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Original Article

Evaluation of the Quality of Life and the Quality of Sleep of postmenopausal osteoporotic women, without evidence of an osteoporotic fracture, who attended an outpatient DXA scan service

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Abstract

Objectives: The present study aimed to investigate whether impairment of health-related quality of life (HRQOL) and possibly, the quality of sleep (Sleep Quality – SQ), of osteoporotic women, may occur, even before the onset of an osteoporotic fracture. **Methods**: The study included 109 women, divided (DXA) into two groups (age-matched): the Control Group (n=68; normal and osteopenic) and the Patient Group (n=41; osteoporotic). Review of medical history of the participants, was followed by evaluation of HRQOL and SQ with the EQ-5D-3L and the PSQI questionnaires, respectively. **Results**: There was no significant difference between the two groups (Control vs. Patient) in terms of average HRQOL and SQ, as measured by the EQ-5D-3L Questionnaire (0.73 vs. 0.70, p>0.05) and the PSQI Index value (5.56 vs. 6.29, p>0.05), respectively. A high percentage of patients was estimated as having a poor SQ (52.9% of the Control Group and 46.3% of the Patient Group, p>0.05). Increasing age, with or without the presence of osteoporosis, seemed to lead to worst QoL (OR<1.00, p<0.05). **Conclusions**: Our study documented homogeneity in HRQOL and SQ, between the two study groups. The strongest predictor for the HRQOL was age (for each year of age increase, the probability of excellent HRQOL significantly decreased).

Keywords: EQ-5D, PSQI, Health-related Quality of Life, Osteoporosis, Quality of Sleep

Introduction

Osteoporosis is a systemic skeletal disease, characterized by low bone mass and structural alteration of bone microarchitecture, both resulting to a decrease in bone strength and an increase in the risk of fractures[1]. The basic structural elements which determine bone strength are bone geometry, bone microarchitecture and bone size. However, 75-90% of the variability of bone strength is determined by Bone Mineral Density (Bone Mineral Density/BMD= the amount of mineral elements of the bone, per unit of its surface area)[2].

According to the World Health Organization (WHO), the diagnosis of osteoporosis in postmenopausal patients is based on the measurement of Bone Mineral Density (BMD), with the method of Dual Energy Photon Absorptiometry (Dual X-Ray Absorptiometry/DXA). According to the guidelines of the International Society for Clinical Densitometry (ISCD), measurement of bone density with DXA, includes the assessment of BMD in three anatomical regions (Lumbar Spine, Total Hip and Femoral Neck). The lowest T-score value

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is then used for the final diagnosis[3]. A T-score ≥-1.0 indicates normal bone density, a T-score <-1.0 and >-2.5 diagnoses osteopenia (low bone mass) and a T-score ≤-2.5 diagnoses osteoporosis[4].

Osteoporosis is the most common chronic metabolic bone disease and represents a very important health problem for the global community. Annually, more than 8.9 million osteoporotic fractures occur, which significantly burden the physical and mental health of the population, the quality of life, and life expectancy[5–7]. Most osteoporotic fractures are recorded in the European continent (34.8%)[7].

The most common sites of osteoporotic fractures are the hip, the lumbar spine, and the wrist. The above-mentioned fracture sites, share common epidemiological features: they are more frequent in women than in men, their frequency increases significantly as age progresses and they involve anatomical regions which are rich in cancellous bone[8]. Osteoporotic fractures may, also, involve other anatomic regions, including the humerus, the pelvis, and the ribs[2].

The term Quality of Life (QoL) is multidimensional, with various epidemiological, functional, economic, biomedical, and cultural extensions. The conceptual pluralism in the definition of QoL, is further enriched (or complicated), by the subjective considerations which result from personal preferences and perceptions[9]. In an attempt to limit the width of the definition, and advance research in the aspects of the QoL related to Health, the term "Health related Quality of Life" (HRQOL) was created. Although clearly limited compared to QoL, the definition of HRQOL still contains subjective elements and remains multilayered. The definition of HRQOL is "limited to the dimension of health and is determined by the effect of disease and treatment, on the individual's ability to perform daily functions"[10]. It should be noted that often, the terms QoL and HRQOL are often interchangeably used, denoting the same concept (usually, that of HRQOL)[11,12].

The term Sleep Quality (SQ) was firstly mentioned in the literature 110 years ago by Rowe[13]. Despite the fact that it has been frequently used in the literature, there is no commonly accepted definition[14]. SQ may be defined as the "satisfaction with the sleep experience, which incorporates elements such as sleep initiation, sleep maintenance, sleep duration and revitalization after awakening"[15]. SQ is a complex clinical tool, consisting of subjective and objective components[16]. The subjective part is summed up in the perceived experience of the patient, especially after waking up[17], while the objective part consists of the laboratory assessment of sleep (polysomnographic studies, sleep recording with portable devices), during which, in addition to sleep duration, various parameters are studied (alternation of sleep phases, latency of arrival, etc.)[17,18].

The aim of our study was to investigate whether osteoporosis, without a known osteoporotic fracture, could be related to the limitation of patients' QoL (HRQOL) and SQ. Regarding the first question, which was, whether osteoporosis could, even without the presence of fracture, affect patients' HRQOL, the literature is relatively poor. The few published studies include a small number of patients, and only a few of the studies are comparatives (e.g., Case - Control). Additionally, in many of them, patients with comorbidities are not excluded, so they have the potential of acting as confounding factors. The above conclusions are summarized in a comprehensive systematic review by Wilson and colleagues (2012)[19]. Regarding the second question, which was, whether osteoporosis can affect, even without the presence of fracture, the SQ of patients, the literature is extremely poor, which makes the present study particularly interesting. It is worth mentioning that sleep disturbances are now accepted to be causally related to low bone mass, and to the frequency of falls, because of which osteoporotic fractures are induced[20,21], which constitutes an inverse association of SQ, with osteoporosis and osteoporotic fractures.

Materials and Methods

Our study was a Case - Control Study, with an approximate 1:2 ratio and age-matched design, in which a total of 109 women were included: a group of 68 women (osteopenia/normal), constituting the Control Group, and a group of 41 women, with osteoporosis, constituting the Patient Group. The first group included women with a T-score >-2.5 and the second group, women with a T-score ≤-2.5.

The allocation of patients into groups was based on the result of their DXA bone density scan, which was performed with the Lunar DPX Pro machine (General Electric). The measurement, according to the International Society for Clinical Densitometry (ISCD) guidelines, included three anatomical locations in all patients (Lumbar Spine, Femoral Neck, Total Hip), and the final categorization was based on the lowest T-score value (according to the ISCD guidelines).

All the participants of the study were examined in two private Diagnostic Imaging Laboratories, in Heraklion, Crete – Greece, during the period between March 2022 - May 2022. Selection of the participants was random, based on the daily examination routine of the laboratories. Since both Imaging Laboratories constitute Primary Health Care Units, the consent of the Scientific Directors of the Laboratories was acquired.

All the participants of the study were postmenopausal, with no evidence or history of osteoporotic fracture and without any coexisting pathology or condition, which could be associated with a reduction of bone mineral density

The questionnaires used to evaluate HRQOL and SQ, were the EQ-5D-3L questionnaire (HRQOL) (https://euroqol.org/eq-5d-instruments/eq-5d-3l-about/) and the Pittsburgh Sleep Quality Index / PSQI (SQ)[22], respectively.

The questionnaires were completed by interview, with the assistance and guidance of the laboratory technologists, following verbal and written debriefing. Informed consent was obtained from all subjects for their participation in the study.

A thorough medical history was initially obtained to exclude women with a history of known osteoporotic fracture

Table 1. Descriptive statistics of the study groups / (Patient vs. Control Group), n=109.

		Groups			
		Patients		Control	
		n	%	n	%
n		41	37.6	68	62.4
Age, years	*mean (stand. dev.)*	64.9 (10.3)		61.8 (8.6)	
	46-64	21	51.2	42	61,8
	65-89	20	48.8	26	38,2
Body weight, kg	*mean (stand. dev.)*	64.7 (11.3) *		73.9 (14.7)	
Body height, cm	*mean (stand. dev.)*	156.8 (6.9)		158.2 (7.3)	
Body Mass Index, kg·m^{-2}	*mean (stand. dev.)*	26.4 (4.7) *		29.6 (5.9)	
	underweight (<18.5)	1	2.4	-	
	normal (18.5-24.9)	16	39.0	11	16.7
	overweight (25.0-29.9)	14	34.1	24	36.4
	obese (30.0+)	10	24.4*	31	47.0

*χ^2 and Student t test: * p<0,05.*

or significant findings / comorbidities which could potentially act as confounding factors, thus influencing the outcome of the study (including long corticosteroid intake, alcohol consumption, smoking history, family history of fracture, systemic diseases and causes of secondary osteoporosis).

For each participant, the date of birth and the basic anthropometric characteristics as weight (kg) and height (m) were recorded. Age (in years) and Body Mass Index (BMI) were then calculated (BMI=kg/m^2).

The EQ-5D-3L Quality of Life Scale (EuroQol five-dimensional questionnaire of three levels) was used to assess HRQOL[23]. This scale consists of two sections: 1) Functional evaluation of 5 health states, including Mobility, Selfcare, Activities of Daily Living, Pain-Discomfort & Anxiety-Distress, evaluated with a 3-point response scale, and 2) the Health State or EQ-VAS Index ("0-100 thermometer"), as currently perceived by the respondents, recorded on a 0-100 scale (EQ visual analogue scale, best state close to 100) (Calculating the U.S. Population-Based EQ-5D Index Score[24,25]. Response combination for each of the 5 conditions are recorded in Section 1 (e.g., 22222 is for the 2nd response in each of the 5 conditions where they state that they have a mobility problem or selfcare problem, etc.). For Section 2, based on the responses of Section 1, in accordance with the U.S. norms that have a range of 0.000-1.000, where values of 1.000 indicate the combination of responses 11111 (excellent health status or absence of functional or other health problem), a final score was calculated. Values <1.000 indicate abnormal levels or at least one problem in a health condition. The overall response consistency of the Scale was assessed with a Cronbach's coefficient as α=0.78.

The Greek version of the Pittsburgh Sleep Quality Index (PSQI) scale was used to assess SQ[22,26–28]. PSQI is a structured scale, which aims to assess SQ during for the last 30 days, consisting of 19 questions and defining 7 components: 1) subjective sleep quality (1 question), 2) sleep onset delay (2 questions), 3) sleep duration (1 question), 4) sleep efficiency (3 questions), 5) sleep disturbances (9 questions), 6) use of hypnotic drugs (1 question) and 7) daytime dysfunction (2 questions). Scoring of responses to each question and/or component spans a 4-point Likert scale, from 0 (never in the past month or very good) to 3 (3 or more times a week or very poor). Combined or stand-alone questions yield a summed total score (PSQI score), with a range of 0 (high sleep quality) to 21 (low sleep quality). A PSQI score score <5 reflects high or good SQ and a PSQI score ≥5 reflects low or poor SQ (higher scores reflect greater impairment of SQ). The overall response consistency of the Scale was assessed by Cronbach's coefficient as α=0.69.

Statistical analysis

Statistical analysis was performed using SPSS software (IBM Corp. Released 2021, IBM SPSS Statistics for Windows, v.28.0, Armonk, NY: IBM Corp.). Frequency distributions of the descriptive characteristics of the two selected Groups in the study were estimated. The χ^2 (Chi-square) and Student t tests as well as the relative of 95% confidence intervals (95% CIs) of comparative parameters were utilized for the comparisons of their baseline characteristics. The χ^2 method was also used for the categorical responses of the Pittsburgh Sleep Quality Index (PSQI) and Quality of Life EQ-5D-3L (EuroQol five-dimensional questionnaire of three levels) scales. For the comparison of the PSQI and EQ-5D-3L scores and the EQ-VAS scales of the two groups, Student t or Mann-Whitney methods were used (following assessment of their distribution using the Blom's method (QQ plot)). Finally, multiple logistic hierarchical regression was used to test their effect on excellent quality of life (versus low/moderate) in terms of characteristics, sleep quality and both study Groups. The acceptable level of significance was set at 0.05.

Table 2. Comparison of the frequencies of the responses of the 5 health states of the EQ-5D-3L HRQOL (EuroQol five-dimensional questionnaire of three levels) / (Patient vs. Control Group), n=109.

Health State	Responses	Groups				p-value
		Patients		Control		
		n	%	n	%	
1. Mobility	1. I have no problems in walking about	28	68.3	47	69.1	0.928
	2. I have some problems in walking about	13	31.7	21	30.9	
	3. I am confined to bed	-		-		
2. Self-care	1. I have no problems with self-care	40	97.6	67	98.5	0.715
	2. I have some problems washing or dressing myself	1	2.4	1	1.5	
	3. I am unable to wash or dress myself	-		-		
3. Usual activities (e.g.. work. study. housework. family or leisure activities)	1. I have no problems with performing my usual activities	40	97.6	61	89.7	0.128
	2. I have some problems with performing my usual activities	1	2.4	7	10.3	
	3. I am unable to perform my usual activities	-		-		
4. Pain/discomfort	1. I have no pain or discomfort	12	29.2	22	32.4	0.739
	2. I have moderate pain or discomfort	25	61.0	42	61.7	
	3. I have extreme pain or discomfort	4	9.8	4	5.9	
5. Anxiety/depression	1. I am not anxious or depressed	10	24.4	17	25.0	0.252
	2. I am moderately anxious or depressed	21	51.2	25	36.8	
	3. I am extremely anxious or depressed	10	24.4	26	38.2	

χ^2 tests.

Results

Descriptive statistics

In accordance with the inclusion criteria, which have been described above, 109 women participated in this study. Based on their DXA measurement, they were assigned into two groups: Patients (n=41) and Controls (n=68). Comparison of their anthropometric characteristics (age-matched) showed no significant difference of the mean age between the two groups (Patient Group and Control Group, 64.9 vs. 61.8 years, respectively, p>0,05). Weight comparison proved that the Patient Group had significantly lower mean body weight, compared to the Control Group (64.7 versus 73.9 kg, p<0.05), BMI (26.4 versus 59.6kg/m^2, p<0.05), or contained less than double the proportion of obese women (24.4% vs. 47.0%, p<0.05) (Table 1).

Table 2 summarizes the comparison of frequencies of responses of the 5 health conditions of the EQ-5D-3L QoL Scale (EuroQol five-dimensional questionnaire of three levels), between the two groups (Patient vs. Control), of the 109 women participating in the study. Each of the five health states, consists of three standardized responses and within them no significantly different frequencies of responses were found between the two groups (p>0.05). Analysis proves that 31.7% of the women in the Patient Group versus 30.9% in the Witness Group have some problems in walking (p>0.05), 61.0% and 61.7% respectively have moderate anxiety or sadness (p>0.05).

Responses of the five health states of the EQ-5D-3L HRQOL Scale define a combined framework of overall responses, which is presented in Table 3. Combination "11111" indicating the first responses of the five health states (no problem, difficulty, pain or anxiety) was found in 17.1% of the women in the Patient Group versus 10.3% in the Control Group. It is remarkable that combination "22222" or higher, was recorded in only 2.4% and 1.5% of the two groups, respectively, while that of "33333", indicating complete deterioration of the health states, was not recorded in any of the participants.

No significant difference of the mean scores of the EQ vas Index (EQ-5D-3L scale) (74.6 vs. 72.1, p>0.05) was found between the women of the two groups (Patient vs. Control), indicating similarly high levels of health. Moreover, statistical analysis of the calculated HRQOL Scale EQ-5D-3L, of the two groups (Patient vs. Control) of the 109 women participating in the study, was performed. As a higher EQ-5D-3L score (→1.000) determines a better quality of life, no significant difference in the mean scores of the groups was found (0.73 vs. 0.70, p>0.05). It is remarkable that a score of 1.000 (excellent quality of live) was only recorded in a low percentage of the participants (17.1% in the Patient Group vs. 10.3% in the Control Group), as summarized in Table 4.

Table 5 presents the frequency of the distribution of the scores of the 7 components of the Pittsburgh Sleep

Table 3. Frequency of combinations of responses to the EQ-5D-3L HRQOL Scale (EuroQol five-dimensional questionnaire of three levels) health states / (Patient vs. Control Group), n=109.

Response combinations of the five health states	Patient		Control	
	n	%	n	%
11111	7	17.1	7	10.3
11112	3	7.3	8	11.8
11113	2	4.9	5	7.4
11121	--		8	11.8
11122	11	26.8	6	8.8
11123	3	7.3	10	14.7
11133	2	4.9	--	
11222	--		2	2.9
11233	--		1	1.5
21112	--		1	1.5
21113	--		1	1.5
21121	2	4.9	1	1.5
21122	6	14.6	6	8.8
21123	3	7.3	7	10.3
21132	1	2.4	--	
21133	--		1	1.5
21221	--		1	1.5
21222	--		1	1.5
21232	--		1	1.5
22231	1	2.4	--	
22233	--		1	1.5

Table 4. Comparison of the EQ-5D-3L HRQOL Scale scores / (Patient vs. Control Group), n=109.

		Groups		p-value
		Patient	Control	
		mean (stand. dev.)		
HRQOL EQ-5D-3L		0.73 (0.20)	0.70 (0.19)	0.642
	low or average (<1.000)	n=34 or 82.9%	n=61 or 89.7%	0.305
	excellent (1.000)	n=7 or 17.1	n=7 or 10.3%	
Average score (in both groups) was 0.71 0.19. Mann-Whitney and χ^2 tests.				

Quality Index (PSQI) / (Patient vs. Control Group), n=109. As scoring of the components is determined by the individual or combined questions, of the 19-question scale, scoring range is from 0 (never had difficulties in the last month or very good sleep quality), to 3 (3 or more times a week or very poor). Statistically significant difference of the distribution of Subjective Sleep Quality was recorded: Patient Group showed a significantly higher frequency of having no difficulties or very good sleep quality (score 0: 48.8% vs. 22.1%, p=0.033), compared to the Control Group. In all other components of the questionnaire, no statistically significant difference was found / (Patient vs. Control Group), n=109 (p>0.05). High frequencies of the questionnaire values which indicate increased sleep difficulties or poor sleep quality (2 and 3), were not generally observed. Direct comparison of the overall Sleep Quality Index Scale (PSQI) scores did not prove any significant difference of the means / (Patient vs. Control Group), n=109 - (5.56 vs. 6.29, p>0.05). On the other hand, a high percentage of poor SQ (score 5.00+) was calculated in both groups (46.3% in the Patient Group versus 52.9% in the Control Group) (p>0.05) (Table 6).

Correlation based on logistic hierarchical regression of

Table 5. Comparison of the frequencies of scores of the 7 components of the Pittsburgh Sleep Quality Index (PSQI) / (Patient vs. Control Group), n=109.

		Groups				p-value
		Patient		Control		
		n	%	n	%	
Subjective Quality of Sleep *(extraction out of one question)*	0	20	48.8	15	22.1	0.033
	1	16	39.0	43	63.2	
	2	4	9.8	7	10.3	
	3	1	2.4	3	4.4	
Sleep latency *(2 questions)*	0	6	14.6	16	23.5	0.724
	1	16	39.0	23	33.8	
	2	13	31.7	19	27.9	
	3	6	14.6	10	14.7	
Sleep duration *(1 question)*	0	13	31.7	17	25.0	0.361
	1	20	48.8	33	48.5	
	2	7	17.1	10	14.7	
	3	1	2.4	8	11.8	
Habitual sleep efficiency *(3 questions)*	0	25	61.0	43	63.2	0.390
	1	5	12.2	13	19.1	
	2	7	17.1	10	14.7	
	3	4	9.8	2	2.9	
Sleep disturbances *(9 questions)*	0	1	2.4	1	1.5	0.457
	1	33	80.5	45	66.2	
	2	7	17.1	20	29.4	
	3	--		1	1.5	
	6	--		1	1.5	
Sleep medications *(1 question)*	0	37	90.2	57	83.8	0.789
	1	1	2.4	2	2.9	
	2	1	2.4	4	5.9	
	3	2	4.9	5	7.4	
Daytime dysfunction *(2 questions)*	0	27	65.9	38	55.9	0.599
	1	11	26.8	25	36.8	
	2	3	7.3	4	5.9	
	3	--		1	1.5	

χ^2 tests.

Table 6. Comparison of the Pittsburgh Sleep Quality Index (PSQI) scores / (Patient vs. Control Group), n=109.

		Groups		p-value
		Patients	Control	
		mean (stand. dev.)		
Sleep Quality Index (PSQI)		5.56 (3.15)	6.29 (3.37)	0.229
	good sleep quality (<5.00)	n=22 ή 53.7%	n=32 ή 47.1%	0.504
	poor sleep quality (5.00+)	n=19 ή 46.3%	n=36 ή 52.9%	

Mean score of all the participants, in both groups, was 6.02 3.29 or 50.5% with poor sleep quality. Mann-Whitney and χ^2 tests.

Table 7. Multiple logistic hierarchical regression of excellent HRQOL (versus low/moderate) in relation with the anthropometric characteristics (age, BMI) and SQ.

	HRQOL score - EQ-5D-3L excellent (1.000) vs. low/average (<1.000)					
	1st model			**2nd model**		
	Odds Ratio	**95%CI**	**p-value**	**Odds Ratio**	**95%CI**	**p-value**
Age (per year change)	0.92	0.85-0.99	0.039	0.92	0.85-0.99	0.047
BMI (per category change / 4 categories)	0.90	0.41-1.97	0.792	0.92	0.42-2.02	0.828
T-score value (per SD change)	0.61	0.29-1.31	0.208	0.73	0.23-2.34	0.596
Sleep Quality Index (PSQI) (poor quality vs. good quality of sleep)	0.59	0.17-2.03	0.402	0.60	0.17-2.06	0.412
Patient vs. Control Group (Patient vs. Control)	--			1.49	0.19-11.61	0.704
Pseudo R^2	*0.126*			*0.129*		
Two participants were excluded (weight and height missing).						

excellent HRQOL (versus low or/and moderate HRQOL) with anthropometric characteristics (age, BMI), T-score values, and SQ is presented in Table 7. According to the 1st model, where analysis is performed for the whole sample of women (both groups), there is a significant inverse association between age and excellent HRQOL, as it appears that, for each year of age increase, the odds of excellent quality of life decrease significantly (OR=0.92, p=0.039). According to the 2nd model, where the separation of the two groups (Patient vs. Control) is introduced, it appears that for each year increase of age, the odds for excellent HRQOL decrease significantly (OR=0.92, p=0.047). There is no significant association of body weight, T-score values, or Sleep Quality Index with excellent HRQOL (p>0.05).

Discussion

Our study was investigating the hypothesis that osteoporosis may be evident, even before an osteoporotic fracture happens. HRQOL and SQ disturbances are the parameters that were studied to test the hypothesis. Analysis of our data did not confirm this hypothesis, by documenting homogeneity in HRQOL and SQ between the osteoporotic women (without evidence of an osteoporotic fracture) and the normal/osteopenic women. Through multivariate correlations, it was found that for each year of age increase, for all women, the probability of excellent quality of life significantly decreases, thus younger age, with or without osteoporosis, is the strongest predictor for the HRQOL.

Literature evidence strongly supports that HRQOL in osteoporotic patients is significantly affected by the presence of osteoporotic fractures[28]. However, it remains uncertain whether HRQOL of osteoporotic patients without fracture, differs from that of subjects without osteoporosis[30,31]. Results of a systematic review were inconclusive - despite the fact that there is some evidence supporting the possible correlation of HRQOL with osteoporosis, without the presence of osteoporotic fracture, there are only limited Case - Control studies, directly comparing a group of osteoporotic women with a non-osteoporotic control group[32].

There is also concern, as it regards the analysis of the results of the studies which investigate HRQOL of osteoporotic patients. HRQOL assessment questionnaires, also assess the perception of the participants, with regard to the parameters they are examining. It is therefore possible that the result is influenced by the fact that the patient has a chronic condition, such as osteoporosis[29]. Even the DXA scan itself, despite being a well-tolerated, painless, and quick procedure, may, theoretically, affect the perception of HRQOL of the patients tested[33].

There is a scientific hypothesis that pain, is likely to pre-exist, even before the clinical appearance of an osteoporotic fracture. This is due to the presence of microscopic disruption of bone architecture (microfractures), which are not detectable by imaging, but are likely to affect the quality of life of osteoporotic patients due to the pain which they cause[29,34].

Confirmation of the above-mentioned hypothesis could result to a policy change, in terms of planning the allocation of health resources and funding, regarding a particularly important public health problem, as osteoporosis[35].

The association of sleep quality and osteoporosis is bidirectional. It is considered highly likely that sleep disturbances, through various pathogenic mechanisms are associated with BMD[36–38]. Particularly, regarding sleep duration, it is suggested by systematic reviews and meta-analyses of published literature, that both short (<6 h) and long (>8 h) sleep duration show an evaluable statistical association with osteoporosis[39,40]. At the same time, sleep quality disorders, directly result to an increase in falls and accidents, hence there is a direct association between sleep disturbances and fracture risk[20,41].

There is research interest regarding the mechanism through which, sleep disturbances, may cause impaired BMD, thus being associated with an increased fracture risk. Bidirectional relationship between osteoporosis and SQ has been limited to the association of osteoporosis with

chronic pain[42,43]. The fact that there may be a relationship between osteoporosis and pain, even in the absence of a diagnosed osteoporotic fracture, could, at least in theory, mean that there may, also, exist a direct relationship between osteoporosis (without fracture) and sleep quality. There is only one published study, with a small number of patients (59), investigating this association[44], which indicates that there is a correlation of osteoporosis, without fracture, with impaired SQ.

Control Group selection in the present study was based on the WHO guidelines for the epidemiological categorization of postmenopausal women screened by DXA, which is the gold-standard for the diagnosis of osteoporosis. On the basis of this categorization, osteoporosis is considered to be a discrete bone disorder (disease). Osteopenia (low bone mass), on the other hand, does not constitute a discrete bone disorder, but an epidemiological observation, therefore, the distinction between the two groups (Control Group and Patient Group), was made on the basis of the normal/abnormal result of the scan (normal/osteopenic vs. osteoporotic). The absence of osteoporotic fracture in both groups further enhances the distinction criteria, since the diagnosis of osteoporosis can be made even with normal BMD (T-score >-2.5), when there is evidence of an osteoporotic fracture.

Results of the statistical analysis of our studies, are summarized as follows:

- Patient Group had significantly lower mean body weight, BMI or less than twice the proportion of obese women ($p<0.05$), compared to the Control Group.
- The Patient Group, at a significantly higher frequency, compared to the Control Group, did not experience difficulties or had very good SQ ($p=0.033$). No significant difference was found in the other components of SQ ($p>0.05$).
- The overall score of the Sleep Quality Index Scale (PSQI) did not differ significantly between the two groups (Patient vs. Control) ($p>0.05$), while a high percentage of participants of both groups, demonstrated poor Sleep Quality (score 5.00+) (46.3% of the Patient Group vs. 52.9% of the Control Group, $p>0.05$).
- No significantly different response rates were found between the two groups ($p>0.05$), regarding the 5 health states of the EQ-5D-3L HRQOL Scale.
- Only a small percentage of the participants of both groups, in the EQ-5D-3L HRQOL questionnaire, revealed the response combination "11111", indicating no problem in any of the 5 health states, while the response combination "33333", which indicates severe problem, in all 5 health states, was not found in any of the participants of both groups.
- No significant difference, between the two groups (Patient vs. Control), in the mean score of the EQ vas Health Status Index was found ($p>0.05$), indicating similarly high levels of health in the two groups of women.
- With the higher EQ-5D-3L score ($\rightarrow$1.000) determining better HRQOL, no significant difference in the mean score was found between the two groups (Patient vs. Control) (0.73 vs. 0.70, $p>0.05$).
- Excellent HRQOL (score 1.000) was demonstrated by a low percentage of the participants in both groups (17.1% in the Patient Group versus 10.3% in the Control Group) ($p>0.05$).
- Through multivariate correlations, it was found that for each year of increasing age, in women of both groups (Patient vs. Control), the odds (probability) for excellent HRQOL significantly decreased (OR=0.92, $p=0.047$). On the other hand, body weight / BMI, T-score or Sleep Quality Index, were not significantly associated with excellent HRQOL ($p>0.05$).
- As a conclusion, younger age in women, with or without osteoporosis, formed the strongest predictor of their HRQOL.

On the basis of the above-mentioned findings, it was clear that there was no statistically significant difference of the HRQOL assessment indicators (EQ-5D-3L questionnaire), between osteoporotic patients and women of the control group. Similar results were obtained with the assessment of sleep quality with the PSQI questionnaire.

The fact that there was no statistically significant difference of the HRQOL between the two groups was not surprising (the opposite would not be surprising either), since, as has been mentioned, similar results were obtained from other published studies[45–47]. Of particular value, however, was the fact that there was no statistically significant difference in SQ, between the control group and the group of osteoporotic women, since the correlation of SQ and osteoporosis, represents a less studied field. It should, in fact, be noted that, between the two compared groups, the EQ-5D-3L questionnaire did not reveal any statistically evaluable differences of the factors which could potentially affect SQ (pain/discomfort and anxiety/sadness), and thus, interfere, as confounding factors, with the results of the study.

Of particular interest were, also, the additional statistical findings, which emerged from the statistical analysis of the data:

(1) The significantly lower mean body weight, BMI or less than twice the proportion of obese women ($p<0.05$), that was observed in the Patient Group. This confirmed, in essence, the statistical correlation between body weight and bone mass, highlighted in a series of studies. In fact, one element that has been recently added to the already known correlation between low body weight and osteoporosis, is the opposite: the correlation between obesity and osteoporosis, as shown by a series of recent scientific publications[48–53].

(2) The statistically proved association of HRQOL with aging. Through multivariate correlations, it was found that for each year of age increase, for all women, the probability of excellent quality of life significantly decreased, thus younger age, with or without osteoporosis, was the strongest predictor for the HRQOL. This means that research should be directed towards the investigation of the causative (aggravating) factors, and their early detection and treatment, in order to determine how to intervene, aiming to modify them, thus improving HRQOL in ageing individuals[54–57].

Among the advantages of the present study was the fact that it was a Case-Control study, since there are very few corresponding studies addressing the specific questions, under the conditions set by research, namely the absence of osteoporotic fracture and comorbidity. Also, the fact that it addressed questions of particular research interest, the answers of which, could direct to a different management and funding policies, for a major public health problem, as osteoporosis.

The main drawback of the present study was the small number of women participating in it (n=109). As a consequence, statistical correlations and trends obtained from the study, will need to be confirmed by larger studies (larger sample of patients and controls), also utilizing other questionnaires, in order to investigate extra parameters and potential correlations.

Conclusion

Our study documented homogeneity in HRQOL and SQ, between the osteoporotic women (without evidence of an osteoporotic fracture) and the normal/osteopenic women. The strongest predictor for the HRQOL was age (for each year of age increase, the probability of excellent quality of life significantly decreased).

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Ethics approval

The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Both Imaging Laboratories constitute Primary Health Care Units, so approval of the Scientific Directors (Dr Konstantinos Chlapoutakis, Dr Georgios Papamastorakis) was obtained.

Consent to participate

Informed consent was obtained from all subjects for their participation in the study.

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