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Mind the gap: Incidence of osteoporosis treatment after an osteoporotic fracture – results of the Austrian branch of the International Costs and Utilities Related to Osteoporotic Fractures Study (ICUROS)

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ABSTRACT

Introduction: Despite availability of effective treatment options proven to prevent osteoporotic fractures, a huge gap in osteoporosis treatment exists. The aim of the present study was to evaluate the treatment rate after a major osteoporotic fracture (MOF) in Austria, one of the 25 wealthiest countries worldwide.

Methods: This analysis is based on the data of the International Costs and Utilities Related to Osteoporotic Fractures Study (ICUROS), a prospective observational study assessing data from patients who suffered a MOF. We stratified these patients by treatment status at time of fracture and compared treatment use following MOF by sex as well as by fracture sites at the time of the index fracture, and 4, 12, and 18 months thereafter. Descriptive statistics, t-tests for continuous variables and chi-squared tests for nominal variables, were performed to compare treatment groups.

Results: A total of 915 patients (78 % female) were recruited at 8 different trauma centers throughout Austria. At the time of fracture, 731 patients (80 %) did not receive osteoporosis treatment. In this group, follow-up analysis after 4, 12 and 18 months revealed a treatment rate of 18 %, 16 %, 15 % in women, and 8 %, 12 %, 10 % in men, respectively. In those who received osteoporosis medication at the time of fracture the treatment rate was 65 %, 54 % and 60 % in women, and comparable results in men.

Conclusions: Only 1 in 10 men, and less than 2 in 10 women of those who did not receive osteoporosis treatment at the time of fracture were prescribed an adequate osteoporosis treatment. Thus, the vast majority of patients who sustained an osteoporotic fracture and thus were at imminent risk of receiving subsequent fractures did not receive an adequate treatment. There is a clear need for the implementation of coordinated, multi-disciplinary models of care for secondary fracture prevention.

1. Introduction

Osteoporosis is a progressive systemic skeletal disease characterized by reduced bone mass leading to bone fragility and higher risk of fractures. In the EU the prevalence of osteoporosis was estimated at 27.6 million in 2010 [1]. The number of osteoporotic fractures is increasing worldwide resulting in a global major public health issue [2]. Osteoporosis is the most common reason among the elderly for non-traumatic or low-energy-induced fractures, notably at the hip, vertebra, wrist and distal forearm [3], which represents the main clinical consequence of the disease. It has been estimated that 8.9 million people worldwide suffer an osteoporotic fracture annually, of which one third occur in Europe [2]. The consequences are serious as osteoporotic fractures are associated with increased morbidity, disability, pain and mortality [4].

Nevertheless, several reports exist, that describe an inadequacy in diagnosis and treatment of osteoporosis worldwide [5,6]. Particularly in the first few months after fragility fracture, the risk for a subsequent fracture is substantially increased and, hence, treatment is vitally important [7]. Numerous approved agents are available to treat osteoporosis effectively [8]. For example, in post-menopausal women with osteoporosis, first line treatment options such as alendronate have been shown to result in a risk reduction of up to 45 % for new vertebral fractures, and up to 30 % for other types of fracture [5]. Moreover,

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teriparatide has been shown to be associated with an even greater reduction of vertebral fracture risk compared to bisphosphonates [9]. It is notable that in men treatment rate after osteoporotic fracture has been shown to be (very) low too, irrespective of the fact that both vertebral and hip fractures are associated with an even higher mortality compared to women, and osteoporosis treatment with proven anti-fracture efficacy is available. For example, treatment with zoledronic acid has been shown to result in a 67 % risk reduction of new vertebral fracture in men [10].

The incidence of osteoporotic fractures in Austria is among the highest worldwide [11–14]. However, so far, no sufficient data has been available on the incidence of osteoporosis treatment in patients suffering an osteoporotic fracture. Furthermore, due to substantial differences in health care systems, results from other countries in which treatment rate after MOFs has been investigated cannot be directly extrapolated to Austria. Ranked as the ninth best health care system in the world by the World Health Organization (WHO), Austria has an excellent health care system based on a two-tier system in which almost all individuals receive publicly funded care, with the option to purchase supplementary private health insurance.

The objective of the current study was to define the incidence of osteoporosis treatment in Austria after a MOF in a) men and women, b) patients with and without prevalent fracture, c) patients with and without prevalent osteoporosis treatment at the time of the index fracture.

2. Methods

This study involves a retrospective analysis based on the data of the International Costs and Utilities Related to Osteoporotic Fractures Study (ICUROS) which was introduced and supported by the International Osteoporosis Foundation (IOF) in 2007 (http://www.icuros.org/). ICUROS is a prospective observational multinational data collection study (Australia, Austria, Estonia, France, Italy, Lithuania, Mexico, Russia, Spain, UK and the USA) with the aim of assessing data from patients suffering an osteoporosis-related fracture providing a deeper insight into the costs and quality of life (QoL) associated with osteoporotic fractures. Unlike in other countries, the Austrian study protocol also included assessment of pharmaceutical treatment with focus on pharmaceutical substances usually used in osteoporosis treatment (i.e.: Calcium, vitamin D, bisphosphonates, estrogens, selective estrogen receptor modulators (SERMs), parathyroid hormone and calcitonin). Patients who were eligible were included at first contact at one of eight participating trauma centers. For inclusion, patients had to be over 50 years of age and be diagnosed with a low-energy-induced fracture of the hip, vertebra, wrist or humerus. Furthermore, only patients living in their own housing prior to the fracture, and who were judged to be capable to answer the patient related questionnaire were included. Recruitment and follow-up interviews were performed by health care providers, and pseudonymized data were entered into the ICUROS database by a study assistant. The Short Portable Mental Status Questionnaire (SPMSQ) [15] was used as a brief cognitive screening instrument to assess a patient's cognitive eligibility for study participation. The first interview was performed during inpatient care or no less than two weeks post fracture. Follow-up interviews were performed by phone-call 4, 12 and 18 months after the fracture. All fractures had to be confirmed via imaging (e.g. X-ray). Patients with fracture as a result of comorbidities (e.g. cancer), those who had multiple fractures during the study period, those who re-fractured during the study period and those who were institutionalized, were excluded. All patients gave their informed consent before being included in the study. They could at any time withdraw from the study by their own choice. The study was approved by the local ethics committee.

The patient cohort was stratified into 2 groups: patients with osteoporosis treatment at time of fracture and patients without osteoporosis treatment at time of fracture. Osteoporosis treatment was defined as receiving one of the following drugs: bisphosphonates, estrogens, SERMs, parathyroid hormone and calcitonin).

Table 1
Overview of whole patient cohort.

	time of fracture	4 months after fracture	12 months after fracture	18 months after fracture
patients	915	624	552	495
men	199 (21.7%)	124 (19.9%)	107 (19.4%)	96 (19.4%)
women	716 (78.3%)	500 (80.1%)	445 (80.6%)	399 (80.6%)
age (years)	75.4 ± 10.2	74.0 ± 9.9	73.8 ± 9.8	73.6 ± 9.9

Table 2
Patient characteristics at time of fracture by treatment status.

	Patients **with** treatment at time of fracture	Patients **without** treatment at time of fracture	p-value
Patients at time of fracture	n = 184 (100%)	n = 731 (100%)	
	(170♀/14♂)	(546♀/185♂)	
Patients 4 months after fracture	n = 142 (77.2%)	n = 482 (65.9%)	p = 0.003
	(130♀/12♂)	(370♀/112♂)	
Patients 12 months after fracture	n = 129 (70.1%)	n = 423 (57.9%)	p = 0.002
	(120♀/9♂)	(325♀/98♂)	
Patients 18 months after fracture	n = 115 (62.5%)	n = 380 (52.0%)	p = 0.01
	(106♀/9♂)	(293♀/87♂)	
age (years)	74.3 ± 8.5	75.8 ± 9.9	p = 0.047
Type of fracture (at baseline)			
proximal femur fracture	73 (39.7%)	417 (57.0%)	p < 0.001
vertebra fracture	44 (23.9%)	115 (15.7%)	p = 0.009
wrist fracture	41 (22.3%)	104 (14.2%)	p = 0.007
humeral fracture	26 (14.1%)	95 (13.0%)	p = 0.69
Prevalent osteoporotic fracture	n = 49 (26.6%)	n = 104 (14.2%)	p < 0.001
Time span to index fracture [years]	2.6 ± 1.5	2.5 ± 1.7	p = 0.79
< 1 year	7 (14.3%)	20 (19.4%)	p = 0.75
1–5 years	28 (57.1%)	69 (70.0%)	p = 0.28
> 5 years	5 (10.2%)	9 (8.7%)	p = 0.77
unknown	9 (18.4%)	5 (4.9%)	
Risk factors for osteoporotic fractures			
Smoking	18 (9.8%)	103 (14.1%)	p = 0.12
Smoking in the past	45 (24.5%)	183 (25.0%)	p = 0.87
Alcohol	6 (3.3%)	50 (6.8%)	p = 0.07
BMI < 20 kg/m^2	19 (10.3%)	69 (9.4%)	p = 0.71
Rheumatoid arthritis	24 (13.0%)	69 (9.4%)	p = 0.15
Proximal femur fracture of parents	27 (14.7%)	68 (9.3%)	p = 0.03
Corticosteroid therapy	38 (20.7%)	98 (13.4%)	p = 0.01
Analgetic medication			
Basic analgetics	89 (48.4%)	279 (38.2%)	p = 0.01
Opioids	14 (7.6%)	33 (4.5%)	p = 0.09

The statistical software package used was IBM® SPSS® Statistics Version 23. A descriptive analysis by treatment group was performed to present treatment rates over time as well as by fracture type. Data are presented as mean (SD) for continuous variables and frequency (%) for categorical variables. The chi-squared test was used to assess the difference in categorical variables by treatment group or sex, and *t*-tests were used to compare continuous variables by treatment group or sex. A p-value of less than 0.05 was considered statistically significant.

3. Results

A total of 915 patients with MOF were enrolled, of whom 716 patients (78.3 %) were women. The mean age was 75.4 ± 10.2 years. For

Table 3
Osteoporosis medication treatment rate.

	Patients **with** treatment at time of fracture n = 184 (20.1%)			Patients **without** treatment at time of fracture n = 731 (79.9%)		
	female n = 170	male n = 14	p-value (within sexes)	female n = 546	male n = 185	p-value (within sexes)
4 months after fracture	85/130 (65.4%)	8/12 (66.7%)	p = 0.93	65/370 (17.6%)	9/111 (8.1%)	p = 0.01
12 months after fracture	65/120 (54.2%)	5/9 (55.6%)	p = 0.94	52/325 (16.0%)	12/99 (12.1%)	p = 0.36
18 months after fracture	64/106 (60.4%)	5/9 (55.6%)	p = 0.78	45/294 (15.3%)	9/87 (10.3%)	p = 0.24

Table 4
Calcium and/or vitamin D treatment rate.

	Patients **with** Ca/vit.D-treatment at time of fracture n = 347 (37.9%)			Patients **without** Ca/vit.D-treatment at time of fracture (n = 568) (62.1%)		
	female n = 311	male n = 36	p-value (within sexes)	female n = 405	male n = 163	p-value (within sexes)
4 months after fracture	169/232 (72.8%)	13/22 (59.1%)	p = 0.17	110/268 (41.0%)	28/102 (27.5%)	p = 0.02
12 months after fracture	167/204 (81.9%)	11/19 (57.9%)	p = 0.01	107/241 (44.4%)	28/88 (31.8%)	p = 0.04
18 months after fracture	137/180 (76.1%)	10/19 (52.6%)	p = 0.03	91/219 (41.6%)	20/77 (26.0%)	p = 0.02

statistical analysis, 624 patients (68.2 %) were available at 4 months, 552 patients (60.3 %) at 12 months, and 495 patients (54.1 %) at 18 months after the index fracture (Table 1). Reasons for loss of follow up were non-availability (60.0 %), patients' withdrawal (22.4 %), death within the study time (6.6 %), another fracture within the study time (5.0 %) and other (5.0 %).

At the time of fracture, 184 patients (20.1 %) received pharmacological treatment while 731 (79.9 %) did not. Comparing demographics between these groups showed significant differences in age (74.3 vs. 75.8 years), fracture prevalence (26.6 % vs. 14.2 %), two risk factors (current corticosteroid therapy: 20.7 % vs. 13.4 %; proximal femur fracture of parents: 14.7 % vs. 9.3 %) and intake of analgesic medication (48.4 % vs. 38.2 %) (Table 2). Except current corticosteroid therapy and proximal femur fracture of parents, there was no difference in risk factors for osteoporotic fractures between these groups.

In women with no osteoporosis treatment at the time of the index fracture, follow up analysis revealed an osteoporosis treatment rate of 17.6 %, 16 % and 15.3 % after 4, 12 and 18 months (Table 3). Accordingly in men, the treatment rate was 8.1 %, 12.1 % and 10.4 %. In patients initially treated for osteoporosis, the treatment rate was 65.4 %, 54.2 % and 60.4 % in women, and 66.9 %, 55.1 % and 55.2 % in men after 4, 12 and 18 months, respectively. At the time of fracture, the most frequently prescribed drugs were bisphosphonates (88.0 %), and then SERMs (4.3 %), calcitonin (4.3 %), estrogens (2.3 %) and parathyroid hormones (1.1 %) at time of index fracture. Similar prescription rates were seen in the follow-up analysis.

Calcium and/or vitamin D replacement therapy was seen in 347 of patients (37.9 %) at time of fracture, while 568 (62.1 %) did not receive treatment with calcium and/or vitamin D. The treatment rates in follow-up-analyses are presented in Table 4.

Osteoporosis treatment was significant lower in men than in women 4 months after fracture (8.0 % vs. 17.6 %; p = 0.01) (Table 3). A significant lower calcium and/or vitamin D treatment rate between sexes was seen in nearly all follow-up analysis (Table 4).

Table 5 presents the osteoporosis treatment rate separated by fracture type. In patients with treatment at time of fracture, the fracture types were proximal femur fracture (n = 73, 39.7 %), vertebral fracture (n = 45, 24.5 %), humeral fracture (n = 26, 14.1 %) and wrist fracture (n = 145, 78.8 %). In patients without treatment at the time of the index fracture, the fracture types were proximal femur fracture (n = 417, 57.0 %), vertebral fracture (n = 115, 15.7 %), humeral fracture (n = 96, 13.1 %) and wrist fracture (n = 115, 15.7 %).

As expected, patients with osteoporosis treatment at the time of fracture were significantly more likely to have a prevalent MOF (26.6 % vs. 14.1 %; p < 0.001). The time span between the fracture in the past and the subsequent fracture at study initiation was comparable between these groups (Table 6). Comparing osteoporosis treatment rate between groups separated by fracture prevalence, the treatment rate at 4 months was significantly higher in patients with a prevalent MOF. However, this significance was not seen in further analysis after 12 and 18 months (Table 7).

4. Discussion

Based on the data of the Austrian ICUROS-branch, we evaluated the treatment incidence in patients with a MOF. In those who did not receive osteoporosis treatment at the time of fracture, only 1 in 10 men and less than 2 in 10 women were prescribed an adequate osteoporosis treatment. In those who had received osteoporosis treatment at the time of fracture, roughly every second patient was deprived of his/her treatment.

We found that the percentage of patients receiving osteoporosis treatment differed significantly between men and women, particularly in regard to treatment initiation of calcium and/or vitamin D. For example, in women with initially no treatment, the osteoporosis treatment rate 4 months after fracture was 17.6 %, whereas the treatment rate in men was only 8.1 % (p = 0.01). Although osteoporosis medication with proven anti-fracture efficacy is also available for men, it is mainly women who receive osteoporosis treatment, indicating a clear gender imbalance. The latter becomes even less plausible, given that men have a higher risk of morbidity and mortality after an osteoporotic fracture compared to women [16].

Analyzing the osteoporosis treatment rate separated by fracture type, the treatment initiation was comparable between all fracture types, whereas numerically the highest treatment rate was seen in patients with vertebra fracture. In those who had already been treated for osteoporosis at time of fracture, the treatment continuation was comparable between all groups separated by fracture type.

In those who had presented with a prevalent fracture at the time of the index fracture (n = 153; 16.7 %) osteoporosis treatment was seen in 32.0 %. In other words, 68.0 % with a clear indication for osteoporosis treatment did not receive such. Our study did not include the assessment of possible reasons underlying the substantial treatment gap. The main causes identified by other studies were ignorance of the indication of treatment [17], incorrect assessment of the patient's fracture risk and comorbidities [18]. Contra-indication like renal failure as a limiting factor for introducing an osteoporosis treatment particularly with bisphosphonates was described as the rarest reason [18]. Furthermore, the majority of vertebral fractures are asymptomatic, they are sometimes underdiagnosed when no imaging is ordered and consequently an initiation of treatment is not enabled [19]. Also the low adherence of patients to medication is a reason leading to poor

Table 5
Site specific osteoporosis medication treatment rate.

	Patients **with** treatment at time of fracture n = 184 (20.1%)				Patients **without** treatment at time of fracture n = 731 (79.9%)			
	Proximal femur fracture n = 73	Vertebra fracture n = 44	Humeral fracture n = 26	Wrist fracture n = 41	Proximal femur fracture n = 417	Vertebra fracture n = 115	Humeral fracture n = 95	Wrist fracture n = 104
4 months after fracture	40/57 (70.2%)	14/23 (60.9%)	14/22 (63.6%)	21/34 (61.8%)	41/259 (15.8%)	16/70 (22.9%)	8/72 (11.1%)	9/81 (11.1%)
12 months after fracture	29/54 (53.7%)	13/23 (56.5%)	11/20 (55.0%)	17/32 (53.1%)	31/221 (14.0%)	14/64 (21.9%)	7/63 (11.1%)	12/75 (16.0%)
18 months after fracture	27/48 (56.3%)	13/22 (59.1%)	11/18 (61.1%)	18/28 (64.3%)	27/198 (13.6%)	10/52 (19.2%)	9/60 (15.0%)	8/70 (11.4%)
Site specific vitamin D and/or calcium treatment rate								
	Proximal femur fracture n = 73	Vertebra fracture n = 44	Humeral fracture n = 26	Wrist fracture n = 41	Proximal femur fracture n = 417	Vertebra fracture n = 115	Humeral fracture n = 95	Wrist fracture n = 104
4 months after fracture	42/57 (73.7%)	17/23 (73.9%)	16/22 (72.7%)	29/34 (85.3%)	117/259 (45.2%)	27/70 (38.6%)	28/72 (38.9%)	41/81 (50.6%)
12 months after fracture	41/54 (75.9%)	17/23 (73.9%)	16/20 (80.0%)	28/32 (87.5%)	108/221 (48.9%)	28/64 (43.8%)	26/63 (41.3%)	48/75 (64.0%)
18 months after fracture	36/48 (75.0%)	16/22 (72.7%)	13/18 (72.2%)	21/28 (75.0%)	87/198 (43.9%)	23/52 (44.2%)	25/60 (41.7%)	37/70 (52.9%)

Table 6
Comparison of patient characteristics.

	Patients dropped out during study period n = 420	Patients observed along the whole study n = 495	p-value
men	103 (24.5%)	96 (19.4%)	p = 0.06
women	317 (75.5%)	399 (80.6%)	
age (years)	77.6 ± 9.7	73.7 ± 9.3	p < 0.001
Type of fracture			
proximal femur fracture	244 (58.1%)	246 (49.7%)	p = 0.01
vertebra fracture	86 (20.5%)	73 (14.7%)	p = 0.02
wrist fracture	47 (11.2%)	98 (19.8%)	p < 0.001
humeral fracture	43 (10.2%)	78 (15.8%)	p = 0.01
Prevalent osteoporotic fracture	69 (16.4%)	83 (16.8%)	p = 0.89
Risk factors for osteoporotic fracture at time of fracture			
Smoking	55 (13.1%)	66 (13.3%)	p = 0.92
Smoking in the past	108 (25.7%)	120 (24.2%)	p = 0.61
Alcohol	33 (7.9%)	23 (4.6%)	p = 0.04
BMI < 20 kg/m^2	54 (12.9%)	34 (6.9%)	p = 0.002
Rheumatoid arthritis	54 (12.9%)	39 (7.9%)	p = 0.01
Proximal femur fracture of parents	38 (9.0%)	57 (11.5%)	p = 0.22
Corticosteroid therapy	59 (14.0%)	77 (15.6%)	p = 0.52
Analgesic medication			
Basic analgesics	172 (41.0%)	195 (39.4%)	p = 0.63
Opioids	25 (6.0%)	23 (4.6%)	p = 0.38

therapeutic outcomes [20].

There are limitations in our analysis. Although the patients included in the Austrian arm of the ICUROS were recruited at 8 different centers from different provinces, a potential bias based on cohort effects cannot be entirely precluded. Nevertheless, our findings are well in line with results of other studies performed in different countries, confirming the insufficient management of patients after an osteoporotic fracture [5,6,21,18]. Furthermore, the studied fracture types may be the most important clinical consequence of osteoporosis, but many other fractures have been described to be associated with low BMD, including fractures of the ankle, ribs, tibia, pelvis and other femoral sites than the proximal one [22]. The selection of just the main types could underestimate the dimensions, burden and extent of osteoporosis. On the other hand, the relatively short observation period of 18 months could further overestimate the adherence to osteoporosis treatment, so the treatment rate may decrease even further.

In conclusion, this analysis revealed a poor treatment rate in patients who sustained a MOF. This low treatment rate persisted over the entire follow-up period of 18 months. Given that Austria is among the wealthiest countries worldwide, it is difficult to understand that the vast majority of patients who sustained an osteoporotic fracture and who are thus at imminent risk of experiencing subsequent fractures, do not receive an adequate osteoporosis treatment.

There is a clear need for the implementation of coordinated, multidisciplinary models of care for secondary fracture prevention.

Declaration of Competing Interest

All authors declare that they have no conflict of interest.

All listed authors have seen and approved the final version of the manuscript.

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Table 7
Osteoporosis medication treatment rate by history of MOF.

	Patients **with** history of MOF n = 153 (130♀/23♂)	Patients **without** history of MOF n = 762 (586♀/176♂)	p-value
At time of fracture	49/153 (32.0%)	135/762 (17.7%)	$p < 0.001$
4 months after fracture	35/109 (32.1%)	132/515 (25.6%)	$p = 0.17$
12 months after fracture	24/92 (26.1%)	110/460 (23.9%)	$p = 0.66$
18 months after fracture	27/83 (32.5%)	96/412 (23.3%)	$p = 0.08$

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