83 ± 2.08	75.40 ± 5.33
BMI [kg/m^2]	25.34 ± 0.83	26.45 ± 0.86	27.33 ± 2.41
Birth weight [g]	3587.50 ± 255.26	3.715.00 ± 70.10	3510.00 ± 141.77
BMD L2–L4 [g/cm^2]	0.98 ± 0.03	0.96 ± 0.04	1.03 ± 0.04
BMD L2–L4 YA [%]	81.64 ± 2.86	80.15 ± 2.90	85.25 ± 2.95
BMD L2–L4 AM [%]	91.23 ± 2.97	89.30 ± 3.39	91.00 ± 2.04
Osteopenia			
T-score	–1.79 ± 0.06	–1.80 ± 0.06	–1.90 ± 0.14
Z-score	–0.86 ± 0.14	–0.81 ± 0.13	–0.92 ± 0.18
Body mass [kg]	66.71 ± 1.94	64.52 ± 1.42	64.36 ± 1.88
BMI [kg/m^2]	25.19 ± 0.71	24.27 ± 0.49	24.43 ± 0.63
Birth weight [g]	3290.00 ± 129.25	3148.57 ± 119.18	3342.50 ± 156.70
BMD L2–L4 [g/cm^2]	0.93 ± 0.04	0.99 ± 0.03	0.99 ± 0.04
BMD L2–L4 YA [%]	77.82 ± 3.45	82.51 ± 2.53	82.50 ± 3.01
BMD L2–L4 AM [%]	86.33 ± 3.62	89.85 ± 2.60	92.00 ± 3.95
Osteoporosis			
T-score	–3.13 ± 0.08	–3.20 ± 0.09	–3.39 ± 0.21
Z-score	–1.71 ± 0.15	–6.10 ± 4.52	–1.37 ± 0.21
Body mass [kg]	62.58 ± 1.43	60.45 ± 1.54	57.57 ± 2.72
BMI [kg/m^2]	24.11 ± 0.47	23.52 ± 0.54	23.52 ± 1.08
Birth weight [g]	3220.00 ± 298.50	3010.00 ± 53.63	3600.00 ± 600.00
BMD L2–L4 [g/cm^2]	1.02 ± 0.03	0.96 ± 0.02	0.92 ± 0.02
BMD L2–L4 YA [%]	84.80 ± 2.35	80.16 ± 1.80	76.33 ± 2.00
BMD L2–L4 AM [%]	93.14 ± 2.39	88.24 ± 1.69	85.87 ± 2.28

Data are mean ± SEM values. None of the parameters showed any significant difference among the genotypes; *p value < 0.05; SEM — standard error of the mean; BMI — body mass index; BMD — bone mineral density

ated with an increased risk of developing osteoporosis and may predispose to its development. For the *RUNX2* polymorphism, no correlation between genotype and clinical parameter was observed.

DISCUSSION

Osteoporosis is a multifactorial disease associated with low bone mass and increased risk of fractures. However, the genetic factors may play a large role in its development. Despite ongoing research, little is known about the genetic mechanisms that control bone growth and formation. To thoroughly understand the molecular mechanisms, polymorphic variants of genes candidate for osteoporosis are still being sought [10]. In our study, the association of *NFκB1* rs4648068 and *RUNX2* rs7771980 polymorphisms with osteoporosis was analyzed. Based on the frequency distribution of individual genotypes and alleles, an attempt was made to determine the genotype or allele predisposing to this disease.

Analyzing the *NFκB1* A>G polymorphism, a slightly more frequent occurrence of the GG genotype was observed in women with osteopenia and osteoporosis compared to control group with normal T-score (osteoporosis 11.40%, osteopenia 10.10% vs control group 8.20%). Patients with the G allele in the osteoporosis group showed lower bone mineral density values, suggesting that the G allele is associated with an increased risk of developing osteoporosis. So far, the impact of the rs4648068 *NFκB1* gene polymor-

Table 5. Characteristics of the postmenopausal women with normal T-score, osteopenia and osteoporosis taking part in the study of the rs7771980 polymorphism of *RUNX2* gene

Genotype	Mean ± SEM	Mean ± SEM	Mean ± SEM
	TT	TC	CC
Controls			
T-score	0.04 ± 0.14	0.26 ± 0.23	–0.95 ± 0.35
Z-score	0.46 ± 0.26	1.01 ± 0.29	–0.35 ± 0.12
Body mass [kg]	66.80 ± 1.52	74.00 ± 3.95	76.00 ± 3.86
BMI [kg/m^2]	25.27 ± 0.59	27.95 ± 1.40	30.33 ± 1.12
Birth weight [g]	3582.14 ± 98.52	3812.50 ± 430.30	3550.00 ± 325.5
BMD L2–L4 [g/cm^2]	0.97 ± 0.03	1.00 ± 0.05	0.79 ± 0.04
BMD L2–L4 YA [%]	80.82 ± 2.23	83.92 ± 3.44	66.50 ± 2.45
BMD L2–L4 AM [%]	90.70 ± 2.27	91.25 ± 4.44	69.40 ± 3.12
Osteopenia			
T-score	–1.81 ± 0.05	–1.80 ± 0.08	–
Z-score	–0.88 ± 0.09	–0.74 ± 0.21	–
Body mass [kg]	65.70 ± 1.31	64.75 ± 1.87	–
BMI [kg/m^2]	24.88 ± 0.47	24.18 ± 0.66	–
Birth weight [g]	3189.52 ± 75.98	3338.57 ± 219.35	–
BMD L2–L4 [g/cm^2]	0.96 ± 0.02	0.97 ± 0.06	–
BMD L2–L4 YA [%]	79.94 ± 1.67	81.88 ± 4.80	–
BMD L2–L4 AM [%]	88.13 ± 1.78	89.62 ± 4.95	–
Osteoporosis			
T-score	–3.19 ± 0.07	–3.15 ± 0.11	–2.84 ± 0.05
Z-score	–4.16 ± 2.53	–1.68 ± 0.16	–0.72 ± 0.21
Body mass [kg]	61.23 ± 1.16	61.39 ± 2.03	57.50 ± 2.45
BMI [kg/m^2]	23.85 ± 0.38	23.71 ± 0.74	22.26 ± 0.67
Birth weight [g]	3095.00 ± 148.70	3410.00 ± 384.30	3050.20 ± 285.40
BMD L2–L4 [g/cm^2]	0.97 ± 0.02	1.02 ± 0.04	0.98 ± 0.14
BMD L2–L4 YA [%]	80.53 ± 1.40	85.27 ± 3.44	81.67 ± 11.70
BMD L2–L4 AM [%]	89.11 ± 1.42	92.91 ± 3.38	91.00 ± 8.74

Data are mean ± SEM values. None of the parameters showed any significant difference among the genotypes; *p value < 0.05; SEM — standard error of the mean; BMI — body mass index; BMD — bone mineral density

phism in the Caucasian group on the development of osteoporosis has not been analyzed. The NFκB transcription factor and its effect on the skeletal system are still under investigation. It has been discovered that the deletion of the gene encoding NFκB in mice, more specifically the p50 (NFκB1) and p52 (NFκB2) subunits, is responsible for rare, hereditary osteopetrosis [11]. Therefore, our studies were undertaken to look for a new genetic marker that could differentiate patients with an increased predisposition to developing osteoporosis.

For the rs7771980 polymorphism of the *RUNX2* gene, the TC genotype was more frequent in the osteopenia group compared to the control group, and the TT genotype was more common in the osteoporosis group. No correlation was observed between the genotype and the clinical parameters, which would indicate a predisposition to the development of osteoporosis. Bustamante et al. studied the effects of -330 G>T polymorphism in promoter P1 and -1025 T>C polymorphism (rs7771980) in promoter P2 of *RUNX2* in 821 Spanish postmenopausal women. The analysis showed that the -330 G>T polymorphism was not associated with any of the phenotypes analyzed, and the -1025 T>C polymorphism was associated with bone mineral density in the femoral neck (FN BMD). Patients with TC genotype had higher mean corrected FN BMD values than patients with TT genotype. No relationship was found between the -1025 T>C polymorphism and bone mineral density in the lumbar spine (LS BMD). Due to the small size of the

group with the CC genotype, no association with FN BMD was observed [12]. Lee et al. analyzed two *RUNX2* polymorphisms: -1492 A>T and -1025 T>C among 729 Korean postmenopausal women. In this study, no significant relationship between the -1492 A>T polymorphism and BMD was found. The analysis showed a significant relationship between the CC genotype and the reduced bone mineral density in the lumbar spine and femoral neck compared to TC heterozygotes and TT homozygotes [13].

In another study, Pined's team investigated the effect of -1025 T>C polymorphism (rs7771980) of the *RUNX2* gene on the development of osteoporosis in 776 Spanish postmenopausal women. Like earlier researchers, they observed the relationship of polymorphism with BMD FN, but not with BMD LS. Women with the TC genotype had a higher BMD FN than women with the TT genotype. Unlike previous researchers, they found a relationship between CC genotype and higher BMD FN than women with TT genotype [14].

In addition, various researchers suggest that several other *RUNX2* gene polymorphisms are associated with the development of osteoporosis. Auerkari et al. [10] studied the variability of -330 G>T (rs59983488) polymorphism in 180 Indonesian postmenopausal women. It has been shown that the TT genotype is associated with an increased risk of developing osteoporosis. Vaughan's team studied -336G>A polymorphism of the *RUNX2* gene in 991 Scottish postmenopausal women. Their data suggest that *RUNX2* alleles are associated with BMD in a manner dependent on menopause and body mass [16].

CONSLUSIONS

In conclusion, based on the literature data, no definite conclusions can be drawn. The *NFκB1* gene rs4648068 polymorphism has not yet been studied in connection with the development of osteoporosis. Our studies have shown that the G allele in the genotype is associated with an increased risk of developing osteoporosis and may predispose to its development. Probably the *RUNX2* gene rs7771980 polymorphism predisposes to the development of osteoporosis, but our studies have not confirmed this fact. Additional studies are required to confirm these relationships. All progress in this field has great potential, because understanding the mechanisms leading to the development of osteoporosis could allow the creation of effective therapies and the introduction of appropriate drugs. Early diagnosis of the disease and the implementation of appropriate treatment adapted to the genotype of patients can slow down or completely prevent its further development.

Conflict of interest

None.

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