Adherence to the recommended prevention strategies before and after a hip fragility fracture: what makes us go blind?

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ABSTRACT

Objectives: Our main objective was to evaluate the percentage of patients under anti-osteoporotic treatment (OT) at the time of hip fracture (HF), and at one and four years after the HF event. We compared these results with the percentage of patients who should be under treatment at all three stages, according to the recently published Portuguese cost-effectiveness recommendations (PCER) for OT. Data regarding the occurrence of new fragility fractures and mortality were, also determined, one and four years after the HF event. Our secondary objective was to evaluate characteristics of patients associated with OT at the time of hip fracture.

Material and Methods: Patients hospitalized due to HF between May 1st and October 31st of 2013 in a single tertiary hospital, were selected for this study. Data regarding demographic, clinical features (including the clinical risk factors for fracture considered by FRAX®), level of independence in daily activities (Katz index), comorbidity (Charlson index) and OT were recorded at the time of the HF. The subsequent risk of fracture was estimated for each patient with FRAX® (without mineral bone density). Mortality and the percentage of patients receiving an OT prescription and suffering a new osteoporotic fracture, at one and four years after the HF event, were established.

Results: One hundred and thirty patients were included, with a mean age of 81.6±8.6 years. At the time of the HF only 28(21.5%) of the patients were receiving some form of OT. According to PCER, 115(88.5%) of these patients should be undergoing treatment according to FRAX® estimated risk, 30(23.1%) based on previous fractures and 119(91.5%) based on either criteria.

The score of comorbidities was negatively associated with the prescription of OT at baseline (OR=0.17 [0.05--0.53], p=0.011) while the level of independence in daily activities was associated with higher probability of being treated (OR=3.20 [1.30-7.89], p=0.003).

At one year after the HF, 39/130(30%) of patients had died. Although, according to PCER, all the remaining patients should be under OT based on the history of HF, only 11/91(12.1%) had received an OT prescription and 5/91(5.5%) suffered a new osteoporotic fracture during this period. At four years after the HF, 65/130 (50%) of patients had died. Only 6 of the remaining 65 (9.2%) were receiving an OT prescription and 9/65(13.8%) had suffered an additional fracture.

Conclusions: Similar to other countries, the percentage of patients receiving OT before and especially after a HF is extremely low. Risk estimations with FRAX® and application of current PCER should allow clinicians to introduce appropriate primary and secondary preventive measures. Comorbidities and dependence seem to be important reasons for this undertreatment.

Keywords: Osteoporosis; Hip fracture; Treatment

INTRODUCTION

Osteoporosis (OP) is a major public health problem. Morbidity, mortality and costs of OP and associated fractures, are already one of the most important burdens faced by health care systems in European countries[1]. Although hip fractures (HF) account for less than 20% of all osteoporotic fractures, they contribute for the majority of fracture-related health care expenditure and mortality, in men and women, over the age of 50 years[2].

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Portugal has one of the lowest rates of HF in Western Europe but, despite that, more than 10.000 patients were admitted every year, to the Portuguese National Health Service, due to hip fragility fractures, between 2006 and 2010, justifying a total health care expenditure of about 216 million euro during 2011[3]. The burden of the problem will tend to increase in coming years, mostly due to the increasing age of the population, unless effective preventive measures are put in place.[3] In fact, it was estimated that the total number of HF worldwide will increase from 1.26 million in 1990 to 2.6 million by 2025 and 4.5 million by 2050[4].

Despite the significant advances registered in the last years in terms of diagnosis and risk fracture assessment, the production of practice guidelines worldwide with validation of country-specific intervention thresholds and the development of effective anti-osteoporotic treatments (OT), there is still an enormous gap between the number of patients at high risk of fracture and those that receive treatment[5-7]. This gap persists even after the occurrence of an osteoporotic fracture (OF), with less than 20% of the patients receiving OT within one year following a hip fracture, even in the most developed countries[7-10].

Although we expect similar osteoporosis care gap to be observed in Portugal, few studies have addressed this important matter. Additionally, multidisciplinary Portuguese cost-effectiveness recommendations (PCER), regarding the estimation of fracture risk and the initiation of OT, were recently published[11]. According to these recommendations, pharmacological treatment should be initiated in all subjects over the age of 50 who have previously experienced: (1) 1 or more fragility fractures of the hip, (2) 1 or more symptomatic vertebral fragility fracture, (3) 2 or more fragility fractures, independently of the site of fracture or the absence of symptoms. Pharmacological treatment with generic alendronate is cost-effective and should be advised in (1) men and women with a ten-year fracture risk according to FRAX®, including dual energy x-ray absorptiometry (DXA), at or above 9% for major fracture or 2.5% for HF and (2) men and women with a ten-year fracture risk according to FRAX®, without DXA, at or above 11% for major fracture or 3% for HF[11].

The main objective of this study was to evaluate the percentage of patients under OT at the time and after a HF, and compare these results with the percentage of patients who should be under treatment according to the recent multidisciplinary Portuguese recommendations. We also ascertain the number of deaths and new OF occurred within 1 and 4 years after the HF. Our secondary objective was to evaluate characteristics of patients associated with OT prescription at the time of HF as a means to identify barriers to OT prescription and foster the implementation of the recommendations in practice.

MATERIAL AND METHODS

PATIENTS

Patients hospitalized for a HF in our tertiary centre – Centro Hospitalar e Universitário de Coimbra – between May 1st and October 31st of 2013, were included in this study. HF cases were identified through medical discharge letters using the International Classification of Diseases, ninth revision (ICD 9), corresponding to codification for hip osteoporotic fractures: ICD 9: 820.08-820.30. A total of 201 such cases were recognized. Patients, their primary caregiver or relatives (the last two in case of death of the patient or patient's inability to communicate) were contacted by phone, to gather informed consent for the participation in the study and, if obtained, to gather data according to a pre-defined and structured questionnaire.

A total of 130 inquiries were done, 32 of which were answered by the patients themselves and 98 by the primary caregiver or relative. It was not possible to collect information regarding 66 patients from the initial sample (n=201), because they (1) did not answer the phone after 3 attempts, (2) working phone number was not available (3) the primary caregiver or relatives ignored essential information or refused to participate. The diagram for patient's distribution is shown on Figure 1.

One and four years after the HF event, the patients or their caregivers were contacted again, by phone, to ascertain death, OF recurrence and OT prescription.

DATA COLLECTION

For each patient we collected data at three time points: baseline (at time of the HF), one and four years after the HF event.

BASELINE

At baseline data collection was done retrospectively

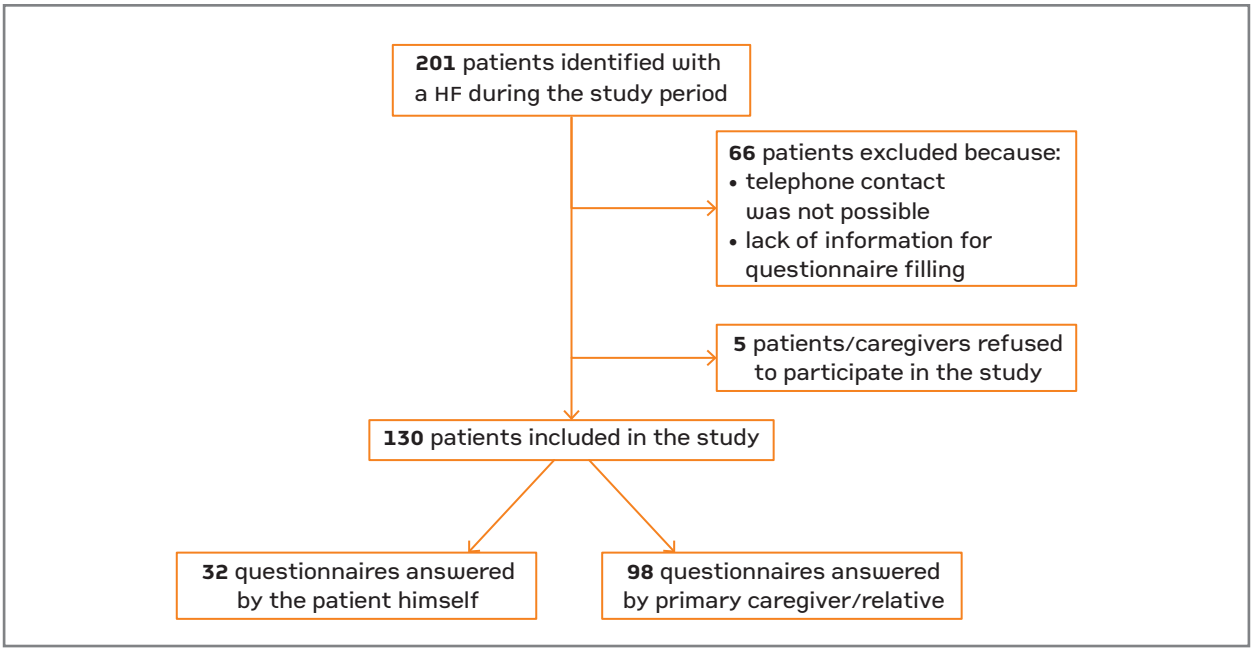

FIGURE 1. Diagram of patients' selection in the study
HF: hip fracture

through application of a structured questionnaire that included data about socio-demographic characteristics: age, gender, residence; clinical characteristics: weight, height, body mass index (BMI), clinical risk factors included in FRAX® - history of previous fracture (including location and number of previous fractures), smoking status, history of corticosteroid therapy, rheumatoid arthritis, alcohol intake, family history of HF and causes of secondary OP – and history of at least one previous fall.

At this time, we inquired two questions regarding OT – was the patient under some kind of treatment for OP at time of the HF? If yes, which? (calcium and vitamin D supplementation/bisphosphonates/strontium ranelate or other medication specified by the patient/caregiver).

Institutionalization status, the level of independence in daily living activities and the level of comorbidities were also recorded at baseline.

Patients were considered institutionalized if they resided on a nursing home or other care unit.

The level of independence was assessed through the Katz score for independence in activities of daily living, commonly referred to as the Katz index. This index ranks adequacy of performance in six functions: bathing, dressing, toileting, transferring, continence, and feeding. Patients are scored yes/no for independence in each of the six functions. A score of 6 indicates full function, 4 indicates moderate impairment, and 2 or less indicates severe functional impairment[12].

The level of comorbidities before the HF was assessed by means of the Charlson Comorbidity Index (CCI). The CCI was developed and validated as a measure of comorbidities and their overall impact on survival, allowing prediction of the risk of mortality over 1 year. The index encompasses 19 clinical conditions, each classified according to a weighting factor ranging from 1-6. Through the sum of the points obtained in each of the variables, a total score is obtained. Higher CCI score indicates greater comorbidity burden and higher risk of mortality[13].

FRAX®, without mineral bone density, was used to estimate the 10 year fracture risk at baseline and so, for the aim of predicting the risk at this time point, the current HF was not considered as previous fracture. For the purpose of FRAX® estimation, patients aged more than 90 years-old were recorded in the FRAX® calculator as having 90 years of age. Thresholds for therapeutic intervention were defined according to recent Portuguese recommendations (without DXA): a 10 year probability of a major osteoporotic fracture ≥ 11% or a 10 year probability of HF ≥ 3% or a history of one or more fragility fracture of the hip, one or more symptomatic fragility vertebral fractures or two or more

fragility fractures, independently of the site of the fracture or absence of symptoms.

ONE AND FOUR YEARS AFTER THE HF

One and four years after the HF event, two questions regarding OT were newly done – had the patient been prescribed with some form of OT? If yes, which? (calcium and vitamin D supplementation/bisphosphonates/strontium ranelate or other medication specified by the patient/caregiver).

We also recorded, at both time-points, the number of patients who died and the number of patients who suffered a new osteoporotic fracture.

All missing data, registered during questionnaire collection, were complemented through consultation of the hospital medical files and/or the Portuguese health database known as "Plataforma de Dados de Saúde (PDS)" - an electronic platform that provides a central system for recording and sharing clinical information, in accordance with the requirements of the National Commission for Data Protection.

ETHICS SECTION

Participation was explicitly voluntary and an informed consent was obtained, through phone contact, from all patients, primary caregiver or relatives (the last two in case of death or patient's inability to communicate). An ethical approval was obtained from the Ethical Committee of the Faculty of Medicine of Coimbra University (Ref. CE-017/2013). Throughout the study, the principles of Helsinki Declaration were respected.

STATISTICAL ANALYSIS

Descriptive statistics of baseline variables was done using means and standard deviations for continuous variables (age, BMI, mean ten-year risk of major OF and HF according to FRAX®, Katz score and CCI) and frequencies and percentages for categorical variables coded as "yes" or "no" (male gender, history of previous fracture, fracture risk factors included in FRAX®, previous falls and institutionalization).

Patients were divided into two groups, according to whether or not they were under anti-osteoporotic treatment at the time of HF, as means to investigate factors associated to OT prescription. Univariable logistic regression analysis was done for each one of the baseline variables: the categorical variables were compared between the two groups using a chi-squared test and the continuous variables were compared using Student's *t* test or Mann-Whitney U test (depending on the presence or absence of normal distribution of the data, respectively).

Multivariable logistic regression was performed and variables with $p<0.1$ in univariate analysis were included in the regression model (age, male sex, BMI, history of previous fracture, history of glucocorticoid therapy, rheumatoid arthritis, alcohol intake, family history of HF, mean ten-year fracture risk according to FRAX® for major OF and HF, institucionalization, CCI and Katz score).

Descriptive statistics of the number of patients who died, who suffered a new osteoporotic fracture and who had been prescribed some form of medication for OP, one and four years after the HF event, was done using frequencies and percentages.

A $p<0.05$ threshold was considered significant for all analyses.

All statistical analyses were performed using the IBM SPSS statistic software version 22.0.

RESULTS

CHARACTERISTICS OF THE POPULATION AT BASELINE

One hundred and thirty patients with a HF were included in the study. The mean age of the study population was 81.6 ± 8.6 years and 69.2% were female. The characteristics of this sample are presented in Table I.

Half of the patients in our study had a history of previous fragility fracture. Of these patients, 8 (12.3%) had one or more fragility fracture of the hip, 6 (9.2%) had one or more symptomatic fragility vertebral fracture, 16 (24.6%) had two or more fragility fractures, independently of the site of the fracture or absence of symptoms, and 35 (53.8%) had a previous fragility fracture, not warranting treatment: forearm (n=12), lower leg (n=4), asymptomatic vertebral (n=10), upper arm (n=4) and ribs (n=5). According to the PCER, based on the history of previous fractures, 30 of all included patients had formal indication to start OT, without the need for FRAX® risk estimation.

All patients presented at least one of the clinical risk factors for fracture included in FRAX® and 43(33.1%) had 2 or more of them.

According to FRAX®, the mean ten-year risk for major OP was 20.9±14% and the mean ten-year risk for HF was 13.4±12.8% before the occurrence of the index HF. Applying the Portuguese Recommendations and taking FRAX® estimates into account (without DXA),

TABLE I. CHARACTERISTICS OF THE STUDY POPULATION (N=130), BEFORE HIP FRACTURE

Characteristics	Population (n=130)
Mean age n(%) (SD) (years)	81.6 ± 8.6
Male gender n(%)	40 (30.8)
Mean BMI (SD) (kg/m2)	25.9 ± 4.4
History of previous fracture n(%)	65 (50)
Fracture risk factors (included in FRAX®) n(%):	
Current smoking	8 (6.2)
History of glucocorticoid therapy	21 (16.2)
Rheumatoid arthritis	15 (11.5)
Alcohol intake (≥ 3 units per day)	23 (17.7)
Secondary Osteoporosis	32 (24.6)
Family history of HF	15 (11.5)
Mean ten-year fracture risk according to FRAX® (SD):	
Major OF	20.9 ± 14
HF	13.4 ± 12.8
Additional factors:	
Institutionalization n(%)	18 (13.8)
Previous falls n(%)	94 (72.3)
Mean Charlson score (SD)	5.5 ± 2.5
Mean Katz index score (SD)	2.6 ± 2.2

HF: hip fracture; SD: standard deviation; BMI: body mass index; OF: osteoporotic fracture

treatment with (at least) generic alendronate would be recommended to 101(77.6%) of the patients based on the 10-year risk of major OF and 115(88.5%) based on the estimated risk of HP. Based solely on the previous fracture criteria, 30(23.1%) of the patients should have received treatment. Altogether, 119(91.5%) of patients should be on OT, based on either of the three criteria.

FREQUENCY OF ANTI-OSTEOPOROTIC TREATMENT AT BASELINE

At baseline only 28 (21.5%) of the patients were under some form of treatment for OP. All these patients had indication for treatment according to the FRAX estimation risk, but they represent only 23.5% of the total number of patients (n=119) who should be under treatment according to national recommendations. Furthermore, only 50% of the total number of patients with a previous fragility fracture (n=30) were receiving treatment before the index HF episode.

The prescribed medications included bisphosphonates (n=4), strontium ranelate (n=3) and calcium+vitamin D supplementation (n=16). The other caregivers did not know the specific ongoing medication, but were sure that the patient had been treated for OP (n=5).

FACTORS ASSOCIATED WITH ANTI-OSTEOPOROTIC TREATMENT AT BASELINE

In univariable analysis, the prescription of OT before fracture was positively and significantly associated with (1) rheumatoid arthritis (OR=15.8 [4.52-55.60], p<0.001), (2) higher ten-year estimated risk for major OF and for HF (p=0.001 and p=0.002, respectively) and (3) a higher Katz score (p<0.001). Prescription of OT before HF was negatively and significantly associated with (1) male gender (OR=0.06 [0.01-0.46], p<0.001), (2) higher CCI (p<0.001), (3) alcohol consumption (OR=0.14 [0.02-1.05], p=0.026) and (4) institutionalization (OR=0.75 [0.68-0.84], p=0.026).

On multivariable analysis, only Katz index and CCI score retained a significant association with the introduction of OT prescription before the HF: for every unit of increase in Katz score the OR for treatment was 3.20 [1.30-7.89] and for every unit increased in Charlson score the OR was 0.17 [0.05-0.53]. Table III represents the results of univariable and multivariable analysis of the factors associated or not with the introduction of OT at baseline.

FREQUENCY OF OSTEOPOROTIC TREATMENT AFTER THE HF

Up to one year after the HF, 39/130(30%) of patients had died. Among the 91 surviving patients, 5(5.5%) had suffered a new osteoporotic fracture. Although, according to PCER, all the surviving patients (n=91) should be under OT based on the history of HF, only 11/91(12.1%) had received some kind of OT prescription: bisphosphonates (n=3), strontium ranelate (n=1) and calcium + vitamin D supplementation (n=7).

Up to four years after the HF and one year after the PCER publication, 65/130 (50%) of patients had died and 9 (13.8%) of the 65 surviving patients had re-fractured. Of the surviving 65 patients only 6(9.2%) had received some kind of OT prescription: bisphosphonates (n=3) and calcium + vitamin D supplementation (n=3). Altogether the percentage of patients being appropriately treated decreased after the fracture. Furthermore, at both time points, all new fragility fractures occurred in non-treated patients.

TABLE II. CHARACTERISTICS OF PATIENTS WITH OR WITHOUT OSTEOPOROTIC TREATMENT, BEFORE THE HIP FRACTURE

Characteristic	Untreated patients (n=102)	Treated patients (n=28)	p value
Age (years), mean±SD	83.9 ± 8.9	80.9 ± 8.4	0.078
Male sex, n(%)	39 (30)	1 (0.8)	<0.001
BMI (kg/m2), mean±SD	26.2 ± 4.7	24.8 ± 2.7	0.044
Previous fracture, n(%)	49 (37.6)	19 (14.6)	0.063
Fracture risk factors (in FRAX®) n(%):			
Current smoking	8 (6.1)	0 (0)	0.200
History of glucocorticoid therapy	13 (10)	8 (6.1)	0.077
Rheumatoid arthritis	4 (3)	11 (8.5)	<0.001
Alcohol intake (≥ 3 units per day)	23 (17.8)	0 (0)	0.026
Secondary osteoporosis	25 (19.2)	7 (5.4)	1.000
Family history of HF	9 (6.9)	6 (4.6)	0.091
Mean ten-year fracture risk according to FRAX® (SD) for:			
Major OF	18.5 ± 11.7	29.7±18	0.001
HF	11.3 ± 9.8	21.3 ± 18.4	0.002
Additional factors:			
Institutionalization n(%)	18 (13.8)	0 (0)	0.013
Previous falls n(%)	71 (54.6)	23 (17.7)	0.189
Mean Charlson Index (SD)	6.4 ± 1.9	2.3 ± 1.5	<0.001
Katz index score (SD)	2.1 ± 2.1	4.6 ± 0.9	<0.001

BMI: Body mass index; OF: Osteoporotic fracture; HF: Hip fracture; SD: Standard deviation

TABLE III. MULTIVARIATE ANALYSIS OF PATIENTS' CHARACTERISTICS ASSOCIATED OR NOT WITH THE INTRODUCTION OF ANTI-OSTEOPOROTIC TREATMENT

	Introduction of OT prescription at baseline			
	Univariable analysis		Multivariable analysis	
Characteristics	OR (CI 95%)	p value	OR (CI 95%)	p value
Age	Not applicable	NS	NS	NS
Male sex	0.06 [0.01-0.46]	<0.001	NS	NS
BMI	NA	0.044	NS	NS
History of previous fracture	NS	NS	NS	NS
History of glucocorticoid therapy	NS	NS	NS	NS
Rheumatoid arthritis	15.80 [4.52-55.6]	<0.001	NS	NS
Alcohol intake	0.14 [0.02-1.05]	0.026	NS	NS
Family history of HF	NS	NS	NS	NS
Ten-year major OF risk (FRAX®)	NA	0.001	NS	NS
Ten-year HF risk (FRAX®)	NA	0.002	NS	NS
Katz score	NA	<0.001	3.20 [1.30-7.89]	0.011
Charlson score	NA	<0.001	0.17 [0.05-0.53]	0.003
Institucionalization	0.75 [0.67-0.83]	0.013	NS	NS

BMI: Body mass index; HF: Hip fracture; OF: Osteoporotic fracture; OR (CI 95%): Odds ratio with confidence interval of 95%; NS: Not significant; NA: Not applicable

TABLE IV. FREQUENCY OF PATIENTS RECEIVING AN OSTEOPOROTIC TREATMENT PRESCRIPTION, NEW OSTEOPOROTIC FRACTURES AND DEATHS, ONE AND FOUR YEARS AFTER THE HIP FRACTURE

	One year after HF	Four years after HF
Patients who died, n(%)	39 (30)	65 (50)
Patients that received an osteoporotic treatment prescription, n(%)	11 (12.1)	6 (9.2)
Patients who should be under osteoporotic treatment according to PCER, n(%)	91 (100)	65 (100)
Patients who suffered a new osteoporotic fracture, n(%)	5 (5.5)	9 (13.8)

PCER: Portuguese cost-effectiveness recommendations; HF: hip fracture

DISCUSSION

According to a recent epidemiological study, OP is the fourth most prevalent rheumatic and musculoskeletal disease in Portugal, with a prevalence of 10.2% among the population aged with more than 18 years-old (17% for women and 2.6% for men)[14]. In a recent Portuguese report, conducted by the Portuguese Society of Rheumatology, less than 10% of 1587 post-menopausal women, in which 43% had Osteoporosis, were receiving OT[15].

In our sample of hip fractured patients, the same treatment lag was found, given that only 21.5% of the patients were receiving some form OT treatment before the HF. Within this percentage, the majority was only on calcium and vitamin D supplementation, and not really on anti-osteoporotic treatment, which further widens the gap. Surprisingly, this proportion was reduced to merely 12.1% at one year and 9.2% at four years after fracture. Within the small group of treated patients, the most prescribed therapeutic was calcium and vitamin D supplementation, with only 4 patients being treated with bisphosphonates before fracture and 3 after fracture (both one and four years' time points), this representing the most cost-effective therapy for OP[11].

According to the recent Portuguese recommendations, a total of 115(88.5%) of these patients should have been recommended for OT before fracture and 100% of them should have been prescribed these medications following the event. Therefore, our study reflects an important gap between best practice recommendations and everyday clinical practice, similar to that observed in other countries[16-19]. The reasons underlying this gap need to be understood if we want to achieve the full social benefit of the current recommendations.

We explored the factors associated with the presence or absence of OT, before the current HF. The univariable analysis suggests that physicians are insufficiently sensitive to the presence of clinical risk factors for fracture. In fact, none of these conditions was associated with a positive odds ratio for treatment, except for rheumatoid arthritis, probably reflecting the intervention of rheumatologists. Alcohol consumption was actually associated with a lower prevalence of treatment. Male gender was associated with a lower rate of treatment compared with female gender. This is consistent with other international studies that conclude that men are less frequently treated than woman, despite the fact that they have a higher risk of morbidity and mortality after a major fragility fracture[17].

On univariable analysis, the overall fracture risk, as estimated by FRAX® was significantly higher in the group of treated patients, suggesting that caring physicians seem to be somewhat sensitive to the overall risk of fracture conveyed by FRAX® but multivariable analysis was not consistent with these findings, proving that either these risk factors are not considered relevant or estimations of risk are nor commonly performed or considered in the decision to treat.

Only two factors remained significantly associated with treatment after multivariable analyses: the Katz and the Charlson scores. The results observed with the Katz index score indicate that patients with higher levels of independence in daily activities are more frequently treated than patients with higher levels of dependence. This may be interpreted as suggesting that physicians tend to disregard the added value of OT and fracture prevention in patients whose functionality (independence) is already significantly compromised and tend to "invest" more to prevent fractures in those with better general heath and quality of life. This interpretation is also sustained by the fact that institutionalized

patients and those with higher burdens of comorbidity were treated less frequently than the ones who were not. Medical comorbidities (presumably due to polimedication) and alcohol abuse have already been identified as significant barriers to initiation of effective OT medication[19-20]. Although this may be understandable to some extent, physicians must be aware that these patients they are leaving untreated are exactly those with the highest risk of fracture and associated mortality[21].

The alarming gap in the secondary prevention of fractures found in our study is, unfortunately, consistent with findings of international reports. In an American retrospective study, the authors reported a fall in osteoporosis medication use between 2001 and 2011 in individuals hospitalized for hip fracture, from 40% to 21%, which suggests that the highest-risk populations are, in fact, not receiving appropriate therapy[21]. Low treatment rates after incident clinical fractures have also been reported from the Global Longitudinal Study of Osteoporosis in Women (GLOW), with only 25% of previously treatment-naïve women taking OT after a hip fracture[22]. Thus, we are facing a global undertreatment of OP, even after the event of a major fracture and physicians are disregarding the fact that the risk fracture rises remarkably after a fracture, especially within the first year of the index fracture event[23].

Our study has some limitations. First, we only included patients with HF, which provided a modest sample of patients. Second, we have a small group of treated patients which could lower the statistical power of logistic regression analysis. Third, information regarding clinical data was provided by the patient himself or by the primary caregivers or relatives, which may represent a recall bias. Even so, medical files and *PDS* were consulted in dubious cases. The list of factors in whom we tested the association with presence of OT is not exhaustive, although they represent important settings and barriers observed in clinical practice. Furthermore this analysis was done using baseline data, regarding the year of 2013. Despite that, given the sustained lack of treatment found in 2017, the authors strongly fell that these findings still represent important settings and barriers in nowadays clinical practice. Finally, we only included patients from one single center, but our findings likely to reflect the reality throughout Portugal.

Nevertheless, our study is, to the best of our knowledge, the first Portuguese study addressing this important matter in both primary and secondary prevention of OF. In addition we also focused on factors associated with OT and barriers limiting the prompt introduction of OT, which has never been studied in our country. In order to foster the application of national recommendations, we need to understand the reasons underlying undertreatment at a national level and design effective strategies to promote awareness and education of physicians, patients and families. Target populations for treatment should be selected according to the risk of fracture and higher number of comorbidities and level of dependence should not represent a barrier for OT, since these features define a population at especially high-risk of fracture. In accordance to international studies, physicians' and patients' concerns about the risk of side effects, such as osteonecrosis of the jaw and atypical femur fractures related to bisphosphonate drug therapy, may also represent important barriers for treatment. Multidisciplinary discussions should be promoted especially among orthopedic surgeons, general practitioners and rheumatologists, including the regular and appropriate assessment of the risk of fracture and the balance of risk and benefits of OT in different ages, independence and general health statuses[24-29].

In conclusion, the percentage of patients under OT before and after a current HF is low and reasons for this undertreatment include a higher level of dependence and the presence of comorbidities. Risk estimation by FRAX® and application of current PCER would allow clinicians to introduce appropriate primary and secondary preventive measures, thus their clinical relevance should be emphasized in the Portuguese medical community.

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