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Anti-osteoporotic treatment after hip fracture remains alarmingly low

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ABSTRACT

INTRODUCTION. Osteoporosis and osteoporotic fractures typically affect postmenopausal women, and osteoporotic fractures significantly increase disability, morbidity and mortality. Several anti-osteoporotic agents are available and have been shown to effectively reduce the incidence of low-energy osteoporotic fractures. However, the post-osteoporotic fracture treatment rate remains low. The purpose of the present study was to follow up on patients with a recent hip fracture with primary focus on anti-osteoporotic treatment and dual-energy X-ray absorptiometry (DXA).

METHODS. We included patients ≥ 65 years of age admitted to a department of orthopaedic surgery in Denmark from 1 June 2019 to 30 May 2020.

RESULTS. In this period, 570 patients ≥ 65 years were treated for a hip fracture. A total of 16.7% of the patients received anti-osteoporotic treatment at follow-up and 6.5% initiated anti-osteoporotic treatment or had a relevant change in anti-osteoporotic treatment. Only 9.8% had a DXA after their fracture; and among this group, 48% received anti-osteoporotic treatment.

CONCLUSION. The majority of patients with a recent low-energy hip fracture did not receive a DXA, did not have a relevant follow-up or received any anti-osteoporotic treatment. The problem is global and needs to be addressed. Starting treatment with anti-osteoporotic medicine before discharge from the orthopaedic department and referring the patient to a DXA at the same time may be part of the solution.

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Post-osteoporotic fracture treatment remains suboptimal despite the availability of a well-tolerated, effective, low-cost treatment with bisphosphonates such as alendronate. The daily presence of geriatricians in the orthopaedic department with a focus on the post-operative treatment was expected to be a part of the solution.

Osteoporosis is defined by a low bone mineral density (BMD) leading to bone frailty and increased risk of fracture. The diagnostic criteria include a dual-energy X-ray absorptiometry (DXA) with a T score ≤ –2.5 with or without the presence of a fragility fracture (spine and/or hip) [1]. Osteoporosis most commonly affects postmenopausal women, and it is estimated that 9 mill low-energy fractures occurred in year 2,000 including fractures of the forearm, hip and spine [2]. Osteoporosis is believed to be markedly underdiagnosed which has serious implications for the prevention of osteoporotic fractures [3, 4]; and osteoporotic fractures significantly increase disability, morbidity and mortality [2]. Thirty to fifty percent of patients never regain their pre-fracture

function [4, 5], and mortality after a hip fracture remains around 20% within the first year of the fracture [6, 7]. Furthermore, one osteoporotic fracture increases the risk of a second osteoporotic fracture more than six-fold [8, 9], which decreases the post-fracture functional status even further.

Several anti-osteoporotic agents are available and have been shown to effectively reduce the incidence of low-energy osteoporotic fractures [10]. Antiresorptive agents, such as bisphosphonates, are a well-tolerated [11], safe [12, 13] and cost-effective treatment to prevent osteoporotic fractures [1]. Even so, several studies have shown a low anti-osteoporosis drug treatment rate following an osteoporotic fracture [14-18].

METHODS

The purpose of the present study was to calculate the number of patients with a hip fracture who subsequently initiate treatment with anti-osteoporotic medicine. This was a one-centre, retrospective observational study, and we included all patients ≥ 65 years admitted to the department of orthopaedic surgery of the Copenhagen University Hospital, Herlev, with a hip fracture or other fractures close to the hip, from 1 June 2019 to 30 May 2020. This department of orthopaedic surgery has a catchment area of about 435,000 inhabitants.

Data, including number of deaths, were collected from the electronic hospital medical charts (Sundhedsplatformen). Prior medication review including purchased prescriptions are accessible through the Shared Medication Record (FMK). The last day of data collection was 28 December 2020, thus allowing a follow-up of 6-18 months, depending on the fracture date.

On day two after surgery, all hip fracture patients ≥ 65 years of age received a geriatric assessment by an orthogeriatric team. The team consisted of one geriatric specialist and one younger/non-specialised medical doctor, who were present in the orthopaedic department five days a week. Measures were obtained on heart rhythm, blood pressure, medication, previous mobility, etc., and the geriatricians focused on the reason for the fall, blood tests including vitamin D status, and decided whether the patient was a candidate for anti-osteoporotic treatment. Patients who were too frail or whose estimated remaining lifespan was shorter than 18 months were considered unsuitable for anti-osteoporotic treatment. Generally, patients with a new hip fracture who already received treatment for osteoporosis were recommended a new DXA to evaluate the efficacy of their pre-existing medication. When a patient was not referred for follow-up and further examinations in the Falls Clinic, the geriatrician encouraged the GP in the discharge letter to see to further examination and treatment for osteoporosis at the next visit. In case of a short admission, patients were in some cases discharged without a geriatric assessment during weekends and holidays.

All patients received a supplement of calcium and vitamin D twice daily (400 mg calcium and 19 µg vitamin D_3). When the vitamin D level was below 50 nmol/l, the patient was further supplemented with additional D-vitamin twice daily for three months. The dosage depended on the level of deficiency. Further examination for osteoporosis awaited the normalisation of vitamin D levels.

The primary outcome was any anti-osteoporotic medication, a DXA following the fracture, initiation of anti-osteoporotic treatment or re-evaluation of pre-existing osteoporotic treatment.

Trial registration: not relevant.

RESULTS

A total of 627 patients were admitted with a hip or near-hip fracture in the one-year study period. At the time of the hip fracture, 570 patients were 65 years of age or older, 74% were women. Men were slightly younger than

women at the time of fracture. At follow-up, 26% of the patients had died. No difference was recorded in age at the time of death between men and women. However, men had a higher death rate than women. On average, death occurred after three months, range: 1-400 days (**Table 1**).

TABLE 1 Demographics and clinical characteristics.

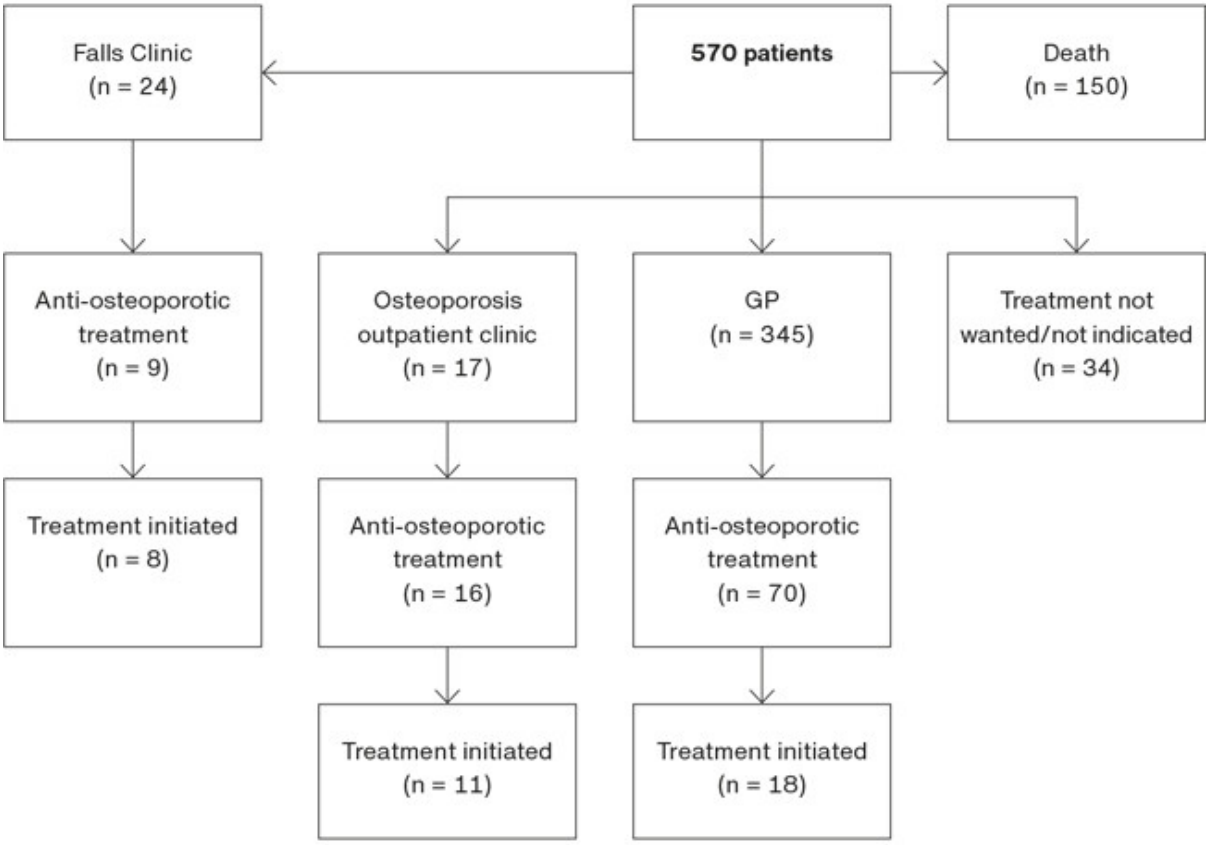
	All patients (N = 570)	Women (N = 422 (74%))	Men (N = 148 (26%))
Age, mean/median, yrs	83.3/83	83.5/84	82.7/83
Patients who had died at follow-up, n (%)	150 (26.3)	100 (23.6)	50 (33.8)
Age at death, yrs	86.2	86.1	86.6
Time until death, mean/median (IQR[a]), days	93.4/43.5 (112)	94/44.5 (118.25)	92/41.5 (108.5)
Fracture diagnosis, %			
Femoral neck	48.4	47.7	46.5
Oher near-hip fractures	51.6	52.3	53.5
Type of surgery, %			
Hemialloplastic + total alloplastic	36.5	35.9	35.2
Osteosynthesis	63.5	64.1	64.8
Anti-osteoporotic medicine initiated			
Patients, n (%)	37 (6.5)	32 (7.6)	5 (3.4)
Age mean/median, yrs	80.6/80	80.8/82	79.6/79

IQR = interquartile range.
a) IQR is used instead of spread as data were set with a high level of positive skew.

Post-hip fracture treatment with alendronate was initiated in 27 patients (4.7%). Treatment with Zoledronic Acid and Denosumab was initiated in seven and three patients, respectively. In all, 37 patients (6.5%) initiated anti-osteoporotic medication or had a relevant change in anti-osteoporotic treatment. A total of 73 patients (12.8%) received alendronate, and 95 patients (16.7%) received some type of anti-osteoporotic treatment at follow-up (Table 1).

Out of 570 patients, 24 (4.2%) were referred to the Falls Clinic before discharge for further examination for osteoporosis. Seventeen patients (3%) were already in an outpatient clinic that managed osteoporosis at the time of their fracture. Further examination for osteoporosis/anti-osteoporotic treatment was not recommended in 73 (12.8%) patients. In the majority of cases, this was due to frailty, but also to kidney failure, disseminated cancer and pathological fractures, or in respect of the patient's wishes. A total of 39 of these 73 patients (53.4%) died during follow-up. Therefore, the GP was expected to follow up on anti-osteoporotic treatment in 345 patients (60.5%). At follow-up, 70 (20%) of these patients were being treated with anti-osteoporotic medication. Treatment was initiated in 18 patients (5.2%) who underwent follow-up at their GP (**Figure 1**).

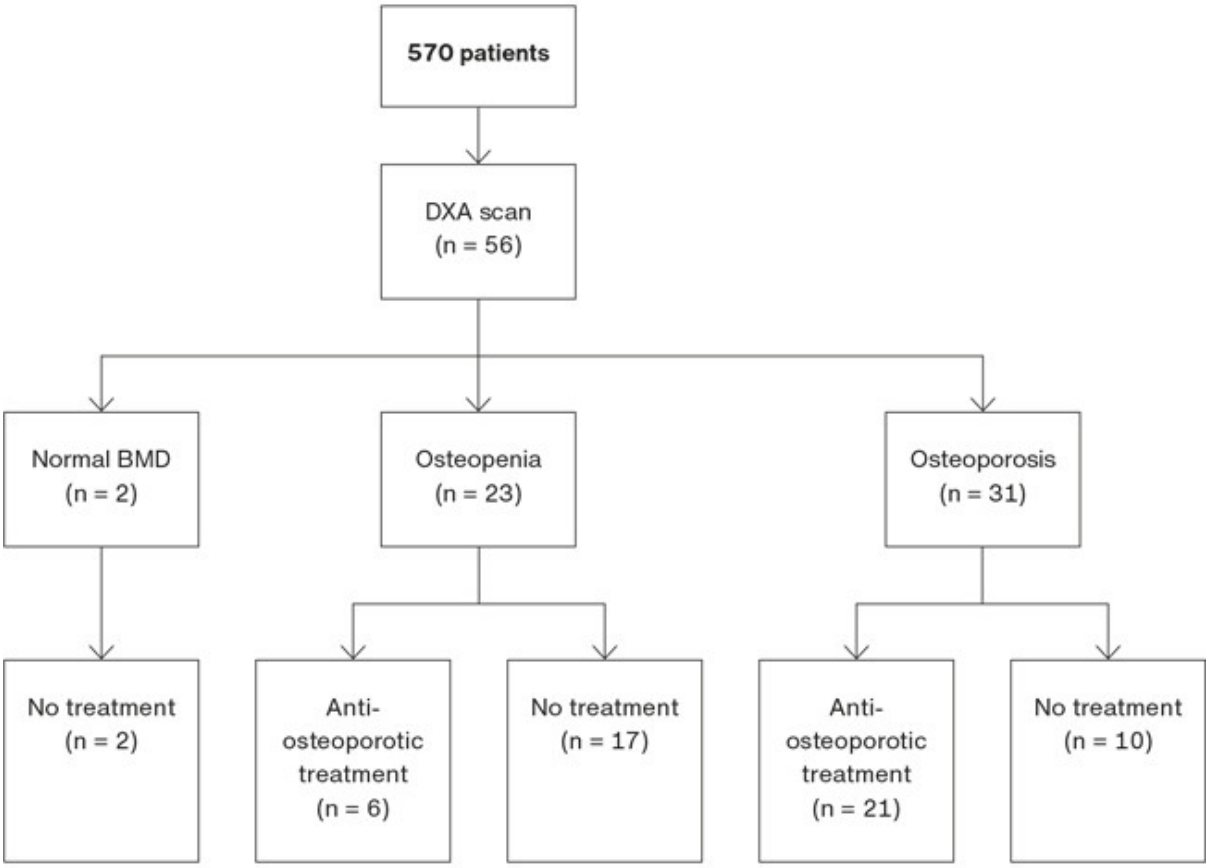
FIGURE 1 Overview of follow-up on hip fracture patients and initiation of anti-osteoporotic treatment.



GP = general practitioner.

A total of 56 patients out of 570 (9.8%) had a DXA following their hip fracture, two had a normal BMD, 23 had osteopenia and 31 had osteoporosis. Among 56 patients, 27 (48%) were treated with anti-osteoporotic medication at follow-up (**Figure 2**).

FIGURE 2 Dual-energy X-ray absorptiometry results and anti-osteoporotic treatment.



BMD = bone mineral density; DXA = dual-energy X-ray absorptiometry.

DISCUSSION

In line with several other studies, we found that embarrassingly few patients with a recent low-energy hip fracture received anti-osteoporotic treatment [14, 17]. The majority of those who did receive treatment had been initiated on anti-osteoporotic medication already before their recent low-energy hip fracture, and a fracture seldomly leads to a re-evaluation of pre-existing anti-osteoporotic treatment.

In this catchment area, the GP is responsible for the management of anti-osteoporotic treatment in most of the patients, i.e. all patients except for those who are followed in an outpatient clinic responsible for the management of osteoporosis, or where the patient is referred to the Falls Clinic following a hip fracture, in this case a total of 41 patients (7.1%). However, GPs do not have any outreach responsibility. This leaves it up to the patient or his or her next of kin to make an appointment with the GP to be examined for osteoporosis, which might be too great a burden to place on their shoulders immediately after a hip fracture which may have changed their mobility and affected their life considerably.

Even though a low-energy hip fracture is sufficient to diagnose a patient with osteoporosis, a DXA is recommended to determine the severity of bone demineralisation and to monitor treatment effects. We were surprised to find that only 9.8% had a DXA after their fracture and only 48% received anti-osteoporotic treatment at follow-up. Hence, we recorded a low DXA rate and insufficient follow-up if a DXA was, in fact, performed. This, again, may be linked to the fact that the patient or their next of kin is responsible for making an

appointment with their GP both for the DXA and for the corresponding follow-up. Furthermore, 25 out of 56 patients (44.6%) who were evaluated by DXA had either osteopenia or a normal BMD, and only six of them received anti-osteoporotic treatment (24%). Even so, these patients have osteoporosis by definition and should be treated with anti-osteoporotic medication as such (Figure 2).

Only nine patients out of the 24 (37.5%) referred to the Falls Clinic were initiated on anti-osteoporotic treatment. An examination in the Falls Clinic can be time-consuming and requires a considerable amount of energy that hip fracture patients typically do not have. Therefore, we observed that appointments were frequently cancelled. Hence, the Falls Clinic may not be the best solution to ensure post-fracture anti-osteoporotic treatment. In addition, some patients had their appointment postponed due to COVID-19 or cancelled their appointments due to the fear of becoming infected with COVID-19, which decreased the overall attendance rate for visits to the Falls Clinic and for DXA in general.

The lack of treatment for osteoporosis is clearly a serious problem that needs to be addressed. The optimal solution may be to initiate treatment when the patient is in the hospital, before discharge. Alendronate remains the first-choice treatment, but taking alendronate can be challenging for some patients. Alendronate must be taken on an empty stomach, at least 30 min. before breakfast, and the patient must remain in an upright position for at least 30 min. after taking the tablet before eating or drinking. It may be difficult to comply with these requirements. Furthermore, the medication is taken only once a week and that may be difficult to remember. When the medication is administrated by a home nurse, it may give rise to several practical problems. After giving alendronate to the patient, the nurse must wait or come back 30 min. later to give the patient the rest of the medicine.

When alendronate is not an option, zoledronic acid may be used instead. Zoledronic acid is a bisphosphonate that is administered intravenously every 12 months and has a similar low-energy-fracture-reducing effect and side effect profile as other bisphosphonates. A single study including 90 patients with hip fracture showed that zoledronic acid may be used in the treatment of osteoporotic hip fractures with proximal femoral nail anti-rotation when given within one week after fracture [19]. Another study in which zoledronic acid was given to frail elderly osteoporotic women showed that the treatment improved their BMD for two years [20]. These results seem very promising and may be part of the solution.

The advantage of administering bisphosphonates to these patients is that it accumulates in the bone minerals and is released slowly. Therefore, the effect persists for some time after the treatment stops, whereas receptor activator of NF-κB ligand (RANK-L) antibodies has a rebound effect and cannot be discontinued without considering further anti-osteoporotic medication.

CONCLUSION

The post-hip-fracture anti-osteoporotic treatment rate remained alarmingly low and few patients were examined with DXA. The reasons are numerous including poor compliance, forgetfulness, contraindications and practical problems, etc.; and the considerable responsibility for initiating treatment typically rests with the patients and their next of kin. Starting treatment with anti-osteoporotic medicine before discharge from the orthopaedic department and referring the patient for a DXA at the same time may be part of the solution. Even so, we are far away from the goal.

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