

Osteoporosis-osteopenia and patients' quality of life: A systematic review

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ABSTRACT

Background: Osteoporosis is a systemic skeletal disease that affects over 200 million people worldwide, most of them women, during or after menopause.

Aim: The present study investigates the quality-of-life levels of patients with osteopenia and osteoporosis.

Material and method: A systematic search of the literature was performed in the PubMed and Scopus databases from October 18 to November 1, 2019.

Results: After the application of exclusion and admission criteria, 21 studies remained, in which a total of 18,525 people were evaluated. The majority of research has been done on postmenopausal women. The quality of life of women with osteoporosis and fractures was found to be lower, compared to the quality of life of women with osteoporosis and without fractures, but also compared to the quality of life of healthy women. No definite conclusions can be drawn about the extent to which osteoporosis and osteopenia affect patients' quality of life, with an absence of fractures, as systematic review studies have yielded conflicting findings. The areas of quality of life that seemed to be most affected in osteoporotic and osteopenic patients were mainly pain followed by social function, physical function and mental function.

Conclusions: Osteoporosis in the presence of fractures helps to reduce the quality of life of women suffering from the condition, but, in the absence of fractures, the effect of the condition remains unclear. More studies are needed to investigate the relationship between bone density and quality of life, but also to investigate the quality-of-life levels of men with osteoporosis. It is important for women with osteoporosis to be evaluated early for the risk of fracture, and to receive appropriate interventions.

Keywords: Osteoporosis, osteopenia, quality of life, life of people with osteoporosis, levels of quality of life.

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INTRODUCTION

Health-related quality of life is a multi-dimensional concept that reflects all aspects of individual well-being and how these aspects are affected by the existence of a disease. Osteoporosis, which this study focuses on, is a systemic disease characterized by low bone mass and deterioration of bone microarchitecture, with consequent increase in their fragility and

increased susceptibility to fractures¹. Osteoporosis, but also osteopenia, which is a precursor to osteoporosis characterized by low levels of bone density, currently affect more than 1/3 of postmenopausal women (IOF, 2019)² and its prevalence is more than three times higher in women than in men. Quality of life is an issue that has been frequently studied to date in patients with osteopenia and osteoporosis and previous



studies have found that the quality of life of patients with osteoporotic fractures is low compared to healthy individuals^{3,4}. The quality of life of patients with osteopenia or lower bone density than normal has not been studied to date in a systematic review. Specifically, the lack of a systematic research study into osteoporosis in Greece is obvious. Likewise, it is obvious that there is a serious lack of studies into the quality of life of men with osteoporosis⁵. It is glaringly obvious that there is an absolute necessity for such studies to be carried out. The aim of this study was to investigate the quality of life of patients with osteopenia and osteoporosis, regardless of the presence or absence of fractures, through the systematic search and study of the literature. Evaluating the quality of life in osteoporosis is important because it can predict the clinical course of the disease and the functional changes of patients with osteoporosis, as well as understanding the conditions that will lead to the development of better treatments for osteoporosis, thus improving the patient's health, reversing bone loss and reducing the risk of fractures.

MATERIAL AND METHOD

The following questions require to be answered:

[1] What are the quality-of-life levels of patients with osteopenia and osteoporosis with or without fractures?

[2] Is there a difference in quality of life between patients with osteopenia / osteoporosis with and without fractures?

[3] Which dimensions of quality of life are most affected in patients with osteopenia and osteoporosis?

It was decided to conduct a systematic literature review as an appropriate method to answer the questions. Specifically, the following steps were followed: 1) We searched the literature electronically, 2) We selected the studies that met specific criteria for admission and exclusion, and 3) We presented and carried out a comparative analysis of the results of the studies.

The research was conducted on electronic databases of scientific articles, specifically on PubMed and Scopus. In addition to the studies identified by the search in the above databases, the list of their bibliographic references was studied, in order to identify additional studies, which may not have been identified based on the search strategy followed. For the studies found in this way, their full text was searched in the Google Scholar database.

To search for the studies, a specific systematic search procedure was followed. The search terms were in English and were combined using logical Boolean operators (AND, OR). A set of search terms was used in more detail for each of the basic search topics, which are: 1) osteopenia and osteoporosis and 2) the

quality of life of patients. The search was carried out in the context of the Advanced Search of electronic databases. The search was carried out during the period October 18th 2019 to November 1st 2019.

RESULTS

Presentation of study results

The systematic search of the literature, led to the identification of 21 studies in which a total of 18,525 people is studied. 75% of these people were postmenopausal women (13,989 women), and only 6.2% were men (1,151). Of the 21 studies, only 1 investigated exclusively the quality of life of men with osteoporosis⁵. Among the others, 4 studied samples that included both men and women^{6,7,8,9} while the remaining 16 studied only women.

The scales most commonly used to assess the quality of life of patients with osteopenia and osteoporosis were QUALEFFO-41 (6 studies) and SF-36 (6 studies). Two studies used either OPAQ, ED-Q5, or a combination of QUALEFFO-41 and SF-36, respectively. The SF-12, mini-OQLQ scales, and in combination QUALEFFO-41 and ED-Q5, were used in one study each to assess the quality of life of patients with osteopenia / osteoporosis.

In terms of study design, the majority were synchronous studies (18 studies), while there were also two diachronic studies^{6,10} and one prospective study¹¹, in which no comparisons were made between groups. Among the

contemporary studies, two were done to study the validity and reliability of quality-of-life assessment tools^{12,5}. Three studies were also conducted to compare quality of life rating scales^{13,8,14}.

In the 20 systematic review studies, comparisons were made between groups. The groups that were compared were:

[1] Women with osteoporosis without fractures - women with osteopenia without fractures - women with normal bone density values^{15,16,17}.

[2] Women with osteoporosis and fractures - women with osteoporosis without fractures^{18,10,12,19,14}

[3] Women with osteoporosis and fractures - women with osteoporosis without fractures - healthy women^{20,21}

[4] Women with osteoporosis and fractures - women with osteoporosis without fractures - women with osteopenia and fractures - women with osteopenia without fractures - healthy women²²

[5] Women with osteopenia with wrist fractures - healthy women²³

[6] Women with osteoporosis regardless of the presence of fractures - women with osteopenia regardless of the presence of fractures - women with normal bone density values^{24,25}

[7] Osteoporotic women regardless of the presence of fractures - healthy women¹³

[8] Osteoporotic patients, men and women, with fractures - osteoporotic patients men and women without fractures^{8,9}

[9] Osteoporotic and osteopenic patients, men and women - healthy individuals ^{6,7}

[10] Men with osteoporosis without fractures - men with osteoporosis and fractures ¹²

Quality of life for women with osteoporosis / osteopenia without fractures

Four studies evaluated the quality of life of women with osteoporosis / osteopenia without fractures versus healthy women^{15,16,21,17} or the quality of life of osteoporotic women without fracture, versus osteopenic women with fractures⁸. Three of them found no differences in the quality of life of osteoporotic women without fractures, compared with healthy women (with normal bone density values), nor with women with osteopenia^{16,21,17} (respectively the levels of statistical significance were $p > 0.05$, $p < 0.01$, not recorded). Two studies found that the quality-of-life levels of women with non-fracture osteoporosis were lower than those of women with normal bone density values^{15,8} (statistical levels significance was respectively < 0.05 and in the second case not calculated).

Quality of life of patients with osteoporosis / osteopenia with and without fractures

A total of ten studies compared the quality of life of osteoporotic / osteopenic women with and without fractures and healthy women ^{18,23,10,20,12,22,21,17,19,14}

Eight studies compared the quality of life of osteoporotic women with fractures and those without fractures^{18,10,12,22,21,17,19,14} Among these, seven found statistically significant differences between the two groups of women, with osteoporotic women with fractures having statistically significantly lower living standards compared to osteoporotic women without fractures^{10,12,22,21,17,19,14}. In more detail, Ramírez Pérez et al.,¹² found that the quality of life of women with fractures was lower than that of women without fractures in the dimensions of pain ($p < 0.05$), physical function ($p < 0.01$), social function ($p < 0.01$) and mental function ($p < 0.05$), Romagnoli et al.,²² found that the quality of life of osteoporotic women with fractures was significantly lower than that of osteoporotic women without fractures, in the areas of physical function ($p = 0.002$), social function ($p < 0.001$) and general health ($p = 0.011$), Sallafi et al.,²¹ found that osteoporotic women with fractures had a significantly lower standard of living than osteoporotic women without fractures, in all areas of SF-36 ($p < 0.01$), Van Schoor et al.,¹⁴ found that the

quality of life levels of osteoporotic women with fractures were significantly lower than those without fractures in Eur ($p < 0.043-0.001$) and Silverman et al.,¹⁹ found that osteoporotic women with fractures had a significantly lower quality of life in terms of physical function, emotional state and clinical symptoms than osteoporotic women without fractures (all $p < 0.01$).

Only the study by Bianchi et al.,¹⁸ concluded the opposite result, i.e., that the quality-of-life levels of osteoporotic women without fractures were significantly lower than those of women with a history of fracture, in the areas of pain ($p < 0.005$) and general health ($p < 0.05$). However, it should be noted that in this study the women had a history of fractures and had received and completed their treatment for their fractures. Therefore, quality of life was not assessed at the time of fracture, as in the previous five studies. A single study found no differences in quality of life between osteoporotic women with fractures versus women without fractures, or those women who had healthy bone density²⁰. It should be noted that only women with thoracic fractures were evaluated in this study.

Two studies also made comparisons between patients, mixed men and women, with and without fractures^{8,9}. Statistically significant differences were found between the two groups in both, with osteoporotic patients

with fractures recording statistically significantly lower quality of life levels compared to osteoporotic patients without fractures [but also compared to osteoporotic patients without fractures]. In the research of Kwon et al.,⁹ this finding referred only to vertebral fractures. Specifically, osteoporotic patients with fractures recorded lower quality of life in all areas of EQ-5D, and this difference was significant only for vertebral fractures ($p = 0.0016$).

One study compared the quality of life of osteopenic patients with fractures versus healthy ones²³ and this study showed that osteopenic women with fractures recorded significantly lower quality of life levels compared with healthy ones, although they were evaluated only for wrist fractures. The areas affected were physical role limitations ($p = 0.014$), physical pain ($p = 0.025$) and vitality ($p = 0.015$).

Finally, one study¹¹, assessed the quality of life of osteoporotic women with fractures, however, no comparisons were made between groups. In this research the mini-OQLQ tool was used and the results showed that the quality-of-life levels of women with osteoporosis were moderate [(range 3.9-4.9)] and were lower in the areas of physical function and carrying out activities of daily living.

Quality of life of patients with osteoporosis / osteopenia regardless of the presence of a fracture

A total of five studies evaluated the quality of life of patients with osteoporosis / osteopenia, whether or not they had a fracture ^{24,25,13,6,7}. These studies evaluated the overall quality of life of osteoporotic patients versus osteopenic patients or healthy patients. Three of these were performed exclusively on women^{24,25,13} and two on men and women together ^{6,7}. Three studies in women have shown that the quality of life of osteoporotic women was statistically significantly lower than that of healthy women ^{24,25,13}. However, this finding was common in all three studies, only for the pain sector, as all three studies used the same quality of life assessment tool (QUALEFFO-41). Specifically, Baczyk et al.,²⁴ found that the quality-of-life levels of osteoporotic women were statistically significantly lower than those of healthy women only in the pain dimension ($p < 0.01$), while Baczyk et al.,²⁵ also found that this was true for the dimensions of social function ($p = 0.001$) and mental function ($p = 0.001$), while De Oliveira Ferreira et al.,¹³ found that this finding was important for all sectors of QUALEFFO-41 ($p = 0.012- 0.001$). In the other two studies in patients, mixed men and women with osteoporosis, it was also found that the quality of life of osteoporotic patients was statistically significantly lower than that of

healthy individuals ^{6,7}. In particular, Dennison et al., ⁶ found that the quality of life of osteoporotic patients was lower in the areas of physical function and general health, both for men ($p = 0.03$) and for women ($p > 0.05$), compared with healthy individuals, while Dhillon et al., ⁷ found that patients with osteoporosis recorded lower quality of life compared to healthy individuals in all areas of EQ-5D ($p < 0.01$).

Quality of life for men with osteoporosis

A total of five studies included evaluations of the quality of life of men with osteoporosis ^{6,7,8,9,5} although in four of these, results are mixed with those of women ^{6,7,8,9}. A study focusing exclusively on the male population⁵, showed that osteoporotic fractures worsen the quality of life of men with osteoporosis in all dimensions of the OPAQ assessed (physical function $p = 0.020$, emotional function $p = 0.009$ and symptoms $p = 0.004$). Men with osteoporosis without fractures were found to have higher levels of quality of life compared to men with osteoporosis with fractures.

In the research of Jahelka et al., ⁸ and Kwon et al. ⁹, in which the quality of life of both sexes was assessed, the percentage of men in the sample was much lower than that of women. In the research of Dhillon et al., ⁷ the percentage of men in the sample is not mentioned, while in the research of Dennison et al.,⁶ the percentages of men and women in

the sample were similar. In all four studies, the quality of life of people (men and women together) with osteoporotic fractures was statistically significantly lower than that of people with osteoporosis without fractures, and also lower than that of patients with osteopenia. None of these studies, however, assessed the differences between the sexes, nor did they provide separate results for men and women.

Areas of quality of life most affected in patients with osteoporosis and osteopenia

In order to study which areas of quality of life are most affected in patients with osteoporosis and osteopenia, the results were analyzed based on the scale used in each study to assess the quality of life.

The QUALEFFO-41 scale was used in a total of 9 studies^{16,24,25,18,13,8,14,12,22}. The pain dimension was found to be affected in eight of the nine studies and was the only one found to be affected in Baczyk et al's research²⁴ for osteoporotic / osteopenic women regardless of fracture ($p < 0.01$). Only in the research of Romagnoli et al.,²² the quality of life of women with fractures was not affected in the dimension of pain. Three studies found that the quality of life of patients with osteopenia and osteoporosis and fractures was affected in all areas of QUALEFFO-41^{13,8,14}. Three studies found that the quality of life of patients with osteoporosis was affected in

three areas of QUALEFFO-41. The only common area between these three studies was social function^{25,12,22}. Analytically, in the research of Baczyk et al.,²⁵ the three dimensions of quality of life of osteoporotic and osteopenic women who were affected, regardless of the existence of a fracture, were pain ($p = 0.006$), social function ($p = 0.001$) and mental function ($p = 0.001$). In the study of Ramírez Pérez et al.,¹² the dimensions of quality of life of osteoporotic women with fractures most affected were pain ($p < 0.05$), physical function ($p < 0.01$), social function ($p < 0.01$) and mental function ($p < 0.05$), while in the research of Romagnoli et al.,²¹ the three dimensions of QUALEFFO-41 most affected in osteoporotic women with fractures were physical function ($p = 0.002$), social function ($p < 0.001$) and general health ($p = 0.011$).

The SF-36 scale was used in a total of 7 studies^{15,13,6,23,10,20,21} while its short version, SF-12 was used in 1 study¹⁷. Five studies, including the one in which quality of life was assessed with the SF-12, found that the quality of life of women with osteopenia and osteoporosis without fractures¹⁵ and with fractures^{13,14,21,17} were affected in all areas of the SF-36. Among the other two studies, in one, the quality of life of patients with osteoporosis, regardless of the presence of fractures, was affected in the areas of physical function and general health for both men ($p = 0.03$) and women ($p (0.05)$)⁶, while in the

research of Hakestad et al.,²³ the results showed that the areas affected were physical pain ($p = 0.025$) and vitality ($p = 0.015$).

The ED-Q5 scale was used in two studies^{9,7} where both found that the quality of life of patients with osteoporosis and fractures was affected in all areas of ED-Q5 ($p = 0.0016$ and $p < 0.01$ respectively).

The OPAQ scale was also used in two studies^{19,5}. In both it was found that the quality of life of osteoporotic women with fractures¹⁹ ($p < 0.01$) and of osteoporotic men with fractures⁵ was affected in all areas of OPAQ (physical function $p = 0.020$, emotional function $p = 0.009$ and symptoms $p = 0.004$).

Finally, the mini-OQLQ scale was used in one study, which showed that the quality of life of osteoporotic patients with fractures was affected in all areas, but more in physical function and activities of daily living¹¹.

Factors affecting the quality of life of patients with osteoporosis and osteopenia

Among the 21 systematic review studies, four performed correlation analyzes on factors affecting the quality of life of patients with osteoporosis and osteopenia^{15,13,9,11}. In the research of Aktas et al.,¹⁵ the quality of life of osteoporotic women without fractures was associated with bone density and in particular it was found that the decrease in bone density was associated with the reduction of quality of life ($p < 0.05$). In the research of Kwon et

al.,⁹ quality of life levels was associated with comorbidities, beyond fractures. Specifically, it was found that the quality of life of osteoporotic patients with fractures was significantly lower for those with comorbidities and especially osteoarthritis, rheumatoid arthritis, hypertension, diabetes, chronic obstructive pulmonary disease and cardiovascular events, compared with those who had no other co-existing conditions ($p < 0.0001$). Similarly, Papaioannou et al.,¹¹ found a deterioration in the quality of life of osteoporotic patients with fractures when there were co-morbidities and in particular when there was atherosclerotic disease and hypertension. The quality of life of osteoporotic patients with fractures was also impaired for those who smoked, for those who lived for long periods in care facilities, for those who had previously undergone hip or spine surgery, and for those receiving sedatives and anticonvulsants. Education and in particular the completion of post-secondary education, receiving treatment for osteoporosis, work and exercise were all positively correlated with quality of life, as well as a lack of family history of osteoporosis. Finally in the research of DeOliveira Ferreira et al.,¹³ the quality of life of osteoporotic women with fractures was associated with BMI and lifestyle and work. In particular, women with osteoporosis and fractures who had a BMI > 25 (those who were overweight

or obese) and those who lived a sedentary life were more likely to have reduced quality of life, compared with those with a normal weight and those who followed a more active lifestyle respectively, while women with osteoporosis and fractures who worked had better quality of life levels than those who did not work ($p > 0.05$).

DISCUSSION

From the results of the abovementioned studies 21 articles were included for analysis in this paper. There was significant heterogeneity between studies, both in terms of the tools used to assess quality of life and in terms of patient characteristics studied and comparisons made between groups.

Initially, the majority of research was conducted on women and especially on postmenopausal women. This is not surprising as it is already known that the incidence of osteoporosis is 3-4 times higher in women compared to men²⁶ and thus the increased interest in research into the quality of life of women with osteoporosis, versus men is justified.

Also, the majority of the studies studied concerned patients with osteopenia / osteoporosis and fractures and the comparison of their quality of life with that of either healthy individuals or patients with osteoporosis without fractures. Again, the increased research interest in the quality of

life of osteopenic / osteoporotic patients with fractures versus osteopenic / osteoporotic patients without fractures is justified both by the increased incidence of fractures and the consequent morbidity / mortality in these patients, and by the significant negative impact of fractures on their quality of life. Osteoporotic patients with fractures experience higher levels of morbidity, increased risk of subsequent fractures and higher mortality rates compared to osteoporotic patients without fractures²⁷.

Consistent with the results of previous research, the present systematic review showed that the quality of life of women with osteoporosis and fractures is lower, compared to the quality of life of women with osteoporosis and without fractures, but also compared to the quality of life of healthy women, i.e. those who have normal bone density values. In addition, studies in the present systematic review that did not focus exclusively on patients with osteoporosis / osteopenia with fractures, but mixed samples including patients with or without a fracture history, showed that the quality of life of osteoporotic women and men was statistically significantly lower than that of healthy women and men, especially in the field of pain, again supporting the view that fractures have a significant and negative impact on the quality of life of patients with osteoporosis. Fractures lead to back pain, disability and

limitations in physical function and psychosocial dysfunction²⁸ and many previous studies have shown the relationship between the existence of fractures and reduced quality of life in postmenopausal women with osteoporosis^{29,30}.

Regarding the quality of life of men with osteoporosis and fractures, only one study of the present systematic review focused exclusively on men⁵. This study showed, similar to previous research, that osteoporotic fractures worsen the quality of life of men with osteoporosis, as men with osteoporosis without fractures were found to have a higher quality of life compared to men with osteoporosis and fractures. The rest of the studies, whose samples included men, did not analyze the results for both sexes separately, and thus the conclusions about the quality of life of men with osteoporosis are significantly reduced. Drawing conclusions becomes difficult, as the research of Solimeo et al.,⁵ was a study conducted primarily to investigate the validity of the OPAQ tool for men. However, a previous study in agreement with the results of Solimeo et al.,⁵ showed that fractures worsen the quality of life of men with osteoporosis. Specifically, Voigt et al.,³¹ investigating the quality of life of older men with osteoporosis in Germany, found that overall quality of life scores, as assessed on the EQ-5D scale for male patients with osteoporosis, were higher than those of the

general population. Patients with more than 2 fractures had the highest level of attenuation in quality of life, and the dimension of quality of life most affected was pain. When quality of life was assessed with the QUALEFFO-41 scale in the same study, the areas most affected were general perception of health, mental function and pain³¹.

These first data show, however, a possible effect of fractures on the quality of life of osteoporotic men. However, this is a relationship that needs to be further explored in the future, as some previous research has shown that men are less likely to seek preventive medical care or engage in health maintenance behaviors, which may eventually raise public health issues³². Risk factors for fracture development in men are similar to those in women, and include high BMI, smoking, family history, a history of bone fractures, and glucocorticoid intake. Other risk factors reported in the literature include age (> 70 years), personal fracture history, alcohol consumption, weight loss, and lack of exercise³³. Male patients at high risk of fracture should be screened prophylactically. Although the link between osteoporotic fractures and reduced quality of life is well established today (at least for women), it is not certain whether the quality of life of patients with osteoporosis and osteopenia without fractures or a previous history of fracture deteriorates after the development of

the disease. Studies comparing the quality of life of osteoporotic and osteopenic patients without fractures with the quality of life of individuals with normal bone density values have yielded opposite results. Three of the five studies which studied the above subject^{16,21,17} did not find that quality of life in osteopenia and osteoporosis worsens when there is no fracture, while two studies^{15,8} found that the quality of life of women with osteoporosis without fracture was lower than that of women with normal bone density values.

It is important to note that in only two of the above studies^{15,16} the primary purpose of the researchers was to study the relationship between quality of life and osteoporosis / osteopenia for patients without fractures, while in the other studies the analysis of this issue was of secondary importance. The research of Aktas et al.,¹⁵ has shown that the reduction of bone density is associated with a decrease in quality of life, and this has also been suggested by other studies, arguing that the effect of osteoporosis is cumulative over time and that as the disease progresses, quality of life levels decrease³⁴. These differences in results between the above studies can be attributed to the different tools used to evaluate the quality of life and the different characteristics of the samples, such as the age and the co-morbidity factors of the patients. A previous systematic review of the

quality of life of patients with osteoporosis without fractures found that the quality of life was adversely affected by osteoporosis in the absence of fractures, mainly in the areas of pain and physical function, but the researchers noted significant variability between studies depending on the quality of life assessment tools used, as well the researchers highlighted the heterogeneity of the samples and the fact that some studies had not adjusted their data for confounding factors such as age and possible comorbidities³⁵. Therefore, the quality of life of patients with osteoporosis without fractures needs to be further studied in the future.

With regard to the quality-of-life stresses most affecting women and men with osteoporosis, drawing conclusions also becomes difficult, due to the many different tools used to assess quality of life. The most commonly used tools in the research of this systematic review were the QUALEFFO-41 and SF-36 which are reliable and valid tools. Other scales used were OQLQ, OPAQ and ED-Q5. QUALEFFO-41 has been developed specifically to assess the quality of life of people with osteoporosis, with or without fractures, and previous research has shown that it is a reliable and valid tool with good resolution³⁶. The OQLQ scale, although used in a single study of the present systematic review¹¹, is also a valid and reliable tool, and a

previous study showed that OQLQ performance was superior to that of QUALEFFO (better psychometric properties) for evaluating the quality of life of osteoporotic patients with vertebral fractures³⁷. However, in clinical practice and research it is used more for the evaluation of pharmacological treatments and physical rehabilitation programs in osteoporosis³⁸. On the other hand, the scales SF-36, SF-12 (short version of SF-36) and ED-Q5 are general measures that assess the quality of life related to health, with good internal coherence, reliability and validity³⁹.

In the studies that used the QUALEFFO-41 scale, the area that was found to be affected in all studies was pain. Social function, physical function and mental function were also affected in many studies, which examined the quality of life of patients with osteopenia-osteoporosis and fractures. The dimensions of pain and physical function were also affected in patients in studies using the SF-36 tool. In osteoporosis, patients may not experience pain, but are more likely than not to experience it⁴⁰. Although pain is not a classic symptom of osteoporosis, acute pain is characteristic of vertebral fractures in osteoporosis. Fractures usually cause sudden and severe pain, while vertebral fractures also result in chronic pain. On the other hand, pain can also be present in patients without fractures. Certain metabolic disorders that

contribute to low bone density, such as vitamin D deficiency and osteomalacia, can cause bone and muscle pain and weakness in osteoporotic patients due to fractures⁴⁰. Fracture-related pain has also been shown in previous research to be an important factor in lowering the quality of life of patients with osteoporosis⁴¹. Psychological function can also be affected as osteoporotic patients often experience anxiety and fear about the progression of the disease. They often have low self-esteem and may even experience depression and social isolation⁴². Diminished physical function is also common in patients with osteoporosis, as the ability to walk and perform simple, daily activities is reduced, especially in patients with fractures, even if they have completed their treatment⁴.

Finally, in this systematic review, factors that affect the quality of life of patients with osteoporosis and osteopenia were also evaluated. Four of the systematic review studies looked at factors that affect the quality of life of patients with osteoporosis, in addition to fractures. Two studies have shown that co-morbidity factors further worsen the quality of life of osteoporotic patients^{9,11} as well as harmful habits of daily living, such as smoking, and a sedentary way of life^{13,11}. On the other hand, work was associated with higher quality of life in osteoporosis in two studies^{15,13}. These factors have also been reported in other previous studies^{43,44}.

CONCLUSIONS

An important distinction when evaluating the results is the presence or absence of fractures. Osteoporosis in the presence of fractures helps to reduce the quality of life of women suffering from the condition, but, in the absence of fractures, the effect of the condition remains unclear. It is noteworthy that several studies found no difference in the quality of life of osteoporotic women without fractures compared with neither that of healthy women (with normal bone density values) nor with the quality of life of women with osteopenia. Also because the quality of life of osteoporotic patients with fractures was further impaired for those who smoked, for those who lived for long periods in care facilities, for those who had previously undergone hip or spinal surgery and for those receiving sedatives or anticonvulsants it is considered necessary that intervention in the form of both preventative measures [e.g. education on the effects of smoking] and/or active measures [e.g. by paying special attention to post-operative patients]. Furthermore the lack of studies concerning male patients was obvious throughout the investigation. More studies are needed to investigate the relationship between bone density and quality of life, but also to investigate the quality-of-life levels of men with osteoporosis. It is important for

women with osteoporosis to be evaluated early for the risk of fracture, and to receive appropriate interventions.

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ΠΑΡΑΡΤΗΜΑ

Flowchart 1. Graphical representation of the flow of systematic search results

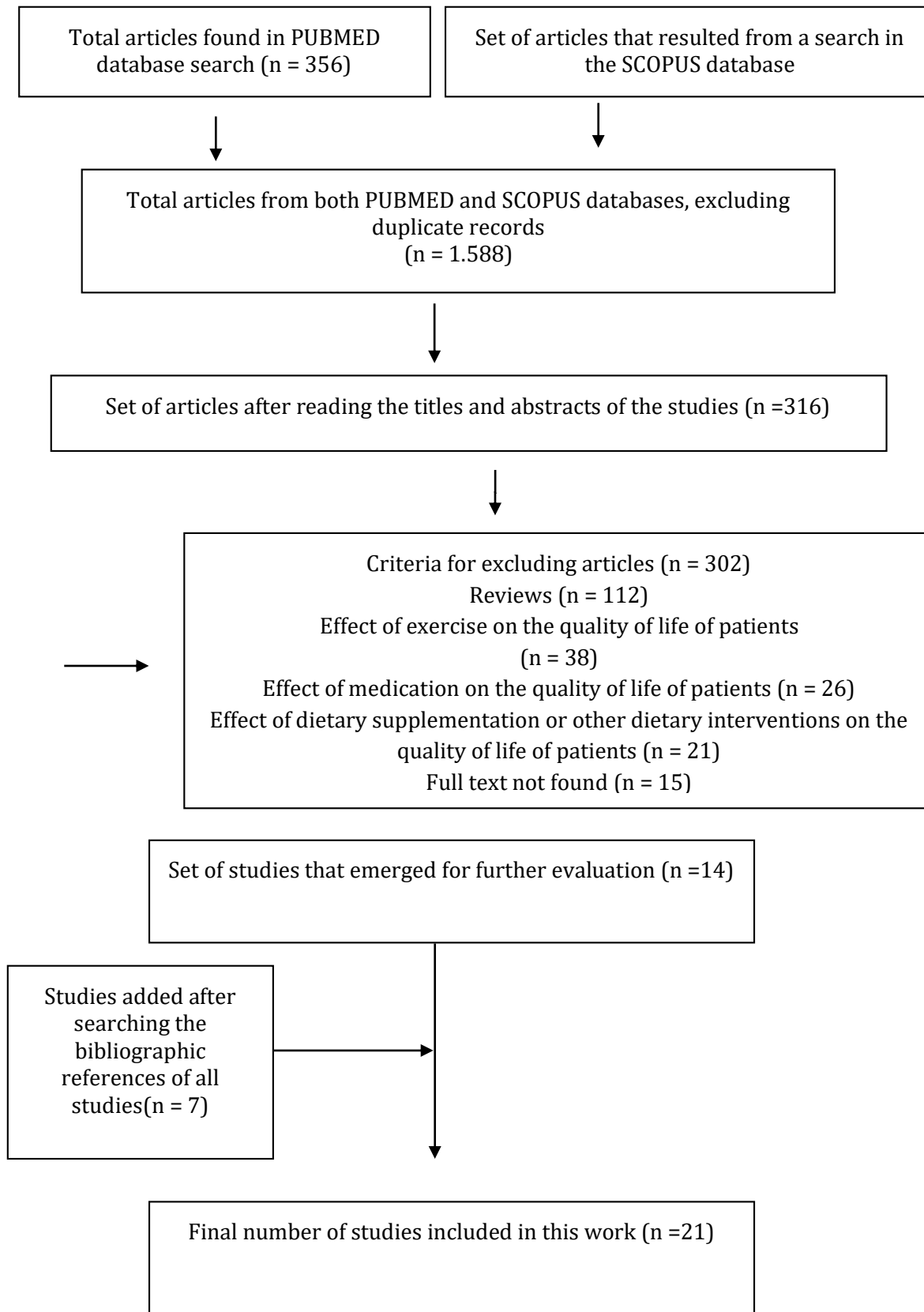


TABLE 1. Characteristics of systematic review studies

Authors/ Country	Purpose of research	Sample	Groups	Quality of life measures	Results
Aktas et al., (2018) Turkey	Investigating the relationship between bone density and quality of life in postmenopausal women	172 postmenopausal women	1) Osteoporotic women without fractures 2) Women with osteopenia without fractures 3) Women with normal bone density values *	SF-36	Decreased bone density was associated with decreased quality of life ($p < 0.05$).
Albayrak et al., (2016) Turkey	Evaluation of quality of life of postmenopausal women with fracture-free osteoporosis	387 postmenopausal women	1) Osteoporotic women without fractures (n = 113) 2) Women with osteopenia without fractures (n = 172) 3) Women with normal bone density values (n = 102)	QUALEFFO-41	No statistically significant differences were observed between the three groups of women in quality of life ($p > 0.05$)
Baczyk et al., (2016) Poland	Evaluation of quality of life of women with reduced bone density, regardless of fracture history, compared to women with normal bone density values	304 women	1) Osteoporotic women (n = 85) 2) Women with osteopenia (n = 122) 3) Women with normal bone density values (n = 97)	QUALEFFO-41	Women with osteopenia and osteoporosis had significantly lower quality of life levels in the areas of pain ($p = 0.006$), social function ($p = 0.001$) and mental function ($p = 0.001$), compared to women with normal bone density values.
Kwon et al. (2016)	Evaluation of quality-	2,078 patients	1) Osteoporotic patients with	EQ-5D	Osteoporotic patients with fractures recorded lower



Authors/ Country	Purpose of research	Sample	Groups	Quality of life measures	Results
Korea	of-life standards of patients with osteoporosis and impact of fractures and co-morbidity factors on their quality of life	with osteoporosis (328 men and 1,750 women)	fractures (n = 229) 2) Osteoporotic patients without fractures (n = 1.849)		quality of life levels in all areas of EQ-5D, and this difference was significant only for vertebral fractures ($p = 0.0016$). Quality of life levels were significantly lower for patients with co-morbidity (osteoarthritis, rheumatoid arthritis, hypertension, diabetes, chronic obstructive pulmonary disease and cardiovascular events) compared with those without co-morbidity ($P < 0.0001$).
Hakestad et al., (2014) Norway	Evaluation of physical function and quality of life of postmenopausal women with osteopenia and wrist fractures	36 postmenopausal women	1) Osteopenic women with wrist fracture (n = 18) 2) Healthy women (n = 18)	SF-36	Osteopenic women with wrist fractures recorded significantly lower levels of quality of life in the areas of physical role limitations ($p = 0.014$), physical pain ($p = 0.025$) and vitality ($p = 0.015$)
Solimeo et al., (2012) North Carolina	Evaluation of quality of life of men with osteoporosis with and without fractures	37 men > 50 years old	1) Men with osteoporosis without fractures (n = 19) 2) Men with osteoporosis with fractures (n = 18)	OPAQ	Men with osteoporosis and without fractures had higher quality of life, compared to men with osteoporosis and fractures, in all dimensions of OPAQ (physical function $p = 0.020$, emotional function $p = 0.009$ and symptoms $p = 0.004$)
Baczyk et al., (2011) Poland	Evaluation of quality of life of postmenopausal women	385 women after menopause	1) Osteoporotic women (n = 85) 2) Women with osteopenia (n = 168)	QUALEFFO-41	Osteoporotic women had significantly lower quality of life levels only in the pain dimension ($p < 0.01$), compared with women with

Authors/ Country	Purpose of research	Sample	Groups	Quality of life measures	Results
	with osteopenia or osteoporosis		3) Women with normal bone density values (n = 132)		normal bone density values.
Sanf�lix- Genov�s et al., (2011) Spain	Investigation of quality of life of postmenopausal women with osteopenia and osteoporosis, with or without vertebral fractures	735 postmenopausal women > 50 years old	1) Osteoporotic women without fracture (n = 168) 2) Women with normal bone density values (n = 146) 3) Women with osteopenia without fracture (n = 364) 4) Women with osteopenia and fracture (n = 57)	SF-12	No differences were recorded in HRQOL between non- fractured osteoporotic women and women with normal bone density values. The quality of life of women with fractures was lower than that of all women without fractures (including women with normal bone density values)
De Oliveira Ferreira et al., (2009) Brazil	Evaluation of quality of life of postmenopausal women with osteoporosis and factors that affect it	220 women after menopause	1) Osteoporotic women with or without fracture (n = 110) 2) Healthy women (n = 110)	QUALEFFO -41 και SF- 36	The quality of life of women with osteoporosis was lower in all areas of Qualeffo-41 and SF-36 compared to women without osteoporosis (p = 0.012- 0.001 for Qualeffo-41 and p = 0.008- 0.001 for SF- 36). No differences in quality of life were found between fractured and non-fractured osteoporotic women, based on Qualeffo-41 (p> 0.05) BMI> 25 and sedentary lifestyle were associated with lower quality of life, while working was associated with better quality of life
Jahelka et al., (2009)	Evaluation of quality of life of	220 patients with	1) Osteoporotic patients without a fracture history (n =	QUALEFFO -41 and	The quality of life of osteoporotic patients without a fracture history was lower

Authors/ Country	Purpose of research	Sample	Groups	Quality of life measures	Results
Austria	patients with osteopenia and osteoporosis with and without fracture history	osteoporosis > 60 years (173 women and 49 men)	1) 89 2) Patients with osteopenia without a history of fracture (n = 44) 3) Osteoporotic patients with a fracture history (n = 87)	SF-36	than that of patients with osteopenia without a fracture history. The quality of life of osteoporotic patients with a fracture history was lower than that of the previous two groups.
Van Schoor et al., (2009) Czech Republic Hungary Italy Slovakia Spain Sweden England	Evaluation of quality of life of women with osteoporosis and fractures, compared to osteoporotic women without fractures, in 25 countries around the world	7,117 postmenopausal women aged 50-85	1) Osteoporotic women with fractures 2) Osteoporotic women without fracture **	QUALEFFO-41 and EQ-5D	The quality of life of women with osteoporosis was lower in Africa, Asia and Europe compared to other countries on both scales (p <0.001). The best quality of life was recorded for osteoporotic women in North America and Oceania. The quality of life of osteoporotic women with fractures was significantly lower than those without fractures in Africa, Asia, Oceania and South America. The quality of life of osteoporotic women with fractures was significantly higher than those without fractures in Europe (p <0.043-0.001)
Ramírez Pérez et al., (2007) Mexico	Study of quality of life of women with osteoporosis with and without	160 women > 50 years old	1) Osteoporotic women without fractures (n = 80) 2) Osteoporotic women with at least one fracture (n = 80)	QUALEFFO-41	The quality of life of women with fractures was lower than that of women without fractures in the dimensions of pain (p <0.05), physical function (p <0.01), social function (p <0.01) and mental

Authors/ Country	Purpose of research	Sample	Groups	Quality of life measures	Results
	fractures				operating ($p < 0.05$).
Sallafi et al., (2007) Italy	Evaluation of the effect of fractures on the quality of life of postmenopausal women with osteoporosis	961 postmenopausal women	1) Osteoporotic women without fractures ($n = 244$) 2) Osteoporotic women with at least one fracture ($n = 234$) 3) Healthy women ($n = 483$)	SF-36	No differences in quality of life were recorded between women with osteoporosis and without fracture and healthy women ($p < 0.01$). Osteoporotic women with fractures had significantly lower standard of living than osteoporotic women without fractures, in all areas of SF-36 ($p < 0.01$).
Dennison et al., (2006) England	Evaluation of quality of life of patients with osteopenia and osteoporosis and comparison with healthy individuals	1,412 people (675 women and 737 men)	1) Patients with osteoporosis and osteopenia 2) Healthy (with normal bone density values) *	SF-36	The quality of life levels of osteoporotic patients were lower in the areas of physical function and general health, both for men ($p = 0.03$) and for women ($p > 0.05$), compared to healthy individuals.
Papaioannou et al., (2006) Canada	Evaluation of quality of life of osteoporotic patients with fractures and investigation of factors that affect their quality of life	1,129 postmenopausal women	-	mini-OQLQ	The quality of life levels of women with osteoporosis ranged from moderate (range 3.9-4.9) and were lower in the areas of physical function and carrying out activities of daily living. Quality of life levels were positively correlated with education, family history of osteoporosis, work, exercise, and treatment. Quality of life was negatively correlated with smoking, long-

Authors/ Country	Purpose of research	Sample	Groups	Quality of life measures	Results
					term living in care facilities, previous hip or spine surgery, sedatives and anticonvulsants, atherosclerotic disease, and hypertension.
Bianchi et al., (2005) Italy	Evaluation of the effect of osteoporosis on quality of life in patients without fractures	97 postmenopausal women	1) Osteoporotic women without fractures (n = 62) 2) Osteoporotic women with a history of fracture who had received and completed their treatment (n = 35)	QUALEFFO-41	The quality of life levels of osteoporotic women without fractures were significantly lower than those of women with a fracture history in the areas of pain (p <0.005) and general health (p <0.05).
Dhillon et al., (2005) England	Evaluation of quality of life of patients with osteoporosis and comparison with healthy individuals	325 people (men and women)	1) Patients with osteoporosis (n = 159) 2) Healthy people (n = 166)	EQ-5D	Patients with osteoporosis reported lower quality of life compared to healthy individuals in all areas of EQ-5D (p <0.01)
Lombardi et al., (2005) Brasil	Evaluation of quality of life of postmenopausal women with osteoporosis	55 postmenopausal women	1) Osteoporotic women without thoracic fracture (n = 20) 2) Osteoporotic women with thoracic fracture (n = 15) 3) Healthy women (n = 20)	SF-36	No differences in quality of life were recorded between the three groups of women

Authors/ Country	Purpose of research	Sample	Groups	Quality of life measures	Results
Hallberg et al, (2004) Sweden	Evaluation of the effect of fractures on the quality of life of postmenopa usal women with osteoporosi s	939 postmen opausal women	1) Osteoporotic women with fractures (n = 292) were followed for a period of 84 days 2) Women with fractures without diagnosis of osteoporosis (n = 647), among them 412 were followed for a 2-year period	SF-36	The quality of life of osteoporotic women with fractures deteriorated significantly after 84 days in all areas of the SF-36. For all the types of fractures mentioned, after 2 years there were improvements in all areas of quality of life. Nevertheless, for hip fractures, the quality of life remained lower than normal in the areas of physical function, social function and physical role.
Romagnoli et al.,(2004) Italy	Evaluation of quality of life of postmenopa usal women with osteoporosi s with and without fractures	361 postmen opausal women	1) Osteoporotic women without fractures (n = 93) 2) Osteoporotic women with fractures (n = 52) 3) Osteopenic women without fractures (n = 120) 4) Osteopenic women with fractures (n = 30) 5) Healthy women (n = 66)	QUALEFFO -41	The quality-of-life levels of osteoporotic women with fractures were significantly lower than those of osteoporotic women without fractures, in the areas of physical function (p = 0.002), social function (p <0.001) and general health (p = 0.011).
Silverman et al, (2001) 25 countries around	Effect of vertebral fractures on quality of life in postmenopa	1,395 postmen opausal women	1) Osteoporotic women without fractures (n= 190) 2) Osteoporotic women with	OPAQ	Spinal fractures have been associated with reduced quality of life in all OPAQ areas. Osteoporotic women with fractures had significantly lower quality of



Authors/ Country	Purpose of research	Sample	Groups	Quality of life measures	Results
the world	usual women with osteoporosi s		fractures (n = 1.205)		life levels in terms of physical function, emotional state, and clinical symptoms, compared with osteoporotic women without fractures (all p <0.01).

* The number of people in each group is not stated

** The number of people in each group was different for each country