Journal of Bone and Mineral Metabolism (2019) 37:327–335
https://doi.org/10.1007/s00774-018-0923-2

ORIGINAL ARTICLE

Failure in diagnosis and under-treatment of osteoporosis in elderly patients with fragility fractures

Sofia Bougioukli[1] · Panagoula Kollia[2] · Theodora Koromila[2] · Sokratis Varitimidis[1] · Michael Hantes[1] · Theofilos Karachalios[1] · Konstantinos N. Malizos[1] · Zoe H. Dailiana[1]

Received: 22 January 2018 / Accepted: 24 March 2018 / Published online: 17 April 2018

Abstract

We evaluated whether osteoporosis is adequately managed and treated in patients suffering from fragility fractures. Factors that influenced osteoporosis diagnosis and treatment rates were also assessed. To this end, patients with the principal diagnosis of low-energy hip, vertebral, or distal radius fractures were recruited for the study. Collected data included risk factors for osteoporosis, history of previous fractures, known history of osteoporosis, and osteoporosis treatment at the time of admission. The patients' prefracture risk profile was also assessed to determine whether osteoporosis could have been identified prior to the index fracture. We identified 308 patients with fragility fractures, including 214 hip, 41 vertebral, and 53 distal radius fractures. Overall, 238 patients (77.3%) had at least one risk factor for osteoporosis. Eighty-eight patients (28.6%) had sustained ≥ 1 prior fragility fractures in the past. However, only 79 patients (25.6%) were aware that they had osteoporosis and even fewer (66 patients, 21.4%) had been receiving osteoporosis treatment preceding the current admission. Anti-osteoporotic agents were more commonly prescribed in patients 66–75 years old ($p=0.008$), with a family history of osteoporosis ($p=0.009$) or history of a prior fragility fracture ($p=0.012$). The treatment rate was higher in women than men ($p=0.026$) and in patients with vertebral or multiple prior fractures compared to patients with prior hip fractures. The current study provides evidence that individuals who experience fragility fractures are not adequately managed for osteoporosis. Only few of the historically known risk factors for osteoporosis were adequately recognized and associated with osteoporosis evaluation and treatment.

Keywords Fragility fracture · Osteoporosis · Osteoporosis risk assessment · Anti-osteoporotic treatment

Introduction

Osteoporosis and its subsequent fractures have been identified as a major public health problem in aging populations, since they are associated with increased morbidity, mortality, and healthcare costs. Due to the increasing life expectancy, the incidence of osteoporosis-related fractures is expected to increase significantly. It has been estimated that the number of hip fractures occurring globally each year will rise from 1.66 million in 1990 to 6.26 million by 2050 [1]. At present, the lifetime risk for a fragility fracture at any site at the age of 50 is approximately 40–53% in women and 13–21% in men [2]. The risk of a future osteoporotic fracture increases significantly in patients with the previous low-energy fractures [3]. A systematic review and metanalysis of the literature has demonstrated a 2.3-, 7.2-, and 1.8-fold increased risk of sustaining a future wrist, spine, and hip fracture, respectively, in patients with a history of fragility fracture at any site [4]. Other factors that have also been associated with an increased risk of osteoporotic fractures include but are not limited to age, female sex, low body mass index (BMI), premature menopause, family history of osteoporosis, co-morbidities related to secondary osteoporosis, low calcium intake, and smoking [5].

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00774-018-0923-2) contains supplementary material, which is available to authorized users.

✉ Zoe H. Dailiana
dailiana@med.uth.gr

1 Department of Orthopaedic Surgery, Faculty of Medicine, University of Thessaly, 3 Panepistimiou St, Biopolis, 41500 Larissa, Greece

2 Department of Genetics and Biotechnology, Faculty of Biology, National and Kapodistrian University of Athens, Athens, Greece

Despite the clear association between prior fragility fractures and subsequent osteoporotic fractures, the presence of adequate diagnostic methods in identifying patients at high risk of osteoporosis, and the availability of effective anti-osteoporotic treatment regimens, only a few patients with non-traumatic fractures undergo further evaluation and treatment for osteoporosis, to prevent the risk for a subsequent osteoporotic fracture [6, 7].

The aim of the present study was to assess the trends in evaluating and managing osteoporosis in patients presenting with fragility fractures, within a University tertiary referral hospital setting in Greece between 2007 and 2013. In addition, we investigated which factors influenced osteoporosis diagnosis and treatment rates.

In this study, we hypothesized that secondary fracture prevention services and initiatives like the International Osteoporosis Foundation's "fracture liaison service" [8] and the American Orthopaedic Association's "Own the Bone" [9] would be adopted by a growing number of hospitals and clinics in our country, with resultant improvement in rates of osteoporosis testing and treatment in high-risk populations as compared to prior studies in the US and Europe. We also hypothesized that the presence of well-established risk factors for osteoporosis would affect evaluation and treatment rates.

Materials and methods

Patient selection

Patients over 45 years of age who were admitted to the Department of Orthopaedic Surgery of a University hospital between 1/2007 and 2/2013 with the principal diagnosis of a fragility fracture of the distal radius, vertebral body, or proximal femur participated in this retrospective cohort study. Fragility fractures were defined as fractures that resulted from a fall from a standing height or less, or presented in the absence of obvious trauma, that would be insufficient to fracture a normal bone [10]. Patients were excluded if they had bone cancer, Paget's disease, osteomyelitis/septic arthritis, severe dementia, or were unwilling to participate in the study. The hospital's institutional review board reviewed and approved the protocol before the commencement of the study.

Data collection

Data were collected through patients' interviews during their hospitalization. An assessment of prefracture risk status was made to determine whether osteoporosis could have been identified prior to the index fracture. Obtained data included the patients' age, sex, site, and etiology of the present fracture, risk factors for osteoporosis (Supplementary Table 1), prior history of osteoporosis, and/or fragility fractures and use of anti-osteoporotic medications. In cases of prior fragility fractures, the patients were asked whether they had undergone further evaluation for osteoporosis while hospitalized or during the follow-up visits following the primary fracture and whether anti-osteoporotic agents were prescribed. Clinical examination included height and weight measurement to assess BMI. Vertebral fractures were assessed clinically and radiographically using lateral plain radiographs of the spine to determine vertebral shape (wedge, concave, or crush) and height decreases in anterior, middle, and posterior vertebra as described by Genant et al. [11]. The FRAX tool was also used to calculate the 10-year probability of a major fracture or hip fracture alone for all patients aged < 90 years, based on the patients' risk factors prior to the index fracture, without the addition of BMD.

Definitions and diagnostic criteria

Late menarche was defined as the absence of menarche by age 15 [12]. Premature menopause was defined as the absence of menstruation for at least 12 months before the age of 40 years [13]. Any BMI < 20 kg/m^2 was defined as low. Corticosteroid use was considered a risk factor for osteoporosis in patients receiving orally administered glucocorticoids in a dose of at least 5 mg for longer than 2 months. The term diabetes mellitus (DM) was used interchangeably for DM type 1 and 2 as a risk factor for osteoporosis. We did not attempt to differentiate between DM type 1 and 2, since there is strong evidence in the literature in support of high fracture risk in both types of DM in elderly patients. Low dietary calcium intake was defined as a daily intake of calcium of < 500 mg [14]. Immobilization was recognized as a risk factor in patients with chronic paresis or hemiparesis/hemiplegia caused by trauma, poliomyelitis, multiple sclerosis, or cerebrovascular events [15].

Statistical analysis

Statistical analysis was performed with SPSS with the significance level set at 0.05. Demographic characteristics, presence of risk factors, and osteoporosis diagnosis/treatment rates preceding the index fracture were estimated overall and according to fracture site. Descriptive statistics are reported as the mean (and standard deviation) or the number (and percentage). One-way ANOVA and post hoc analysis with Bonferroni test were used to compare age, BMI, and menopause age between patients with different fracture types (hip, wrist, and spine). Independent samples *t* test was used for age and BMI comparisons between male and female patients and patients with or without history of osteoporosis treatment. Mann–Whitney *U* test and Kruskal–Wallis test were used for comparisons in FRAX scores between patients with or without history of osteoporosis treatment and between patients with different fracture types, respectively. Chi-square tests were used for the rest of the calculations. A multivariate analysis, including only the variables with $p < 0.05$ in the univariate analysis, was performed to assess the factors that influenced osteoporosis treatment rates.

Results

General characteristics

A total of 308 patients (257 female, 51 male) with the principal diagnosis of fragility fracture of the hip, spine, or wrist met the eligibility criteria and were included in the study (Table 1). In detail, 214 patients had sustained a proximal femur fracture (69.5%), 41 a vertebral body fracture (13.3%), and 53 a distal radius fracture (17.2%). There was a significant difference in fracture site between males and females (hip 88.2 vs 65.8%, spine 7.8 vs 14.4%, wrist 4 vs 19.8%, respectively, $p = 0.003$). The overall mean age of the enrolled patients was 75.9 ± 11.5 years. Patients admitted with a hip fracture were significantly older than those with spine or wrist fractures ($p < 0.001$). No differences with respect to mean age were observed between male and female patients (78.7 ± 12.5 vs 75.9 ± 11.5 years, $p = 0.06$). In the female population, 255 patients were postmenopausal (mean age of menopause = 47.7 ± 6.3 years) and 2 peri-menopausal. No difference in the menopause age was seen between patients with different fracture types. The overall average BMI was 27 ± 4.8 kg/m^2, with hip fracture patients having a significantly lower BMI ($p = 0.001$).

Prior history of fractures

Of the 308 patients, 88 (28.6%) had sustained a prior non-traumatic fracture, including 37 hip, 10 vertebral, 13 wrist, and 17 other (proximal humerus, calcaneus, distal femur, etc.) fragility fractures. Eleven patients (all of them in the hip fracture group) had sustained more than one previous fragility fractures. There was no association between the presence of a prior osteoporotic fracture and gender ($p = 0.117$). However, there was an association between the present fracture site and the history of a previous osteoporotic fracture; patients with hip fractures had a higher prevalence of fragility fracture history compared to patients with the other two fracture types ($p = 0.029$). The most common prior fracture type was a contralateral hip fracture in the hip group (49.3%), vertebral body fracture in the spine group (62.5%), and contralateral distal radius fracture in the wrist group (88.9%) (Supplementary Figure).

Other risk factors for osteoporosis

The majority of patients (238/308, 77.3%) reported at least one risk factor for osteoporosis. The most commonly reported risk factors in decreasing order were low calcium nutrition, diabetes mellitus, family history of osteoporosis, use of osteoporosis-associated medications, and thyroid disorders (Table 2). No difference was observed between patients admitted for different fragility fractures with respect to the presence of risk factors in general. However, there were certain differences when examining the different risk factors individually. Patients with a distal radius fracture reported family history of osteoporosis more often compared to hip fracture patients (32.1 vs 11.2%, $p < 0.001$). On the other hand, diabetes mellitus and prolonged immobilization were significantly more common in hip versus wrist fracture patients (22 vs 9.4%, $p = 0.036$ and 15 vs 3.8%, $p = 0.035$). Moreover, significant differences were noted in the FRAX scores when comparing patients admitted with hip fractures to the other two groups. In detail, patients in the hip fracture group had a higher 10-year probability of a major fracture (21.8 ± 13.2%) and hip fracture (13.2 ± 12.2%) versus wrist ($p < 0.001$) and vertebra ($p = 0.001$) fracture patients (Table 1).

Table 1 Patient demographics overall and by fracture type

Characteristic	Fracture type			Overall
	Hip	Spine	Distal radius	
No of patients (%)	214 (69.5%)	41 (13.3%)	53 (17.2%)	308
Sex				
Male	45 (88%)	4 (7.8%)	2 (3.9%)	51 (16.6%)
Female	169 (65.8%)	37 (14.4%)	51 (19.8%)	257 (83.4%)
Age (mean ± SD)	79.6 ± 10	69.5 ± 9.4	66 ± 10.7	75.9 ± 11.5
Age of menopause (mean ± SD)	47.8 ± 6.3	47.9 ± 6.4	47.3 ± 6.3	47.7 ± 6.3
BMI (mean ± SD)	26.1 ± 4.4	29.1 ± 5.9	28.8 ± 4.4	27 ± 4.8
FRAX-major fracture	21.8 ± 13.2	14.2 ± 9.7	12.9 ± 10	19.1 ± 12.8
FRAX-hip fracture	13.2 ± 12.2	6.3 ± 6.9	5.5 ± 7.7	10.8 ± 11.4

Table 2 Risk factors for osteoporosis in the study population overall and by fracture type

Risk factors for osteoporosis	Fracture type			Overall
	Hip	Spine	Distal radius	
Any risk factor	168 (78.5%)	30 (73.2%)	40 (75.5%)	238 (77.3%)
Genetic/constitutional				
Previous fragility fracture	71 (33%)	8 (19.5%)	9 (17%)	88 (28.6%)
Family history of osteoporosis	24 (11.2%)	8 (19.5%)	17 (32.1%)	49 (15.6%)
Late menarche	20 (9.3%)	6 (14.6%)	7 (13.2%)	33 (10.7%)
Premature menopause	20 (9.3%)	4 (9.8%)	8 (15.1%)	32 (10.4%)
Concomitant disorders				
Thyroid disease	25 (11.6%)	5 (12.2%)	10 (18.9%)	40 (13%)
Chronic renal failure	8 (3.7%)	0	0	8 (2.6%)
Rheumatoid arthritis	6 (2.8%)	1 (2.4%)	2 (3.8%)	9 (2.9%)
Endocrinopathies and autoimmune disorders	7 (3.3%)	4 (9.8%)	1 (1.9%)	12 (3.9%)
Chronic obstructive lung disease	11 (5.1%)	1 (2.4%)	1 (1.9%)	13 (4.2%)
Diabetes mellitus	47 (22%)	4 (9.8%)	5 (9.4%)	56 (18.2%)
Prolonged immobilization	32 (15%)	4 (9.8%)	2 (3.8%)	38 (12.3%)
Medications				
Corticosteroids	30 (14%)	2 (4.9%)	3 (5.7%)	35 (11.4%)
Other (PPIs, heparin, antiepileptics, etc.)	29 (13.6%)	7 (17.1%)	5 (9.4%)	41 (13.3%)
Lifestyle				
Low dietary calcium intake	59 (27.6%)	7 (17.1%)	8 (15.1%)	74 (24%)
Nulliparity	16 (7.5%)	5 (12.2%)	3 (5.7%)	24 (7.8%)
Smoking	24 (11.2%)	7 (17.1%)	7 (13.2%)	38 (12.3%)
Low BMI (≤ 20 kg/m^2)	18 (8.4%)	1 (2.4%)	2 (3.8)	21 (6.8%)

Management of osteoporosis preceding the present fracture

At the time of admission, only 79 patients (25.6%) were aware that they had osteoporosis. Sixty six of them were on anti-osteoporotic treatment and reported compliance and adherence to their osteoporosis medication. Supplements of calcium/vitamin D were the most commonly used (40.9%), closely followed by bisphosphonates (39.4%). Other prescribed agents were calcitonin (12.1%), parathyroid hormone (PTH) (1.5%), strontium ranelate (1.5%), and raloxifene (1.5%). Two patients were on multiple anti-osteoporotic drugs (Fig. 1B). The rest of the diagnosed, but not currently treated patients (13/79) were either not prescribed treatment at all or were initiated on osteoporosis therapy, but discontinued therapy by themselves fairly soon after initiation (<6 months). Thus, the patients that reported discontinuation of the anti-osteoporosis medications were considered non-treated and included in the “diagnosed, but not treated” group (Fig. 1a).

Patients receiving treatment for osteoporosis were significantly younger compared to those not treated ($p = 0.026$). Furthermore, women were more likely to have received diagnosis/treatment for osteoporosis compared to men. In detail, 29.6% of women were previously diagnosed with osteoporosis and 24.5% (63/257) were receiving treatment, whereas only 6% of the men had documented osteoporosis with proper therapy ($p < 0.001$ and $p = 0.002$, respectively). There was no association between osteoporosis treatment and BMI or menopause age (Table 3). FRAX scores for major fractures or hip fracture alone did not differ significantly ($p > 0.05$) between treated and not treated patients (Table 3).

Patients with the previous fractures were more likely to have a documented diagnosis of osteoporosis and subsequent anti-osteoporotic treatment compared to patients without prior fractures (diagnosis 34.1 vs 22.5%, $p = 0.036$; treatment 31.8 vs 17.4%, $p = 0.006$). An association was also observed between the prior fracture site and osteoporosis treatment ($p = 0.012$); treatment was initiated in 22% of patients with prior hip fractures, 62.5% with previous vertebral fractures, 57% with known wrist fractures, 18% with other fractures, and 75% with multiple osteoporotic fractures. As per the rest of the risk factors, only few of them were associated with higher rates of osteoporosis management, namely corticosteroid use, and family history of osteoporosis (Table 4).

The statistically significant results of the univariate analysis were used as the independent variables in the multivariate logistic regression model. Through the multivariate analysis, we identified 6 characteristics that were independently associated with the likelihood of receiving anti-osteoporotic treatment: age, sex, history of prior

A

	Hip N=214	Spine N=41	Distal Radius N=53	Overall N=308
Diagnosed and treated	40 (18.7%)	13 (31.7%)	13 (24.5%)	**66 (21.4%)**
Diagnosed but not treated	12 (5.6%)	0	1 (1.9%)	**13 (4.2%)**
Neither diagnosed nor treated	162 (75.7%)	28 (68.3%)	39 (73.6%)	**229 (74.4%)**

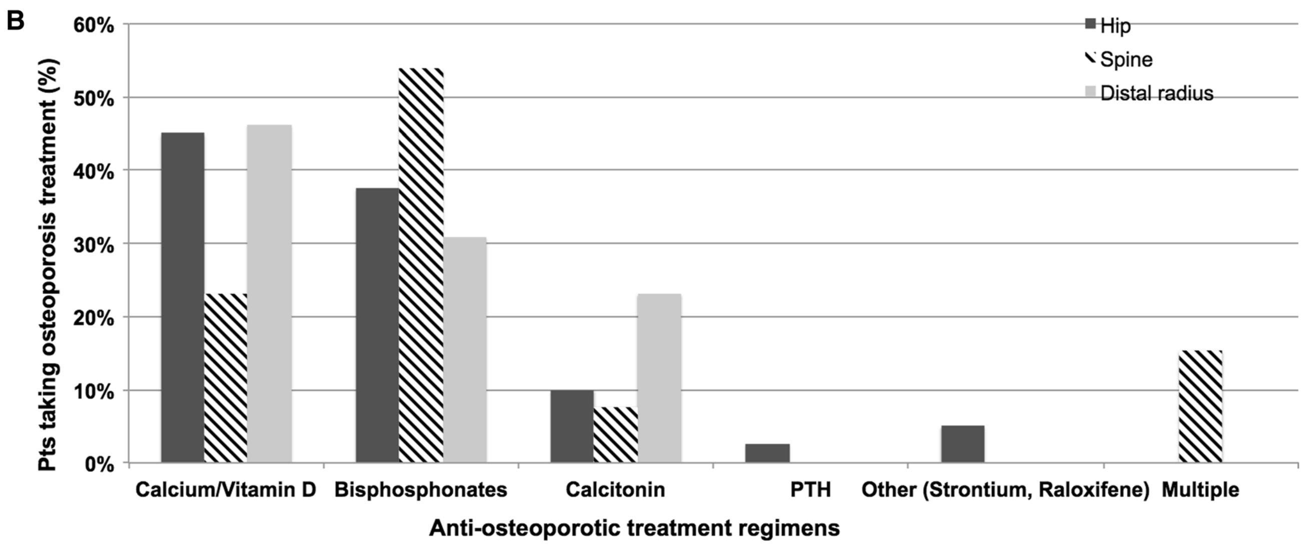

Fig. 1 Management of osteoporosis in patients with low-energy or non-traumatic fractures of the hip, spine or distal radius prior to admission. Previous diagnosis and treatment of osteoporosis is presented overall and by fracture type (**a**). Treatment agents by fracture site are also given (**b**). *Pts* patients, *PTH* parathyroid hormone

Table 3 Univariate analysis of numerical variables between previously treated and non-treated patients

Characteristic	Previous osteoporosis treatment		p value
	Yes	No	
	$N=66$	$N=242$	
Age	73 ± 10.7	76.6 ± 11.6	0.026
BMI	27.3 ± 3.8	26.9 ± 5	0.456
Menopause age	48.1 ± 5.4	47.6 ± 6.6	0.557
FRAX-major fracture	22.2 ± 14.7	18.3 ± 12.2	0.072
FRAX-hip fracture	12.2 ± 13.8	10.4 ± 10.6	0.645

fractures, prior fracture site, diabetes mellitus, and family history of osteoporosis (Table 5). In detail, women were 4 times more likely to receive treatment compared to men (OR 4.28; 95% CI 1.19–15.4). Moreover, patients 66–75 years old were 4 times more likely to receive treatment compared to patients > 86 years (OR 4.60; 95% CI 1.50–14.11). Increased odds of receiving anti-osteoporotic agents were also observed in patients with prior fragility fractures (OR 2.32; 95% CI 1.20–4.48) and family history of osteoporosis (OR 2.71, 95% CI 1.28–5.76) after controlling for other factors. The treatment rate was particularly high in patients with vertebral (OR 5.83; 95% CI 1.07–31.76) or multiple prior fractures (OR 10.50, 95% CI 1.67–66.09) compared to patients with prior hip fractures. Finally, patients with diabetes were less likely to have received treatment for osteoporosis compared to patients without diabetes (OR 0.27, 95% CI 0.09–0.79).

Discussion

Several clinical factors have been associated in the literature with an increased risk for osteoporosis and subsequent fragility fractures, in part independently of BMD. In our series, 77.3% of the enrolled patients had ≥ 1 known risk factors for osteoporosis and 28.6% of them reported ≥ 1 non/low-traumatic fractures during adulthood, preceding the current admission. Regarding the site of prior fracture and the index fracture, there was a remarkable predilection for the involvement of the same (spine) or contralateral (hip and distal radius) site. This observation is consistent with what

Table 4 Univariate analysis of categorical variables in patients treated or not treated for osteoporosis at the time of admission

Studied factors	Osteoporosis treatment $N=66$	No osteoporosis treatment $N=242$	RR (95% CI)	*p* value
Sex				
Female	63 (95.5%)	194 (80.2%)	4.081 (1.34–12.5)	0.002
Male	3 (4.5%)	48 (19.8%)	0.245 (0.08–0.75)	0.002
Any risk factor	56 (84.8%)	182 (75.2%)	1.6 (0.86–2.97)	0.119
Previous fragility fracture	28 (42.4%)	60 (24.8%)	1.82 (1.52–2.78)	0.006
Family history of osteoporosis	19 (28.8%)	30 (12.4%)	2.13 (1.38–3.29)	0.001
Late menarche	7 (10.6%)	26 (10.7%)	0.86 (0.43–1.73)	0.674
Premature menopause	6 (9.1%)	26 (10.7%)	0.75 (0.35–1.60)	0.440
Thyroid disease	11 (16.7%)	29 (12%)	1.34 (0.77–2.33)	0.322
Chronic renal failure	2 (3%)	6 (2.5%)	1.16 (0.34–3.94)	0.684
Rheumatoid arthritis	4 (6.1%)	5 (2.1%)	1 (0.97–4.59)	0.104
Endocrinopathies and autoimmune	5 (7.6%)	7 (2.9%)	2.02 (1–4.08)	0.083
Chronic obstructive lung disease	2 (3%)	11 (4.5%)	0.71 (0.19–2.58)	0.742
Diabetes mellitus	5 (7.6%)	51 (21.1%)	0.37 (0.15–0.87)	0.011
Prolonged immobilization	8 (12.1%)	30 (12.4%)	0.98 (0.5–1.89)	0.943
Corticosteroids	13 (19.7%)	22 (9.1%)	1.9 (1.16–3.13)	0.017
Other relevant drugs	8 (12.1%)	33 (12.4%)	1.01 (0.54–1.89)	0.971
Low dietary calcium intake	14 (21.2%)	60 (24.8%)	0.97 (0.59–1.96)	0.900
Nulliparity	5 (7.6%)	19 (7.9%)	0.97 (0.46–2.02)	0.925
Smoking	8 (12.1%)	30 (12.4%)	0.97 (0.5–1.87)	0.925
Low BMI ($\leq$20 kg/m^2)	2 (3%)	19 (7.9%)	0.43 (0.11–1.62)	0.269

has been reported in the literature. Johnell et al. demonstrated that a prior hip fracture was a significant risk factor for a new hip fracture in both men and women [16]. Klotzbuecher et al. reported a relationship between prior vertebral fractures and future fractures, with the association being the strongest for subsequent vertebral fractures (RR 4.4, 95% CI 3.6–5.4 for peri/postmenopausal women and RR 19, 95% CI 6.5–55.3 for other patient populations) [4]. Moreover, it has been shown that wrist fractures are strong predictors of subsequent wrist fractures (RR 3.3, 95% CI 2.0–5.3) compared to other fracture sites in peri/postmenopausal women [4].

Despite the presence of several clinical risk factors historically known to contribute to fracture risk, including prior fragility fractures, and significantly high FRAX scores, osteoporosis was poorly recognized prior to the present admission. The current study suggests that the management of osteoporosis in patients admitted with fragility fractures is not adequate in our country. At the time of admission, only 21.4% of the patients were aware that they had osteoporosis and were on anti-osteoporosis medications, despite the fact that most of them were at high risk for osteoporosis. This treatment rate is similar to what has been reported in the literature. A retrospective study conducted in Ontario in 2000 showed that patients with fragility fractures had a treatment rate of 18.5% prior to the index fracture [6]. Furthermore, a nationwide survey in Switzerland identified a treatment rate of 23.2% in patients > 50 years of age admitted for fragility fractures [17], with a more recent study in Italy reporting a treatment rate of 22.5% in patients ≥ 65 years old hospitalized with low-energy hip fractures [18]. What is also interesting is the fact that there is no significant difference in the treatment rates of osteoporosis between the aforementioned studies (including our own), despite the fact that they were all done at different time points more than 10–15 years apart. This indicates that little progress has been made in improving clinical practice patterns for osteoporosis management in high-risk patients, despite the fact that there are universally acceptable screening policies to identify patients at high-risk and effective treatment options for osteoporosis.

Regarding the type of treatment received, only some of the treated patients were on optimal therapy for osteoporosis significantly reducing the risk of vertebral, hip, and other non-vertebral fractures (bisphosphonates, strontium ranelate, or combination therapy), whereas the remaining patients were most likely undertreated (e.g., calcium and vitamin D alone, PTH alone, and raloxifene). Calcium and vitamin D supplements alone are usually insufficient to prevent osteoporosis-related fractures especially in low doses (daily supplementation with < 400 IU of vitamin D3 and < 1000 mg of calcium) [19]. However, they may be beneficial in patients > 65 years of age at increased risk for falls, or with calcium or vitamin D insufficiency or when

Table 5 Multivariate logistic regression analysis on factors that may affect the receipt of anti-osteoporotic treatment prior to admission

Characteristic	Odds ratio (95% CI)	*p* value
Sex		
Male	1.00 (Ref)	
Female	4.28 (1.19–15.40)	0.026
Age group		
< 55	1.30 (0.22–7.62)	0.774
56–65	2.41 (0.68–8.54)	0.173
66–75	4.60 (1.50–14.11)	0.008
76–85	1.66 (0.55–5.00)	0.368
> 86	1.00 (Ref)	
Prior fragility fracture		
Yes	2.32 (1.20–4.48)	0.012
No	1.00 (Ref)	
Prior fracture site		
Hip	1.00 (Ref)	
Wrist	4.67 (0.81–26.87)	0.085
Spine	5.83 (1.07–31.76)	0.041
Other	0.778 (0.13–4.62)	0.782
Multiple	10.50 (1.67–66.09)	0.012
Corticosteroid use		
Yes	2.25 (0.83–6.06)	0.110
No	1.00 (Ref)	
Diabetes mellitus		
Yes	0.27 (0.09–0.79)	0.016
No	1.00 (Ref)	
Family history		
Yes	2.71 (1.28–5.76)	0.009
No	1.00 (Ref)	

combined with an antiresorptive or anabolic agent [20]. PTH has been shown to decrease the risk of vertebral fractures, but, to date, has no clear measurable effect in non-vertebral fractures [21]. Raloxifene reduces bone turnover, prevents bone loss, and diminishes the vertebral fracture risk without modifying the risk of non-vertebral fractures. Calcitonin has been shown to reduce bone loss, but no safe conclusions regarding its fracture prevention efficacy can be made [22]. Finally, strontium ranelate, an agent approved in Europe for the treatment of postmenopausal osteoporosis, has been proven to be effective in improving bone strength and preventing vertebral and non-vertebral fractures. Concerns about cardiac safety have led to a recommendation issued by European Medicines Agency for restriction of strontium use only in postmenopausal women or men with severe osteoporosis and increased risk of fracture [23].

Our study also identified predictors of receiving osteoporosis treatment preceding the index fracture. The most likely recipients of anti-osteoporotic drugs were women, patients 66–75 years of age, with a family history of osteoporosis, or a history of prior fragility fractures, especially in the spine or multiple sites. On the contrary, older age (> 86 years), certain prior fragility fractures, and diabetes were inversely related to the likelihood of receiving pharmacological treatment.

The low rate of osteoporosis diagnosis/treatment in men observed in our study is consistent with what has been previously reported in the literature, with treatment rates ranging from 0 to 15% [24–26]. Surprisingly, it seems that there is still the misconception that osteoporosis is a women's disorder only, despite the several studies demonstrating the problem of osteoporosis in male patients and the higher mortality rate associated with all fragility fractures in men compared to women [27]. Another observation is that patients over 86 years of age received poor osteoporosis treatment, although the risk for all major fragility fractures increases significantly with advancing age [28, 29]. This could be related to the fact that elderly patients usually have complex medical histories with multiple co-morbidities and polypharmacy. Prescribing additional medications to elderly patients with polypharmacy might increase the risk of drug–drug interactions, adverse effects, and patient non-adherence [30].

It is also interesting to note that anti-osteoporosis treatment was initiated in only 22% of patients with prior hip fractures compared to the significantly higher treatment rates in patients with wrist or spine fractures. These results fall within the range that has been reported in the literature, with treatment rates following a hip fracture varying from 6 to 22.5% in other European countries [18, 25, 31]. One possible reason could be the belief of many healthcare providers that, once a hip fracture has occurred, it is way too late to alter the progression of the disease. This is particularly true for elderly individuals, who tend to present with these fractures, as compared to the younger patients that usually suffer from distal radius or vertebra fractures and have a higher chance of getting adequate treatment. Another obstacle in properly addressing osteoporosis in hip fracture patients could be the increasing reports for the association of bisphosphonates with atypical femoral fractures. The result of such reports was to make physicians even more reluctant to administer anti-osteoporosis medication. Low treatment rates were also seen in patients with non-hip/non-vertebral fragility fractures (excluding wrist fractures). In general, fragility fractures in sites other than the hip, spine, or wrist tend to be perceived as irrelevant to osteoporosis and thus are not further evaluated, even though there is strong evidence to support the contrary [4, 29].

Finally, diabetes mellitus was not recognized as a risk factor for osteoporosis; on the contrary, it was inversely related to the likelihood of receiving anti-osteoporosis treatment. The rest of the well-known risk factors for osteoporosis did not seem to affect the evaluation and treatment rate in any way, further supporting the hypothesis that there is a gap in osteoporosis care even in high-risk patients. These observations represent either lack of knowledge or poor strategies in translating knowledge into diagnostic and therapeutic practices for osteoporosis.

In 2005, the American Orthopaedic Association launched the secondary prevention program "Own the Bone" to educate physicians and patients on the importance of osteoporosis screening and treatment in individuals with fragility fractures. To date, "Own the Bone" has been implemented in 220 institutions in the USA, leading to significant improvements in the management of osteoporosis postfracture [9]. More recently, the Fracture Working Group of the International Osteoporosis Foundation published a paper describing coordinator-based systems for secondary prevention services in patients suffering from osteoporosis-related fractures [32]. This initiative aims to close the secondary fracture prevention care gap by identifying patients presenting with fragility fractures and coordinating their care for proper evaluation of fracture risk, further assessment, and recommendation of appropriate treatment. The fracture liaison service (FLS) model was originally designed in the UK [8], but, since then, has been implemented in many countries in Europe, Australia, and the USA. Despite the promising preliminary results with regards to osteoporosis intervention rates, reduction in refracture risk, reduced mortality, and cost-effectiveness [33] in certain reference centers, further work needs to be done. Such intervention programs need to be implemented in a larger scale internationally to help change physicians' behavior and positively impact osteoporosis treatment rates and incidence of future fragility fractures.

There are several limitations to our study. First, this study was done in a single hospital, and thus, the results may not be easily generalizable to the whole country's population. However, this hospital is the only tertiary referral center in the central part of the country covering a population of ~ 1.5 million people. Another limitation is the relatively small sample size for spine and wrist fractures compared to the hip fracture patients. In the present study, only inpatients with fragility fractures were recruited. However, most vertebral and distal radius fractures are managed in the emergency room or in the outpatient clinic, in contrast to hip fractures that are always admitted. Finally, BMD was not included in the statistical analysis, since DEXA results were available only in 83/308 patients at the time of admission.

Our study builds upon the findings previously reported in the literature, providing recent data for a Greek population of both male and female patients with different fragility fractures. To our knowledge, this is the first study ever conducted in a homogeneous subpopulation of osteoporotic patients in Greece to determine whether osteoporosis is adequately managed and treated in patients suffering from fragility fractures. Our analysis also provides important insights into the various parameters that may affect the physicians' decision to treat in the respective country. It is also one of the few studies that have been done internationally after the implementation of initiatives like the International Osteoporosis Foundation's "fracture liaison service" and the American Orthopaedic Association's "Own the Bone". Interestingly, our diagnosis/treatment rates were similar to the previous reports, suggesting that there has been no noticeable improvement in recent years, despite the emphasis in secondary fracture prevention services.

In conclusion, the current study provides evidence that the management of osteoporosis in individuals who experience fragility fractures is inadequate, despite the fact that the majority of them have at least one known risk factor for osteoporosis, including prior fragility fractures. Factors such as age, sex, family history of osteoporosis, and prior fragility fractures may influence the patient's likelihood of receiving osteoporosis evaluation and treatment prior to the index fracture, whereas other risk factors are widely disregarded or poorly recognized as relevant to osteoporosis. Interventions to improve rates of risk assessment, early diagnosis, and use of anti-osteoporotic medications are necessary to reverse the current poor trend in osteoporosis care. Physicians need to realize that targeting high-risk patients is critical; adequate osteoporosis management can decrease the risk for a subsequent osteoporotic fracture and its associated personal, social, and economic burden.

Acknowledgements The authors would like to thank Dr. Antonios Koutalos for his invaluable assistance with patient interviews.

Compliance with ethical standards

Conflict of interest The authors declare no conflicts of interest.

Ethical approval The study has been approved by the University's institutional research board and has been performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments.

References

1. Cooper C, Campion G, Melton LJ III (1992) Hip fractures in the elderly: a world-wide projection. Osteoporos Int 2:285–289
2. Johnell O, Kanis J (2005) Epidemiology of osteoporotic fractures. Osteoporos Int 16:S3–S7
3. Center JR, Bliuc D, Nguyen TV, Eisman JA (2007) Risk of subsequent fracture after low-trauma fracture in men and women. JAMA 297:387–394
4. Klotzbuecher CM, Ross PD, Landsman PB, Abbott TA III, Berger M (2000) Patients with prior fractures have an increased risk of future fractures: a summary of the literature and statistical synthesis. J Bone Miner Res 15:721–739
5. Kanis JA (2002) Diagnosis of osteoporosis and assessment of fracture risk. Lancet 359:1929–1936

6. Hajcsar EE, Hawker G, Bogoch ER (2000) Investigation and treatment of osteoporosis in patients with fragility fractures. CMAJ 163:819–822
7. Elliot-Gibson V, Bogoch ER, Jamal SA, Beaton DE (2004) Practice patterns in the diagnosis and treatment of osteoporosis after a fragility fracture: a systematic review. Osteoporos Int 15:767–778
8. McLellan AR, Gallacher SJ, Fraser M, McQuillian C (2003) The fracture liaison service: success of a program for the evaluation and management of patients with osteoporotic fracture. Osteoporos Int 14:1028–1034
9. Bunta AD, Edwards BJ, Macaulay WB Jr, Jeray KJ, Tosi LL, Jones CB, Sietsema DL, Kaufman JD, Murphy SA, Song J, Goulet JA, Friedlaender GE, Swiontkowski MF, Dirschl DR (2016) Own the bone, a system-based intervention, improves osteoporosis care after fragility fractures. J Bone Jt Surg Am 98:e109
10. World Health Organization (1998) Guidelines for preclinical evaluation and clinical trials in osteoporosis. http://apps.who.int/iris/handle/10665/42088. Accessed 28 Feb 2018
11. Genant HK, Wu CY, van Kuijk C, Nevitt MC (1993) Vertebral fracture assessment using a semiquantitative technique. J Bone Miner Res 8:1137–1148
12. Tuppurainen M, Kröger H, Saarikoski S, Honkanen R, Alhava E (1995) The effect of gynecological risk factors on lumbar and femoral bone mineral density in peri- and postmenopausal women. Maturitas 21:137–145
13. Shuster LT, Rhodes DJ, Gostout BS, Grossardt BR, Rocca WA (2010) Premature menopause or early menopause: long-term health consequences. Maturitas 65:161–166
14. Prentice A (2004) Diet, nutrition and the prevention of osteoporosis. Public Health Nutr 7:227–243
15. Epstein S, Inzerillo AM, Caminis J, Zaidi M (2003) Disorders associated with acute rapid and severe bone loss. J Bone Miner Res 18:2083–2094
16. Johnell O, Kanis JA, Odén A, Sernbo I, Redlund-Johnell I, Petterson C, De Laet C, Jönsson B (2004) Fracture risk following an osteoporotic fracture. Osteoporos Int 15:175–179
17. Suhm N, Lamy O, Lippuner K, OsteoCare study group (2008) Management of fragility fractures in Switzerland: results of a nationwide survey. Swiss Med Wkly 138:674–683
18. Ruggiero C, Zampi E, Rinonapoli G, Baroni M, Serra R, Zengarini E, Baglioni G, Duranti G, Ercolani S, Conti F, Caraffa A, Mecocci P, Brandi ML (2015) Fracture prevention service to bridge the osteoporosis care gap. Clin Interv Aging 10:1035–1042
19. USPSTF (2016) Final Recommendation Statement. Vitamin D and calcium to prevent fractures: preventive medication. http://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/vitamin-d-and-calcium-to-prevent-fractures-preventive-medication. Accessed 18 Oct 2016
20. Boonen S, Vanderschueren D, Haentjens P, Lips P (2006) Calcium and vitamin D in the prevention and treatment of osteoporosis—a clinical update. J Intern Med 259:539–552
21. Neer RM, Arnaud CD, Zanchetta JR, Prince R, Gaich GA, Reginster JY, Hodsman AB, Eriksen EF, Ish-Shalom S, Genant HK, Wang O, Mitlak BH (2001) Effect of parathyroid hormone (1–34) on fractures and bone mineral density in postmenopausal women with osteoporosis. N Engl J Med 344:1434–1441
22. Joffe HV (2013) Calcitonin salmon for the treatment of postmenopausal osteoporosis. Silver spring (MD): FDA; http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ReproductiveHealthDrugsAdvisoryCommittee/UCM343748.pdf. Accessed 21 Jan 2017
23. European Medicines Agency's Committee for Medicinal Products for Human Use (2013) Recommendation to restrict the use of Protelos/Osseor (strontium ranelate).http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2013/04/news_detail_001774.jsp&mid=WC0b01ac058004d5c1. Accessed 5 Mar 2018
24. Hawker G, Ridout R, Ricupero M, Jaglal S, Bogoch E (2003) The impact of a simple fracture clinic intervention in improving the diagnosis and treatment of osteoporosis in fragility fracture patients. Osteoporos Int 14:171–178
25. Panneman MJ, Lips P, Sen SS, Herings RM (2004) Undertreatment with anti-osteoporotic drugs after hospitalization for fracture. Osteoporos Int 15:120–124
26. Balasubramanian A, Tosi LL, Lane JM, Dirschl DR, Ho PR, O'Malley CD (2014) Declining rates of osteoporosis management following fragility fractures in the U.S., 2000 through 2009. J Bone Jt Surg Am 96:e52
27. Center JR, Nguyen TV, Schneider D, Sambrook PN, Eisman JA (1999) Mortality after all major types of osteoporotic fracture in men and women: an observational study. Lancet 353:878–882
28. Ensrud KE (2013) Epidemiology of fracture risk with advancing age. J Gerontol A Biol Sci Med Sci 68:1236–1242
29. Ahmed LA, Center JR, Bjørnerem A, Bluic D, Joakimsen RM, Jørgensen L, Meyer HE, Nguyen ND, Nguyen TV, Omsland TK, Størmer J, Tell GS, van Geel TA, Eisman JA, Emaus N (2013) Progressively increasing fracture risk with advancing age after initial incident fragility fracture: the Tromsø study. J Bone Miner Res 28:2214–2221
30. Maher RL, Hanlon J, Hajjar ER (2014) Clinical consequences of polypharmacy in elderly. Expert Opin Drug Saf 13:57–65
31. Rabenda V, Vanoverloop J, Fabri V, Mertens R, Sumkay F, Vannecke C, Deswaef A, Verpooten GA, Reginster JY (2008) Low incidence of anti-osteoporosis treatment after hip fracture. J Bone Jt Surg Am 90:2142–2148
32. Marsh D, Akesson K, Beaton DE, Bogoch ER, Boonen S, Brandi ML, McLellan AR, Mitchell PJ, Sale JE, Wahl DA, IOF CSA Fracture Working Group (2011) Coordinator-based systems for secondary prevention in fragility fracture patients. Osteoporos Int 22:2051–2065
33. Walters S, Khan T, Ong T, Sahota O (2017) Fracture liaison services: improving outcomes for patients with osteoporosis. Clin Interv Aging 10:117–127