



# Correlations between 10-year risk of death from cardiovascular diseases and 10-year osteoporotic fracture risk in postmenopausal women

Korelacja między 10-letnim ryzykiem zgonu z powodu chorób sercowo-naczyniowych i 10-letnim ryzykiem złamań osteoporotycznych u kobiet w okresie postmenopauzalnym

Anna Kawińska-Hamala<sup>1</sup>, Andrzej Kawiński<sup>2</sup>, Krzysztof Stanek<sup>3</sup>, Michał Stuss<sup>4</sup>, Ewa Sewerynek<sup>4</sup>

<sup>1</sup>Clinic of Electrophysiology, Medical University of Lodz, Poland

<sup>2</sup>Clinic of General and Colorectal Surgery, Medical University of Lodz, Poland

<sup>3</sup>Clinic of Endocrinology and Metabolic Disorders, Polish Mother's Memorial Hospital Research Institute in Lodz, Poland

<sup>4</sup>Department of Endocrine Disorders and Bone Metabolism, Medical University of Lodz, Poland

## Abstract

**Introduction:** Osteoporosis and cardiovascular diseases (CVD) are more common in the elderly population and have similar risk factors.

**The goal** was an evaluation of the correlation between 10-year risk of death from CVD and 10-year bone fracture risk (FRAX).

**Material and methods:** A total of 79 patients of the Regional Centre of Menopause and Osteoporosis of the Military Teaching Hospital in Lodz (Poland), aged 50–83 years, consulted for osteoporosis were divided into two groups: study group — with osteoporosis (O; T-score  $\leq -2.5$  SD) and control — without osteoporosis (T-sc  $> -2.5$ ). Bone mineral density was evaluated by densitometric scanning of spine (L2-L4 T-score) and/or femoral neck (Neck T-score) and/or total hip (Total Hip T-score). Total cholesterol (TC), fasting glucose, arterial blood pressure, medical history, and family history were obtained. The risk of fatal-CVD was assessed by Euro Heart Score (EHS), and major osteoporotic (MOFR) and hip fracture risk (HFR) by the FRAX scale.

**Results:** 80% of the patients (32/40) with osteoporosis and 51% (20/39) of the patients without osteoporosis revealed a HeartScore  $\geq 5\%$ . There was correlation in the group of all patients between EHS and Neck T-score ( $p < 0.05$ ; Spearman rank correlation coefficient (Rs) =  $-0.3806$ ), L2-L4 T-score ( $p < 0.05$ ; Rs =  $-0.2891$ ), and Total Hip T-score ( $p < 0.005$ ; Rs =  $-0.3561$ ), and in the control group — between EHS and Neck T-score ( $p < 0.05$ ; Rs =  $-0.3502$ ). There was a 2.33% difference between the average EHS level to the disadvantage of patients with osteoporosis ( $p < 0.05$ ). EHS positively correlated with MOFR ( $p < 0.001$ ) and HFR ( $p < 0.001$ ) in the whole study population and with MOFR ( $p < 0.05$ ) and HFR ( $p < 0.01$ ) in the group of osteoporotic patients. There were differences between groups in TC ( $p < 0.001$ ) and BMI ( $p < 0.001$ ) levels.

**Conclusions:** The 10-year risk of fatal-CVD correlated with osteoporosis and with the 10-year osteoporotic fracture risk. This conclusion may help identify patients who require extended cardiotherapy protocols. (*Endokrynol Pol* 2017; 68 (4): 390–397)

**Key words:** osteoporosis; cardiovascular diseases; fracture risk; fatal CVD; Euro Heart Score

## Streszczenie

**Wstęp:** Osteoporoza i choroby układu sercowo-naczyniowego (CVD) występują częściej w populacji osób w starszym wieku i posiadają podobne czynniki ryzyka.

**Cel:** Ocena korelacji pomiędzy 10-letnim ryzykiem zgonu z powodu CVD oraz 10-letnim ryzykiem złamań kości (FRAX) u pacjentów z osteoporozą.

**Materiał i metody:** 79 pacjentów z Regionalnego Ośrodka Menopauzy i Osteoporozy (Uniwersytecki Szpital im. WAM w Łodzi, Polska), w wieku 50–83 lat, konsultowanych pod kątem osteoporozy, podzielono na 2 grupy ze względu na badanie densytometryczne (T-score): grupa badana — z osteoporozą (O; T-score  $\leq -2,5$  SD) i kontrolna — bez osteoporozy (T-score  $> -2,5$ ). Uzyskano następujące informacje: wywiad medyczny, BMI, elektrokardiogram; za pomocą kwestionariusza: czynniki ryzyka osteoporozy, wywiad w kierunku chorób sercowo-naczyniowych m.in. udaru, zawału serca (MI), choroby niedokrwiennej serca (CAD), nadciśnienia tętniczego (HA), cukrzycy (DM), wywiad rodzinny w kierunku tych schorzeń. Dokonano także densytometrycznej oceny gęstości mineralnej kości (BMD): kręgosłupa (L2-L4 T-score) i/lub szyjki kości udowej (Neck T-score) i/lub całego biodra (Total Hip T-score). Ponadto, oznaczono poziom całkowitego cholesterolu (TC) i glukozy na czczo (GLU) w surowicy oraz zmierzono ciśnienie tętnicze krwi (BP). Ryzyko wystąpienia incydentu sercowo-naczyniowego zakończonym zgonem (Fatal CVD) oceniono przy pomocy skali Euro Heart Score (EHS) dla populacji polskiej. Ryzyko złamań oceniono przy pomocy skali FRAX dla całkowitego ryzyka złamań (Major Osteoporotic Fracture Risk — MOFR), oraz ryzyka złamań kości udowej (Hip Fractures Risk — HFR).

**Wyniki:** 80% pacjentów (32/40) z osteoporozą i połowa pacjentów bez osteoporozy (20/39) uzyskała HeartScore  $\geq 5\%$ . Wykazano istotną statystycznie negatywną korelację w grupie wszystkich pacjentów pomiędzy EHS and Neck T-score ( $p < 0,05$ ; Spearman rank correlation coefficient (Rs) =  $-0,3806$ ), L2-L4 T-score ( $p < 0,05$ ; Rs =  $-0,2891$ ), Total Hip T-score ( $p < 0,005$ ; Rs =  $-0,3561$ ), jak również w grupie kontrolnej tylko pomiędzy EHS and Neck T-score ( $p < 0,05$ ; Rs =  $-0,3502$ ). Stwierdzono również znamienne różnice pomiędzy średnim poziomem EHS w obu grupach



Anna Kawińska-Hamala, MD, Department of Endocrine Disorders and Bone Metabolism, Chair of Endocrinology, Medical University of Lodz, 90-752 Łódź, ul. Żeligowskiego 7/9, Poland, phone/fax: +48 (42) 63 93 127; e-mail: anna\_kaw@wp.pl

( $p < 0,05$ ) — 2,33%, na niekorzyść pacjentów z densytometrycznymi cechami osteoporozy. EHS pozytywnie korelowało z MOFR ( $p < 0,001$ ) i HFR ( $p < 0,001$ ) u wszystkich pacjentów. Ponadto zaobserwowano istotne korelacje pomiędzy EHS i MOFR ( $p < 0,05$ ) i HFR ( $p < 0,01$ ) w grupie pacjentów z osteoporozą. Obie grupy różniły się istotnie pod względem średnich poziomów TC ( $p < 0,001$ ) i wartości BMI ( $p < 0,001$ ).

**Wnioski:** Dziesięcioletnie ryzyko zgonu z powodów sercowo-naczyniowych korelowało z występowaniem osteoporozy oraz 10-letnim ryzykiem złamań osteoporotycznych. Wyciągnięte wnioski mogą pomóc w identyfikacji grupy pacjentów wymagających poszerzenia leczenia kardiologicznego. (*Endokrynol Pol 2017; 68 (4): 390–397*)

**Słowa kluczowe:** osteoporoza; choroby sercowo-naczyniowe; ryzyko złamań; FRAX; Euro Heart Score

## Introduction

The facts and statistics about osteoporosis in the world indicate that approximately 200 million people suffer from this medical condition, with a 15–30% male population above the age of 50 years and 30–40% postmenopausal women. Osteoporosis is a chronic disease, concomitant with other medical conditions, including coronary arterial disease (CAD), arterial hypertension (HA), and other cardiovascular disorders [1–8].

The incidence of both osteoporosis and CVD grows with age [2, 6]. Attention should be drawn to the observed coexistence of the same risk factors for osteoporosis and cardiovascular diseases, except the age, which include sedentary lifestyle, impaired lipid metabolism, tobacco smoking, and excessive alcohol consumption [5], similarly to the presence of the same proinflammatory markers (including CRP, IL6, TNF- $\alpha$ , and TNF- $\beta$ ) [2]. All this suggests a common pathophysiological mechanism, which may underlie both medical conditions.

It is an important fact that both osteoporosis and cardiovascular disorders are associated with a significant risk of disability and mortality, while only a few studies have attempted to analyse both diseases as related conditions [9–12].

Thus, the primary question was raised whether there was any relationship between the 10-year risk of death from cardiovascular diseases and the 10-year risk of osteoporotic fracture.

## Material and methods

The study comprised 79 patients of the Regional Centre of Menopause and Osteoporosis of the Military Teaching Hospital in Lodz (Poland), treated during the years 2009–2013, who signed an informed consent form.

The enrolled patients included postmenopausal women at the age of 50–83 years (the mean age: 67 years).

The patients were randomly assigned to the study and divided into two groups: a group with osteoporosis (40 patients) and a control group without osteoporosis (39 patients, including 29 with osteopenia and 10 healthy subjects). The division was made according to WHO criteria after densitometric scanning of the spine (T-score of lumbar spine [L2–L4]) and/or femoral neck (T-score of

Neck) and/or total hip (T-score of Total Hip), performed by dual-energy X-ray absorptiometry (DXA), where the T-score BMD  $\leq -2.5$  SD revealed osteoporosis. Patients who had T-score BMD from  $-2.5$  to  $-1.0$  SD were diagnosed to have osteopenia. The densitometer GE Lunar Prodigy was used. The minimum acceptable precision for technologists in our facility does not exceed the following values: 1.9% (LSC = 5.3%) for Lumbar Spine, 1.8% (LSC = 5.0%) for Total Hip, and 2% (LSC = 5.5%) for Femoral Neck.

Both groups were at similar ages, without any significant differences. The mean age of the patients with osteoporosis was  $68 \pm 6.8$  years (mean  $\pm$  SD) (56–80 years old; five patients below 60 years old) and of those without osteoporosis was  $66 \pm 7.8$  (mean  $\pm$  SD) years (50–83 years; eight patients below 60 years old).

The data were obtained from medical history. Two questionnaires and additional tests were carried out by means of ESC EuroHeart Score (EHS) [13, 14] and WHO FRAX score [15] requirements.

The acceptance of the Local Bioethical Committee was obtained before setting the study. Patients signed an informed consent form before the study.

## Questionnaires

Two questionnaires were employed: (1) cardiological, enquiring about tobacco smoking, diabetes mellitus (DM), hypertension (HA), ischaemic heart disease (IHD), and myocardial infarction (MI) and/or cerebral stroke, in the examined patients plus the incidence of the same diseases and sudden cardiac death (SCD) in the closest family members (father, mother, siblings); and (2) osteoporotic, where, among others, risk factors for osteoporosis were considered, comprising: occupational activity, manual work, tobacco smoking, coffee consumption, calcium supplementation, fractures in patient's medical history, fractures in family medical history, and chronic glucocorticosteroid (GCS) therapy.

## Additional procedures

Patient's height and weight were measured without shoes and in light clothes. A stadiometer SECA 206 was used to measure height. The arterial blood pressure — systolic and diastolic — was measured (on an arm after a five-minute rest) with a sphygmomanometer. BMI was calculated from body height and weight inputs.

ECG was taken by AsCARD Mr Silver ver. 2.24 (with particular attention paid to features of experienced myocardial infarction and features of ischaemia). Fasting glucose (measured by ContourTS glucometer) and total cholesterol levels (measured by MultiCareIn) were assayed in capillary blood by semi-quantitative method, prior to drug intake (off medications on the day when measurements were made; there was no long-time pause in drug intake).

### **EuroHeart Score**

The 10-year risk of death from cardiovascular diseases was assessed by means of the EuroHeart Score (EHS). The so-called high-risk card was used, which is adequate for countries of Central-Eastern Europe, including Poland. The scale took into account the following five parameters: sex, age, tobacco smoking, systolic blood pressure, and total cholesterol level. Scores  $\geq 5\%$  were regarded as high risk. EuroHeart Score is a broadly used scale recommended by the European Society of Cardiology [13, 14, 16].

### **FRAX Score**

Using the FRAX Score tool, the 10-year fracture risk was evaluated in two domains: major osteoporotic fracture risk (MOFR) and hip fracture risk (HFR), using the Poland-adjusted FRAX version. The scale considered 12 factors: age, sex, weight, height, fracture history, hip fractures in family history, actual tobacco smoking, GCS therapy, rheumatoid arthritis, secondary osteoporosis, alcohol consumption, and Femoral Neck DXA results. According to the Polish guidelines [15], values  $\geq 10\%$  of MOFR and  $\geq 3\%$  of HFR were interpreted as high. The FRAX Score scale is increasingly prevalent and its application is recommended in Poland [15].

### **Statistics**

The mean results were expressed as mean  $\pm$  SD. The level of statistical significance was set at  $p < 0.05$  (5%). Pearson's correlation coefficient ( $R_p$ ) and Spearman's rank correlation coefficient ( $R_s$ ) were used, where  $R = 0-1$  (strong —  $R = 0.5-1$ , weak —  $R = 0-0.5$ ) were assumed to be positive correlations. To check the correlation with 0/1 (absent/present) data the Mann-Whitney test was used.

## **Results**

### **Bone Mineral Density and T-score**

The mean T-score in the control group was  $-1.3 \pm 0.8$  (the lowest score at  $-2.2$  SD), while in the study group, the average and the lowest T-score values were  $-2.9 \pm 0.8$  and  $-4.9$  SD, respectively. The mean T-score in all examined sites (Neck, L2-L4, Total Hip) is presented in Table I.

### **Total cholesterol and BMI**

The mean TC levels significantly differed between the groups ( $p < 0.001$ ). Higher TC levels were observed in patients with osteoporosis (see Table I). The mean TC level value in the control group was  $194 \pm 28$  mg/dL, which was interpreted as slightly elevated (following the recommended by European Society of Cardiology (ESC) norm  $< 190$  mg/dL) [14]. Twenty-one patients obtained the TC levels  $\geq 195$  mg/dL, 4  $\geq 250$  mg/dL, while the mean TC level in the study group was definitely higher, amounting to  $233 \pm 52$  mg/dL (35 patients were  $TC \geq 195$  mg/dL, 13  $\geq 250$  mg/dL: two over 300 mg/dL, and one over 400 mg/dL). The highest TC values were also higher in the study group than in the control group (400 mg/dL and 252 mg/dL, respectively). Conversely, the mean BMI in the control group was  $27.6 \pm 3.5$  (which corresponds to overweight) and  $24.4 \pm 3.4$  in the study group (not exceeding the normal limits). The BMI levels significantly differed between groups ( $p < 0.001$ ).

### **Arterial pressure**

No significant differences were observed between the mean arterial pressure values (systolic and diastolic) (see Table I). However, higher maximal and minimal systolic and higher maximal and minimal diastolic pressure values were noted in the study group. It was most distinctive in the case of the maximal diastolic pressure, which was 106 mmHg in the control group and 138 mmHg in the study group (a difference of 32 mmHg) and, what is more important, in the course of CVD and for the maximal systolic pressure, where it was 202 mmHg in the control group and 223 mmHg in the study group (a difference of 19 mmHg).

### **Fasting glucose level**

An analysis of the mean fasting glucose level and DM occurrence did not indicate any differences between the two groups. The mean fasting glucose level was 94 mg/dL — equal in both groups (see Table I). In the control group there was statistically significant negative correlation between fasting glucose level and L2-L4 T-score ( $p < 0.05$ ;  $R_s = -0.5135$ ).

### **EuroHeart Score and FRAX Score**

The ESC score was significantly higher ( $p < 0.05$ ) in the osteoporotic group ( $7.95 \pm 5.7$ ) than in the control group ( $5.61 \pm 4.3$ ). The maximal EHS value in the group of patients with osteoporosis was 10% higher than in the group without osteoporosis (in the osteoporosis group the highest EHS was 30%, while in the control group it was 20%). None of the patients with osteoporosis obtained EHS  $< 1\%$  (i.e. low mortality risk). It is worth emphasising that 80% of the patients from the study

**Table I. Parameters: measured and calculated (mean  $\pm$  SD; in the upper part of the table) and obtained from Osteoporosis questionnaire (in %; in the lower part of the table). The  $p < 0.05$  (5%) was considered as statistically significant (marked with \*)**  
**Tabela I. Parametry: zmierzone i policzone (średnia  $\pm$  SD; w górnej części tabeli) oraz uzyskane z wywiadu zebranego za pomocą kwestionariusza (%; w dolnej części tabeli).  $p < 0,05$  (5%) — istotne statystycznie (zaznaczone przy użyciu \*)**

Type	Parameter	Control group	Osteoporosis group	p-value
Measured/calculated	<b>Mean <math>\pm</math> SD</b>			
	EHS [%]	5.61 $\pm$ 4.3	7.95 $\pm$ 5.7	< 0.05*
	MOFR [%]	5.53 $\pm$ 2.9	15.36 $\pm$ 11.0	< 0.001*
	HFR [%]	1.47 $\pm$ 1.8	8.61 $\pm$ 9.7	< 0.001*
	T-sc Neck	-1.2 $\pm$ 0.8	-2.4 $\pm$ 0.7	< 0.001*
	T-sc Total	-0.6 $\pm$ 0.9	-1.8 $\pm$ 0.9	< 0.001*
	T-sc L2-L4	-1.1 $\pm$ 1	-2.6 $\pm$ 0.9	< 0.001*
	Age [years]	66 $\pm$ 7.8	68 $\pm$ 6.8	NS
	BP systolic [mmHg]	135 $\pm$ 24.1	138 $\pm$ 20.9	NS
	BP diastolic [mmHg]	79 $\pm$ 11.2	80 $\pm$ 13.4	NS
	Fasting glucose [mg/dl]	94 $\pm$ 12.7	94 $\pm$ 24.8	NS
	TC [mg/dl]	194 $\pm$ 28.4	233 $\pm$ 52.0	< 0.001*
	BMI	27.6 $\pm$ 3.5	24.4 $\pm$ 3.4	< 0.001*
Obtained from questionnaires (towards osteoporosis and towards baseline heart events)	%			
	Tobacco smoking	18	25	NS
	GCS	5	13	NS
	Retired	87	78	NS
	Lack of physical effort	77	68	NS
	Coffee consumption	3	3	NS
	Diet low in calcium	21	18	NS
	Bone fractures	31	43	NS
	Bone fractures in family	18	13	NS
	Stroke	5	5	NS
	MI	13	3	NS
	CAD	31	28	NS
	HA	41	46	NS
DM	5	8	NS	
Obtained from questionnaire (family medical history)	Stroke in family	33	33	NS
	MI in family	23	28	NS
	CAD in family	51	50	NS
	HA in family	51	43	NS
	DM in family	33	23	NS
	SCD in family	16	23	NS

group demonstrated a high 10-year risk of death from cardiovascular diseases, while in the control group it was approximately 50% of the patients.

As we expected, the higher FRAX scores were noted in the group of patients with osteoporosis. The significantly higher values were present in both domains: MOFR ( $p < 0.001$ ), as well as HFR ( $p < 0.001$ ) (see

Table I). According to cut-off MOFR and HFR values, respectively, 60% and 85% of patients with osteoporosis revealed high fracture risk. The corresponding values in the control group were merely 8% and 10%, respectively. The differences between the mean FRAX scores were 9.5% and 8% in the MO and H domains, respectively.

### Correlation between EHS and T-score and FRAX

There were statistically significant negative correlations in the whole study population between EHS and Neck T-score ( $p < 0.005$ ;  $R_s = -0.3806$ ), and L2-L4 T-score ( $p < 0.05$ ;  $R_s = -0.2891$ ) and Total Hip T-score ( $p < 0.005$ ;  $R_s = -0.3561$ ) (see Fig. 1). We found also statistically significant negative correlation in the control group, but only between EHS and Neck T-score ( $p < 0.05$ ;  $R_s = -0.3502$ ) (see Fig. 2). In the study group, we did not observe any significant correlations between EHS and T-score values.

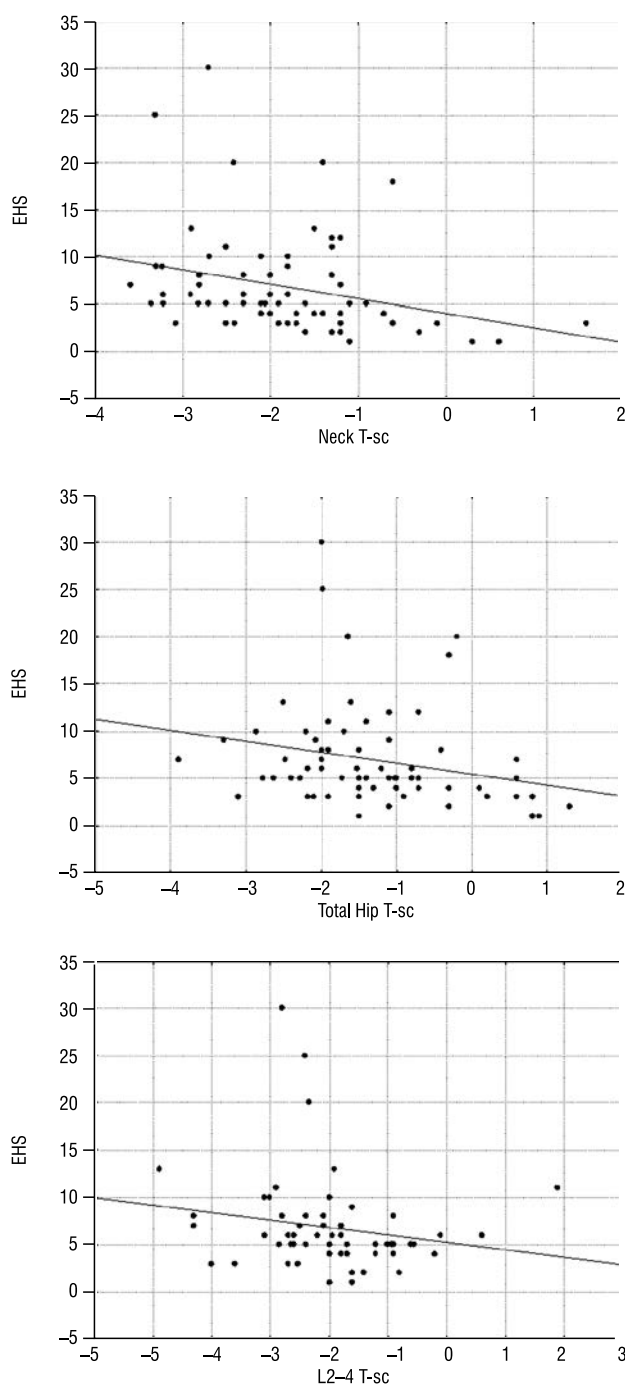
Statistical analysis revealed also a positive correlation between EHS and FRAX score in the whole study population in the MOFR domain ( $p < 0.001$ ;  $R_p = 0.3$ ) and in the HFR domain ( $p < 0.001$ ;  $R_p = 0.34$ ). We have also noticed a positive correlation between EHS and FRAX scores in the MOFR domain ( $p < 0.05$ ;  $R_p = 0.27$ ) and the HFR domain ( $p < 0.01$ ,  $R_p = 0.34$ ) in the study group. It should be noted that in the whole study population and in the group of patients with osteoporosis there was a stronger correlation between the 10-year cardiovascular mortality risk and the 10-year risk of hip fracture than between the above parameter and the 10-year risk of major fractures, the former being in a localisation typical for osteoporosis. We found no statistically significant correlations between EHS and fracture risk values in the control group.

### Cardiological history

We did not find any significant differences between the groups in terms of occurrence of DM, HA, and episodes of stroke or MI in the past. The data on myocardial infarction episodes were verified by ECG recordings. What is interesting, 100% of patients without osteoporosis after MI reported MI in the obtained history, while only one third of the patients with osteoporosis were aware of experienced MI.

There was statistically significant positive correlation between the presence of electrocardiographic signs of MI in the past and EHS in the control group ( $p < 0.05$ ;  $R_s = 0.3678$ ) and in the whole study population ( $p < 0.05$ ;  $R_s = 0.2806$ ). Due to the nature of the variables a Mann-Whitney test was performed, which showed that in both cases there was significant difference in the levels of EHS (Score) depending on the changes in ECG.

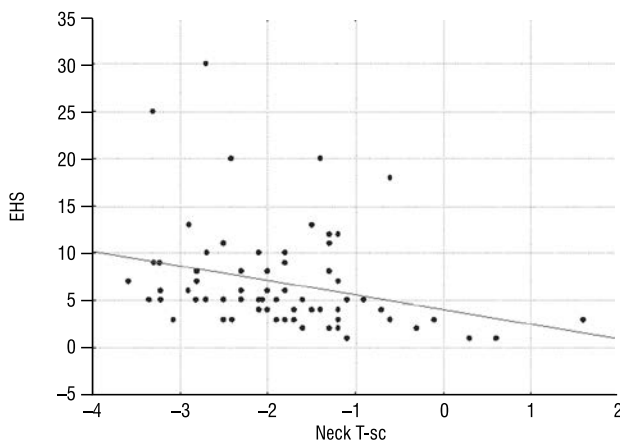
It should be emphasised that the statistical analysis revealed a higher correlation between the risk of mortality for CVD and the number of cardiovascular diagnosed diseases in the patients with osteoporosis than in those without osteoporosis. For example, the same risk of death (e.g., 5%) was found in case of the almost twice lower number of cardiological disorders in the patients with osteoporosis  $-0.4$  ( $p < 0.05$ ;  $R_p = 0.29$ ) than in those without osteoporosis  $-0.9$  ( $p < 0.001$ ;



**Figure 1.** Correlation between Euro Heart Score and Neck T-score ( $p < 0.005$ ;  $R_s = -0.3806$ ), Total Hip T-score ( $p < 0.005$ ;  $R_s = -0.3561$ ) and L2-L4 T-score ( $p < 0.05$ ;  $R_s = -0.2891$ ) in the group of all patients

**Rycina 1.** Korelacja między Euro Heart Score i Neck T-score ( $p < 0,005$ ;  $R_s = -0,3806$ ), Total Hip T-score ( $p < 0,005$ ;  $R_s = -0,3561$ ) i L2-L4 T-score ( $p < 0,05$ ;  $R_s = -0,2891$ ) w grupie wszystkich pacjentów

$R_p = 0.45$ ). There was also statistically significant positive correlation between EHS and cardiological history in the control group ( $p < 0.005$ ;  $R_s = 0.4983$ ) (see Fig. 3) and in the whole study population ( $p < 0.005$ ;  $R_s = 0.3599$ ).



**Figure 2.** Correlation between Euro Heart Score and Neck T-score in control group ( $p < 0.05$ ;  $R_s = -0.3502$ )

**Rycina 2.** Korelacja między Euro Heart Score i Neck T-score w grupie kontrolnej ( $p < 0,05$ ;  $R_s = -0,3502$ )

### Family medical history

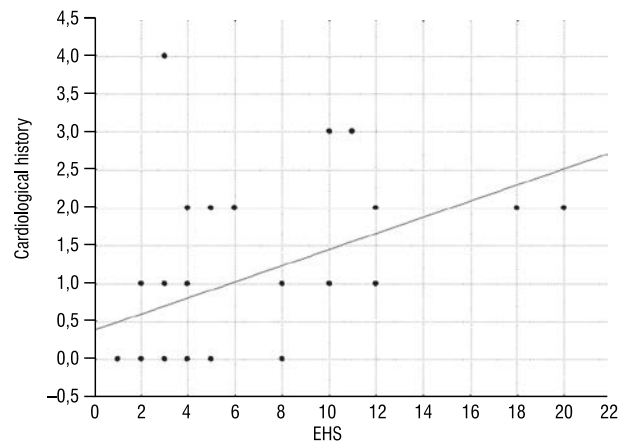
In the subpopulation of patients with osteoporosis we have observed a clear statistical trend to positive correlation ( $R_p = 0.1979$ ;  $p = 0.096$ ), between „better” (less positive) family history towards cardiological episodes (concerning almost all the discussed disease entities) and 10-year risk of fatal CVD.

### Medical history towards osteoporosis

After gathering medical history, we did not find any significant differences between the groups, according to the tobacco smoking, exposition to GCS, coffee consumption, calcium intake with diet, osteoporotic fractures, and bone fractures in family members. However, in the osteoporotic group, there was a higher percentage of patients supplemented with calcium compounds and exercising with physical effort on a daily basis. We were surprised to notice statistically significant positive correlation between L2-L4 T-score and medical history towards osteoporosis (number of osteoporotic risk factors according to a questionnaire) ( $p < 0.05$ ;  $R_s = 0.2636$ ) in the whole study population.

## Discussion

As has been demonstrated, low bone-mineral density (BMD) levels may be associated with cardiovascular diseases [2–4, 6, 7, 17, 18]. The results of our study confirmed higher 10-year risk of fatal CVD in patients with osteoporosis. Moreover, we found that as many as 80% of the patients with osteoporosis qualified to the high (> 5%) 10-year CVD mortality risk group, while in the group of non-osteoporotic patients only 50% of patients had high CVD mortality risk. A similar association



**Figure 3.** Correlation between Euro Heart Score and cardiological history (number of cardiological entities in history) in control group ( $p < 0.005$ ;  $R_s = 0.4983$ )

**Rycina 3.** Korelacja między Euro Heart Score i wywiadem kardiologicznym (liczba jednostek kardiologicznych w wywiadzie) w grupie kontrolnej ( $p < 0,005$ ;  $R_s = 0,4983$ )

between low BMD at the menopause and mortality from cardiovascular diseases can be found in literature [12]. After the MORE study some authors went a step further, describing a strong linear association between the severity grade of osteoporosis and future risk of cardiovascular events [11].

There were similar numbers of patients with HA as well as with DM in both groups (with no statistical significance). The literature reports broadly inform about higher incidence rates of osteoporosis in patients affected by arterial hypertension and type 1 diabetes mellitus [2, 3, 19] and about increased risk of bone fractures in patients with DM t. 2 [20] (RAC-OST-POL study showed also that diabetes t. 1 increased the risk of fall [21]) — in our study, probably, it would be easier to illustrate the difference in the case of a higher number of patients.

The literature reports a higher prevalence of ischaemic heart disease in patients with osteoporosis and osteopenia than in those without these two medical conditions [6]. The results obtained in our study are rather divergent regarding that particular aspect. According to medical history, IHD occurred with similar frequency in both groups of patients (as well as MI). What is interesting, 100% patients without osteoporosis after MI reported MI in the obtained history, while only one third of the patients with osteoporosis were aware of experienced MI (it could be suspected that those patients, being unaware of the cardiac medical condition, did not undertake any secondary prevention, which was associated with a much higher risk of fatal CVD outcome). CT-angiography of the coronary arteries, carried out in that group of patients, would be another important step towards evaluation of the incidence and progression of ischaemic disease.

Moreover, the statistically significant correlations were described between EHS and Neck, Total Hip, and Lumbar Spine (L2-L4) T-score in the whole study population and between EHS and Neck T-score in the control group. Neck T-score seems to be the most valuable predictor of fatal-CVD. What is more, the 10-year risk of fatal CVD risk, observed in that group of patients, significantly correlated with the 10-year risk of major fractures and hip fractures. We also found similar results in the literature: women with the highest risk of CVD have a higher risk of major osteoporotic fractures [10], which may be associated with the pathophysiological disorders common in both processes. A common pathogenesis of the two medical conditions may, for example, indicate mutual correlations of medicinal agents, exerted on particular disease entities. For example, anti-atherosclerotic statins influence BMD levels, while anti-resorptive bisphosphonates reduce the formation of arterial calcifications [18]. On the other hand, cardiovascular episodes are more frequently observed in patients on large-dose (1000–2000 mg) calcium supplementation — lower doses seem to be safe (800 mg should be adequate as long as optimal vitamin D levels are ascertained) [8].

In our study, higher total cholesterol levels (medium, maximal and minimal) were observed in the patients with osteoporosis, which may have supported atherosclerotic changes and atherosclerosis-related complications. Metabolic disorders find solid confirmation in literature reports, which bring up examples of cases with the elderly, in whom metabolic disturbances overtly correlated with atheromatosis and osteoporosis progression. That particular concomitance of medical conditions can be explained by the fact that dyslipidaemia (especially the rise of LDL, with a simultaneous fall of HDL) plays a major role in the process of atheromatous plaque formation (while simultaneously suppressing osteoblast activity in the osseous tissue), enhances calcification processes in vascular walls, and is associated with bone mass losses in postmenopausal women [2]. However, one article reports the opposite, with the suggestion that cholesterol levels in young and middle-aged patients do not appear to have long-term clinical implications for osteoporosis [22].

Statistical evaluation demonstrated higher fatal CVD risk in patients with osteoporosis vs. those without osteoporosis, while there were an equal number of cardiological diseases. It may suggest that, besides cardiological conditions, there might have been another CVD mortality risk factor in the study group, such as osteoporosis. This situation may, as emphasised in many studies, be influenced by the correlation between low bone mineral density and the occurrence of calcifications in arteries, in the aorta and in cusps of the aortal

valve, which is observed in postmenopausal women [1, 4, 7] (aortal calcification is an independent factor, predicting low BMD levels [7]). Another correlation has also been documented, namely that between decreased BMD and increased arterial stiffness, observed in hypertensive patients [3].

The higher cardiovascular death risk among the patients of the study group may suggest the presence of an additional risk factor, which is common for both osteoporosis and CVD. It is important here to consider osteoporosis and metabolic markers associated with this disease. It appears from the literature that the undertaken studies rarely evaluate bone metabolism markers with reference to ischaemic heart disease. It is postulated that multiple factors, e.g. osteoprotegerin, parathyroid hormone, phosphates, vitamins D and K, seem to be involved in both osteoporosis and CVD [23]. Only scarce reports indicate that osteoprotegerin most effectively illustrates the bone-arterial relationships [5, 18] and, while controlling osteoclast activity and functions, it also influences the process of calcification and atherosclerosis (90% of atherosclerotic plaques undergo calcification), being also associated with an increased risk of diabetes mellitus and death from cardiovascular disease [2]. It is also reported that BMPs (bone morphogenetic proteins), ALP (alkaline phosphatase), and OPN (osteopontin) — factors involved in osteogenesis — are correlated with vascular calcification [19]. In the literature there is also suggestion that osteocalcin is important not only for bones but also for glucose and fat metabolism [24].

In the osteoporosis group there was a higher percentage of patients supplemented with calcium compounds and exercising with physical effort on a daily basis. It may have resulted from compliance with medical recommendations in that particular condition — it might be obvious that those patients strictly undergo secondary prevention (but it might be also a paradox that active patients who supplement calcium have higher risk of osteoporosis).

## Conclusions

Summing up, in our study the high 10-year risk of death from cardiovascular diseases was more frequent in patients with osteoporosis, the mean 10-year risk of fatal CVD was higher in the group of patients with osteoporosis, and EHS negatively correlated with T-score of the Neck, Total Hip, and L2-L4 in the whole study population and with Neck T-score in the control group. The EuroHeart Score also correlated with the 10-year risk of major and femoral neck fractures in the whole study population and in the group of patients with osteoporosis. Besides, regarding this group, there

was a higher fatal CVD risk in those with osteoporosis vs. those without osteoporosis, with the same number of cardiological diseases in both groups. Taking into account the demonstrated correlations, basic cardiological diagnostic methods (ECG, lipids, arterial blood pressure) are suggested in patients with osteoporosis and, vice-versa, basic examinations towards bone metabolism disorders (total calcium and vitamin D levels) are recommended in cardiological patients because simple screening may help prevent potentially more serious consequences. A more detailed analysis of this issue is highly justified (mostly for the rather low number of patients in the presented study), although the indicated statistical significance and conformity with literature reports improve the reliability of the attained results. We are aware of the limitations of our study, especially the small number of patients in the study groups. This was a pilot study — it is planned to conduct the study on a greater number of patients in the future.

## References

- Cepollaro C, Monaco R, Marcucci G. Cosegregation of cardiovascular diseases and osteoporosis: instrumental diagnosis. *Clin Cases Miner Bone Metab.* 2008; 5(1): 40–44, indexed in Pubmed: [22460844](#).
- Danilevicius CF, Lopes JB, Pereira RMR. Bone metabolism and vascular calcification. *Braz J Med Biol Res.* 2007; 40(4): 435–442, indexed in Pubmed: [17401486](#).
- Masugata H, Senda S, Inukai M, et al. Association between Bone Mineral Density and Arterial Stiffness in Hypertensive Patients. *Tohoku J Exp Med.* 2011; 223(2): 85–90, doi: [10.1620/tjem.223.85](#).
- Rubin MR, Silverberg SJ. Vascular calcification and osteoporosis—the nature of the nexus. *J Clin Endocrinol Metab.* 2004; 89(9): 4243–4245, doi: [10.1210/jc.2004-1324](#), indexed in Pubmed: [15356015](#).
- Shen C, Deng J, Zhou R, et al. Relation Between Bone Mineral Density, Bone Loss and the Risk of Cardiovascular Disease in a Chinese Cohort. *The American Journal of Cardiology.* 2012; 110(8): 1138–1142, doi: [10.1016/j.amjcard.2012.05.053](#).
- Yesil Y, Ulger Z, Halil M, et al. Coexistence of osteoporosis (OP) and coronary artery disease (CAD) in the elderly: it is not just a by chance event. *Arch Gerontol Geriatr.* 2012; 54(3): 473–476, doi: [10.1016/j.archger.2011.06.007](#), indexed in Pubmed: [21723624](#).
- Wagenaar P. Osteoporosis: a cardiovascular risk factor equivalent to type 2 diabetes. *Cardiovasc J Afr.* 2010; 21(5): 295, indexed in Pubmed: [20972521](#).
- Meier C, Kränzlin ME. Calcium supplementation, osteoporosis and cardiovascular disease. *Swiss Med Wkly.* 2011; 141: w13260, doi: [10.4414/smw.2011.13260](#), indexed in Pubmed: [21882122](#).
- Farhat GN, Cauley JA. The link between osteoporosis and cardiovascular disease. *Clin Cases Miner Bone Metab.* 2008; 5(1): 19–34, indexed in Pubmed: [22460842](#).
- Makovey J, Macara M, Chen JS, et al. High osteoporotic fracture risk and CVD risk co-exist in postmenopausal women. *Bone.* 2013; 52(1): 120–125, doi: [10.1016/j.bone.2012.09.025](#), indexed in Pubmed: [23023015](#).
- Tankó LB, Christiansen C, Cox DA, et al. Relationship between osteoporosis and cardiovascular disease in postmenopausal women. *J Bone Miner Res.* 2005; 20(11): 1912–1920, doi: [10.1359/JBMR.050711](#), indexed in Pubmed: [16234963](#).
- von der Recke P, Hansen MA, Hassager C. The association between low bone mass at the menopause and cardiovascular mortality. *Am J Med.* 1999; 106(3): 273–278, doi: [10.1016/s0002-9343\(99\)00028-5](#), indexed in Pubmed: [10190374](#).
- Lloyd-Jones DM. Cardiovascular Risk Prediction: Basic Concepts, Current Status, and Future Directions. *Circulation.* 2010; 121(15): 1768–1777, doi: [10.1161/circulationaha.109.849166](#).
- Perk J, De Ba, Helmut G, et al. Europejskie wytyczne dotyczące zapobiegania chorobom serca i naczyń w praktyce klinicznej na 2012 rok. *Kardiol Pol.* 2012; 70(supl. 1): 1–100.
- Goncz G. Polskie zalecenia postępowania diagnostycznego i leczniczego w osteoporozie – podsumowanie aktualizacji 2013. *Med Prakt wyd specj Reumatologia.* 2013; 1: 33–46.
- Gierch M, Gierch J, Junik R. The evolution of lipid profile in patients with metabolic syndrome according to the cardiovascular risk calculated on the basis of SCORE chart. *Endokrynol Pol.* 2016 [Epub ahead of print] doi: 10.5603/EP.a.2016.0020, doi: [10.5603/EP.a.2016.0020](#).
- Sewerynek E, Stuss M, Sewerynek E, et al. Bisphosphonates and the risk of atrial fibrillation. *Endokrynol Pol.* 2011; 62(1): 93–96, indexed in Pubmed: [21365587](#).
- Hamerman D. Osteoporosis and atherosclerosis: biological linkages and the emergence of dual-purpose therapies. *QJM.* 2005; 98(7): 467–484, doi: [10.1093/qjmed/hci077](#), indexed in Pubmed: [15955801](#).
- Spirini D, Rini GB, Di St, et al. Correlation between osteoporosis and cardiovascular disease. *Clin Cases Miner and Bone Metab.* 2014; 11(2): 117–119, doi: [10.11138/ccmbm/2014.11.2.117](#).
- Miazgowski T, Krzyzanowska-Swiniarska B, Ogonowski J, et al. [Does type 2 diabetes predispose to osteoporotic bone fractures?]. *Endokrynol Pol.* 2008; 59(3): 224–229, indexed in Pubmed: [18615397](#).
- Pluskiewicz W, Adamczyk P, Czekajlo A, et al. Falls in RAC-OST-POL Study: epidemiological study in postmenopausal women aged over 55 years. *Endokrynol Pol.* 2016; 67(2): 185–189, doi: [10.5603/EP.a.2016.0015](#), indexed in Pubmed: [26884285](#).
- Samelson EJ, Cupples LA, Hannan MT, et al. Long-term effects of serum cholesterol on bone mineral density in women and men: the Framingham Osteoporosis Study. *Bone.* 2004; 34(3): 557–561, doi: [10.1016/j.bone.2003.11.024](#), indexed in Pubmed: [15003803](#).
- Lello S, Capozzi A, Scambia G. Osteoporosis and cardiovascular disease: an update. *Gynecol Endocrinol.* 2015; 31(8): 590–594, doi: [10.3109/09513590.2015.1041908](#), indexed in Pubmed: [26036806](#).
- Garanty-Bogacka B, Syrenicz M, Rać M, et al. Association between serum osteocalcin, adiposity and metabolic risk in obese children and adolescents. *Endokrynol Pol.* 2013; 64(5): 346–352, doi: [10.5603/EP.2013.0016](#), indexed in Pubmed: [24186590](#).