



Intensive screening for osteoporosis in patients with hip fracture

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Abstract

Summary Opportunities to evaluate, treat, and prevent future osteoporotic fractures are often being overlooked, especially in patients with a prior osteoporotic fracture. We find that an intensive outreach osteoporosis investigation strategy can help increase the number of patients investigated and treated for osteoporosis following a hip fracture.

Purpose Patients experiencing a hip fracture are subject to an increased risk of subsequent fractures. This suggests an urgent need to develop strategies that will allow a higher number of patients with fragility hip fractures to be investigated and treated for osteoporosis. In accordance, we developed a secondary osteoporosis prevention program and evaluated the results of the program.

Methods In the study period, 1071 patients with a hip fracture were admitted to Hvidovre University Hospital. Eligible patients were offered an osteoporosis investigation program, which included a DXA-scan with vertebral fracture assessment and a medical consultation. The data retrieved from this program were registered and analyzed. The primary goal of the study was to describe the number of subjects, who completed the program, and to characterize the initiated osteoporosis treatment. Secondary outcomes evaluated were prevalence of DXA-verified osteoporosis, changes in T-score due to treatment, and 1-year mortality rate.

Results In total, 557 patients were offered participation of which 333 patients completed the full program. Among these, 159 patients had DXA-verified osteoporosis and 192 patients were started treatment. This resulted in a significant higher T-score at the lumbar spine and femoral neck compared with subjects not treated. Additionally, we report a 1-year mortality rate of 27.7% among all patients with hip fracture.

Conclusion We report that an intensive outreach osteoporosis investigation program can help increase the number of hip fracture patients being tested and treated for osteoporosis. Further, the initiation of treatment can significantly increase the T-score.

Keywords Osteoporosis · Hip fractures · DXA-scan · T-score · Anti-osteoporotic treatment · Fracture liaison service

Introduction

Osteoporosis is typically asymptomatic until a fracture occurs. Classical sites for osteoporotic fractures are the spine, hip, proximal humerus, and the distal forearm. Osteoporotic fractures are typically associated with a low-energy trauma and are a major

cause of morbidity [1]. Of these, the hip fracture is the most severe type carrying the highest morbidity and mortality [2].

The clinical significance of osteoporosis is related to the increased risk of fractures, but due to the lack of symptoms prior to the fracture, osteoporosis is underdiagnosed and consequently undertreated. The purpose of osteoporosis treatment is to prevent these fractures by increasing bone mass, but patients rarely receive adequate information, evaluation, and treatment following a hip fracture. In general, investigation and treatment rates following a fragility hip fracture are low [3–5]. However, there is a reason for some optimism, with recent studies showing an increase in both investigation and treatment rates, primarily due to the introduction of secondary prevention programs, such as the fracture liaison service (FLS) [6, 7].

Patients experiencing a hip fracture are subject to an increased risk of subsequent fractures, and considering the fact

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that patients with a fragility fracture warrant the diagnosis of osteoporosis, they should be treated accordingly [8, 9]. Yet, opportunities to evaluate, treat, and prevent future fractures are unfortunately often being overlooked. This emphasizes the pressing need to develop secondary prevention strategies to address osteoporosis in patients with hip fractures and other osteoporosis-related fractures, in order to prevent subsequent fractures and additional disability and mortality [10–12].

In accordance, we developed the osteoporosis investigation program (OIP) in order to allow a higher number of patients with hip fractures to be investigated and treated for osteoporosis. The primary aim of this study has been to evaluate the results of the program with regard to the number of hip fracture patients investigated and treated for osteoporosis.

Methods

Study population

This is a cross-sectional study with follow-up. The population consisted of all patients admitted to the Department of Orthopedic Surgery at Hvidovre University Hospital with a hip fracture, in the period from 1 January 2013 to 31 December 2014. Subjects with a pathological fracture related to malignancies were excluded and referred to the Department of Oncology. Both high- and low-energy hip fractures were eligible to be offered the OIP and therefore included in the study.

All patients had their electronic medical records reviewed by a nurse from the Osteoporosis Unit at the Department of Endocrinology at Hvidovre University Hospital, using the following exclusion criteria:

1. Dementia¹ and > 90 years of age
2. Dementia¹ and a new mobility score (NMS) ≤ 1 [14]
3. Dementia¹ and a serious comorbidity (i.e., stroke, Parkinson's disease)
4. Patients, who were not motivated for rehabilitation following the fracture
5. Weakened general health condition
6. Life expectancy of less than 12 months
7. Disseminated cancer
8. Patients already investigated or treated for osteoporosis by the Department of Endocrinology at Hvidovre University Hospital
9. Patients investigated or treated for osteoporosis by their general physician
10. Patients transferred to another hospital during admission

¹ Defined as a Hindsoe-test score < 5 [13]

Subjects would not be offered the OIP, if one of the above criteria was present. Patients who were not interested in any further investigation or treatment would also not be offered the OIP.

The program consisted of a bone mineral density (BMD) measurement including vertebral fracture assessment and a consultation with a physician specialized in endocrinology and bone diseases. The purpose of the medical consultation was to establish the diagnosis and to start treatment of osteoporosis, if needed.

Measurement of BMD was performed by dual-energy x-ray absorptiometry (DXA) at the lumbar spine, femoral neck, and total hip. In-house test on a standard phantom was performed every morning to assess precision and coefficient of variation (CV) on the different machines used. CV of the individual scanners were in general low with values below 0.9% at the lumbar spine. Three different models of Hologic (Hologic, Inc., Bedford, MA, USA) DXA-scanners were used in this study. Every 6 months, multiple scans of the same phantom on different machines were performed and difference in mean BMD was assessed. A statistically minor systematic difference was detected between one machine and the two others. The difference between means of BMD was < 0.01 g/cm² corresponding to less than 1.2% of the average BMD and therefore not corrected for in this study [15]. All patients were scanned on the same machine at the initial scan and at follow-up. Spinal T-scores of patients were calculated using peak reference values and standard deviation (SD) from the Hologic study [16]. T-scores, of the total hip and femoral neck, were calculated using data from the NHANES phase III study [17]. According to the World Health Organization (WHO) criteria, patients were classified as having osteoporosis if the T-score was ≤ -2.5 and osteopenia if the T-score was between -2.5 and -1.0 at one of the measured sites.

Collection of data

A total of 1089 patients with a hip fracture were admitted during the study period. Of these, 18 patients were readmitted for a hip fracture in the same period, resulting in 1071 subjects with at least one hip fracture. Due to the exclusion criteria, 389 (36%) subjects were not offered the program and 125 (12%) subjects declined any further investigation or treatment. In total, 557 (52%) subjects were offered participation in the OIP.

A nurse from the Osteoporosis Unit documented the fracture date and registered all information involved in the OIP, including any anti-osteoporosis drugs initiated by a physician and the type of treatment initiated. Patients were not offered entry in the program if they were already on treatment for osteoporosis. Calcium and/or vitamin D were not considered independent anti-osteoporosis treatments. For this reason, patients receiving calcium and vitamin D supplements prior to the fracture would still be included in the study. After

12 months, the nurse would review the patients' electronic medical record and register relevant health data, such as low- or high-energy hip fractures and death.

If a patient had more than one DXA-scan performed, the results of the first scan after the fracture was retrieved, as well as the results of the follow-up scan (defined as the most recent scan, after the first DXA-scan). Any DXA-scan results performed prior to the fracture or after the follow-up DXA-scan, if such was present, were not retrieved. We were unable to access or review the subjects' electronic medical journal any further. For this reason, any medical history or prior medicine use could not be registered or reported in this study.

The study was done as a part of the quality assurance project for the Department of Endocrinology at Hvidovre University Hospital.

Outcomes

The primary outcomes of the study were to describe the number of subjects, who completed the full OIP, and to characterize the initiated anti-osteoporosis treatment.

Secondary outcomes reported were prevalence of DXA-verified osteoporosis and changes in T-score following the initiated treatment as well as 1-year mortality.

Analysis

Statistical analysis was performed using RStudio software (version 1.1.383). Continuing variables are presented as mean value and standard deviation (SD). Categorical variables are presented as number and percent of observations. Numerical data comparison between groups was done using *t* test. Categorical data compared between the groups was done using χ^2 test or Fisher's exact test. A paired *t* test was used, when analyzing the change in T-score in patients between the initial DXA-scan and the follow-up scan. A test of association between changes in site-specific T-scores and treatment versus no treatment was done using Welch's two-sample *t* test and multiple regression models. Statistical significance was defined as a two-tailed *p* value < 0.05.

Results

The total population consisted of 1071 patients with a least one hip fracture in the study period. The mean age was 78.6 years, and the majority of patients were women. One-year mortality for the total population was 27.7%. A total of 29 (2.7%) fractures were classified as high-energy trauma. General characteristics of the study population are listed in Table 1.

Subjects offered the OIP were significantly younger and had a significant lower mortality compared with subject not offered the program. These differences are most likely due to

the exclusion criteria. A significantly higher proportion of fractures in the OIP group were due to high-energy trauma. There were no significant differences in gender ratio between the two groups.

A flowchart of the completion of the OIP is shown in Fig. 1. A total of 557 subjects were offered the OIP; of these, 333 (59.8%) subjects had a DXA-scan performed and the results of the DXA-scan including VFA could be retrieved in 314 (56.4%) subjects. We were unable to retrieve the DXA-scan results of 19 patients due to the upgrading of the electronic database systems.

Table 2 shows the prevalence of osteoporosis and mean T-scores at the lumbar spine, femoral neck, and total hip at the initial and follow-up scan. At the initial scan, we retrieved results from 314 subjects at the lumbar spine and 270 patients at the femoral neck and total hip. A total of 159 subjects had a T-score ≤ -2.5 . The most common site for osteoporosis was at the femoral neck. Mean T-scores were lowest at the femoral neck. The mean interval between the fracture and the initial DXA-scan was 6 months (SD = 0.5).

At the follow-up scan, 172 patients had a DXA-scan performed at the lumbar spine and 143 at the femoral neck and total hip. A total of 98 subjects had a T-score ≤ -2.5 . The most common site for osteoporosis was the femoral neck. Mean T-scores were lowest at the femoral neck. The mean time between the initial and follow-up DXA-scan was 18 months (SD = 0.6).

Of the 314 patients having the initial DXA-scan performed at the lumbar spine, 44 (14%) were unable to have a scan performed at the femoral neck and total hip due to hip replacement.

Table 3 shows the treatment initiated according to T-scores. Treatment was initiated in 122 (76.7%) subjects with osteoporosis, in 47 (37.6%) subjects with osteopenia, and in 13 (43.3%) subjects with a T-score > -1 , while 10 subjects were initiated treatment in the group without retrievable DXA-scan results. In total, treatment was initiated in 192 (57.7%) subjects. The most frequently used treatment was zoledronic acid followed by alendronate. In addition to the 192 patients initiated in treatment, there were 39 patients who were offered calcium and vitamin D supplements without being prescribed an anti-osteoporotic drug.

There were 37 (23.3%) patients with a T-score ≤ -2.5 , who were not prescribed any other treatment. The most common cause for this was patients not showing up for the planned medical consultation after the DXA-scan; other reasons included patients declining any further treatment or having severe renal impairment.

Effect of initiated treatment on the T-score

Table 4 shows the change in T-score between the initial and follow-up scan in patients initiating osteoporosis treatment and

Table 1 General characteristics of the study population and comparison of subjects offered the OIP and subjects not offered the program. *p* values are calculated differences between the offered and not offered group

	Total population <i>n</i> = 1071	Offered the OIP <i>n</i> = 557	Not offered the OIP <i>n</i> = 514	<i>p</i> value
Age (SD), <i>n</i>	78.6 (12.1), 1066	75.5 (12.3), 554	82.0 (11.0), 512	< 0.01
Sex (women), <i>n</i> (%)	724/1071 (67.6%)	379/557 (68.8%)	345/514 (67.1%)	0.79
Death within 12 months of fracture, <i>n</i> (%)	297/1071 (27.7%)	67/557 (12.0%)	230/514 (44.7%)	< 0.01
Lifespan from fracture to death in months (SD), <i>n</i>	3.1 (2.9), 297	4.6 (3.5), 67	2.6 (2.5), 230	< 0.01
High-energy fractures, <i>n</i> (%)	29/1071 (2.7%)	26/557 (4.7%)	3/514 (0.6%)	< 0.01
More than one hip fracture in the study period, <i>n</i> (%)	18/1071 (1.7%)	10/547 (1.8%)	8/514 (1.6%)	0.82

in patients not treated. Patients accepting osteoporosis treatment had a significant increase in lumbar spine T-score, but no significant change at the femoral neck or total hip. In the group without treatment, no significant change in T-score was observed at the lumbar spine; however, a significant decrease in T-score was observed at the femoral neck and total hip.

Table 5 shows the estimated increase in T-scores in patients with anti-osteoporosis treatment compared with patients without treatment. In the univariate analysis, there was a significant increase in lumbar spine T-score and a borderline significant increase at the femoral neck, but no significant changes at the total hip.

In a multivariate regression model, we adjusted for age and sex. The increase in T-score at the lumbar spine persisted after adjustment, and there was a significant increase in T-score at the femoral neck in this model, but no significant changes at the total hip. Additional adjustment for T-scores at baseline did not significantly change the estimates.

In a subgroup analysis, there was no significant differences in age, sex, or mortality between the group, who received

treatment versus the group not receiving treatment. Patients, who were initiated in treatment, did have significantly lower T-scores at the initial scan (data not shown).

Discussion

The main findings of the present study are that 60% of subjects invited to participate in the OIP had a DXA-scan performed. The main reason for not having a DXA-scan performed was patients not showing up at the planned DXA-scan, despite attempts to book a new visit. This resulted in 40% of eligible subjects not having a DXA-scan performed. Among subjects showing up, 50.6% had osteoporosis verified by DXA-scan and 57.7% were prescribed treatment. Patients were more likely to be initiated in treatment if they had a T-score ≤ -2.5 . Nevertheless, 23.3% of subjects with a T-score ≤ -2.5 were not initiated in treatment.

In our study, no patient with a presumed high-energy hip fracture had a T-score ≤ -2.5 , which questions the need for

Fig. 1 A flowchart of the completion of the OIP

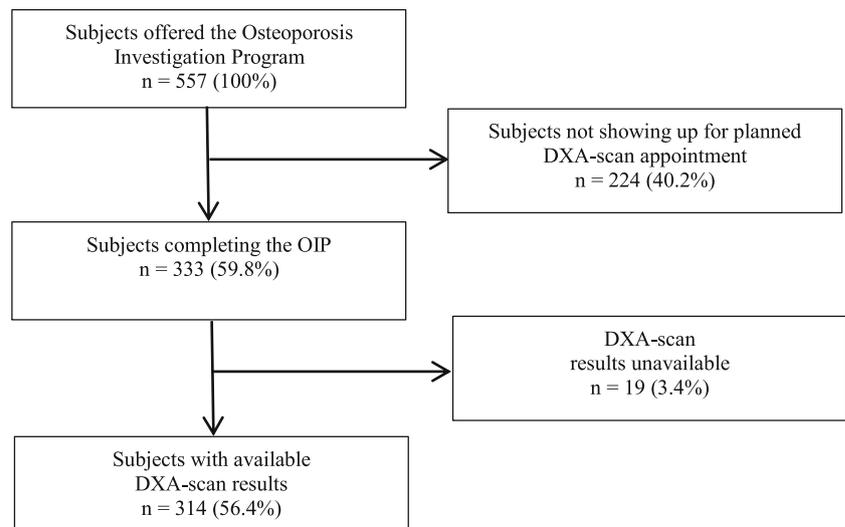


Table 2 Prevalence of DXA-verified osteoporosis at the initial and follow-up scan according to scan site

	Initial DXA-scan <i>n</i> = 314		Follow-up DXA-scan <i>n</i> = 172	
	Mean T-score (SD)	Osteoporosis, <i>n</i> (%)	Mean T-score (SD)	Osteoporosis, <i>n</i> (%)
Lumbar spine	- 1.32 (1.65)	74/314 (23.2%)	- 1.47 (1.51)	43/172 (25.0%)
Femoral neck	- 2.36 (0.90)	132/270 (48.9%)	- 2.60 (0.79)	85/143 (59.4%)
Total hip	- 2.06 (0.99)	95/270 (35.2%)	- 2.25 (0.89)	55/143 (38.5%)
DXA-verified osteoporosis (%)	159/314 (50.6%)		98/172 (57.0%)	

further osteoporosis investigation in this group. However, we recognize that this is a small sample and that larger studies are needed in order to confirm this. In addition, the separation between high- and low-energy trauma can be difficult, especially in the acute clinical setting.

We report a 1-year mortality rate of 27.7%. This is comparable with the mortality found in other studies of patients with hip fractures [18]. Life expectancy was found to be significantly shorter in those not found suitable for participation in the OIP.

We were able to show that patients initiating treatment had a significant increase in T-score at the follow-up DXA-scan at the lumbar spine after 1.5 year and that subjects not initiating treatment had a significant decrease in T-score at the femoral neck and total hip. Comparison of changes in T-score among subjects with or without treatment showed that the T-score in treated patients increased significantly at the lumbar spine with a borderline significant increase at the femoral neck. This increase persisted after adjustment for age and sex at the lumbar spine and became significant at the femoral neck. No significant change between the groups was observed at the total hip. However, subjects initiating treatment are more likely to have a lower T-score at the initial scan. To address this issue, we adjusted for the T-score at baseline, which did not change the overall results.

These findings should serve as an incentive for the physician to initiate osteoporosis treatment in patients with fragility hip

fractures. Even so, osteoporosis is still being underdiagnosed and undertreated in patients following a hip fracture and other osteoporosis-related fractures. Saad et al. showed that only 12% received a BMD measurement following the hip fracture [19]. Nguyen reported that 32% had a DXA-scan performed and only 26.9% were prescribed anti-osteoporosis treatment following a hip fracture [5]. Antonelli et al. showed that, within 1 year of a hip fracture, 10% had a DXA-scan planned and 19% had anti-osteoporosis medication prescribed [3]. Although this indicates a very scarce use of osteoporosis treatment following a hip fracture, studies have shown that treatment rates in general have increased over time [20, 21]. Recently, Klop et al. reported that, in year 2000, only 7.4% of patients received osteoporosis treatment after experiencing a hip fracture, which increased to 45.5% by the year 2010 [22].

It is surprising, that osteoporosis is being underdiagnosed and undertreated, when in fact all patients with fragility fractures at the spine or hip warrant the diagnosis of osteoporosis, according to the International Society for Clinical Densitometry (ISCD) and the Danish National Treatment Guidelines [8, 23]. Ideally, osteoporosis should be prevented before a fracture occurs. This is not always possible, so an important strategy would be to identify patients, who have had a fragility fracture, and offer treatment in order to prevent any subsequent fractures. It is well-known that the risk of subsequent fractures can be reduced by initiation of osteoporosis treatment. In a double-blinded randomized clinical trial,

Table 3 Selection of treatment initiated according to DXA-scan

	Osteoporosis <i>n</i> = 159	Osteopenia <i>n</i> = 125	T-score > - 1 <i>n</i> = 30	DXA-scan results not available <i>n</i> = 19	Total <i>n</i> = 333
Alendronate (%)	37 (23.3%)	24 (19.2%)	4 (13.3%)	4 (21.1%)	69 (20.7%)
Zoledronic acid (%)	71 (44.7%)	21 (16.8%)	7 (23.3%)	6 (31.6%)	105 (31.5%)
Ibandronate (%)	3 (1.9%)	0 (0%)	0 (0%)	0 (0%)	3 (0.9%)
Teriparatide (%)	3 (1.9%)	1 (0.8%)	0 (0%)	0 (0%)	4 (1.2%)
Denosumab (%)	8 (5.0%)	0 (0%)	2 (6.7%)	0 (0%)	10 (3.0%)
Estrogen (%)	0 (0%)	1 (0.8%)	0 (0%)	0 (0%)	1 (0.3%)
Total treatment	122 (76.7%)	47 (37.6%)	13 (43.3%)	10 (52.6%)	192 (57.7%)

Table 4 Estimated change in T-scores in patients initiating osteoporosis treatment and the patients not treated

	Treatment				No treatment			
	Estimate (SD)	95% CI	<i>p</i> value	<i>n</i>	Estimate (SD)	95% CI	<i>p</i> value	<i>n</i>
Lumbar spine	0.28 (0.40)	0.21 to 0.34	< 0.01	144	-0.03 (0.41)	-0.19 to 0.13	0.71	28
Femoral neck	-0.03 (0.27)	-0.08 to 0.02	0.24	123	-0.19 (0.33)	-0.35 to -0.04	0.02	20
Total hip	-0.03 (0.61)	-0.13 to 0.08	0.65	123	-0.17 (0.24)	-0.28 to -0.05	0.01	20

Lyles et al. found that zoledronic acid significantly reduced the incidence of subsequent fractures by 35% and mortality by 28%, compared with placebo. Zoledronic acid also significantly increased BMD at the total hip by 5.5% and by 3.6% at the femoral neck after 36 months [10]. Bawa et al. found that osteoporosis therapy significantly lowered the incidence of subsequent fractures at all sites by 40% and by 33.8% at the hip over 3 years [24].

The reasons for the gap between evidence-based treatment guidelines and actual initiation of treatment rates remain partly unclear. It is possible that clinicians are less likely to initiate treatment of osteoporosis in patients lacking BMD measurement or if a patient has a T-score > -2.5, as seen in our study. Another reason could be confusion regarding which physician is responsible for the treatment. Giametti et al. found that no single specialist was the source of counseling after a fragility fracture, indicating uncertainty about, who is to handle the responsibilities of follow-up care [25]. However, a planned strategy would clear up this issue. In our study, all patients who participated in the program were consulted by an endocrinologist, who would assume the responsibilities of both the diagnosis and treatment.

In our study, no gender difference in offered osteoporosis investigation or treatment was observed; however, other studies have shown that osteoporosis investigation and treatment is more common in women. Antonelli et al. showed that women were more likely to have a DXA-scan performed and be initiated in osteoporosis treatment [3]. This is confirmed by several other studies [5, 19, 22]. It is likely that osteoporosis is still being misconceived as a female disease; however, a

planned strategy would diminish the difference between the genders, as seen in our study.

When reviewing the literature evaluating secondary prevention programs in osteoporosis management, it is clear that these programs have a higher proportion of patients receiving investigation and treatment following a fragility fracture. Roy et al. found that implementation of their secondary prevention program resulted in 89% of patients with a fragility hip fracture being investigated for osteoporosis compared with 24% before implementation of the program [26]. A Danish hospital implemented the FLS, and it resulted in 92.9% having a DXA-scan performed with an osteoporosis prevalence of 14.9% [7]. A Canadian study showed that implementation of FLS resulted in 86.1% having a DXA-scan performed. The prevalence of osteoporosis was 15.3% [27]. These studies included all types of fragility fractures, with hip fractures only constituting 5% and 10%, respectively. This might explain why the prevalence of osteoporosis was much higher in our study and why less patients in our study had a DXA-scan performed. Axelsson et al. compared BMD measurement and treatment rates in a two-year period before and after FLS implementation [6]. The study showed that, before implementation, only 7.6% received BMD measurement compared with almost 40% after implementation. When looking at treatment rates, only 3.4% were initiated in treatment following a fragility fracture compared with 22.1% after implementation of FLS. These studies all suggest that a secondary prevention program can increase the number of patients being tested and treated for osteoporosis; however, it had been widely discussed whether this practice is cost-effective. A recently published Australian study showed that a FLS saves up to \$880,000 per 1000 patients

Table 5 Estimated effect on the T-score in patients initiated in anti-OP treatment compared with patients without treatment

	Univariate analysis			Multiple regression ^a			Multiple regression ^b		
	Estimate	95% CI	<i>p</i> value	Estimate	95% CI	<i>p</i> value	Estimate	95% CI	<i>p</i> value
Lumbar spine <i>n</i> = 172	0.30	0.13 to 0.47	< 0.01	0.29	0.13 to 0.46	< 0.01	0.32	0.15 to 0.48	< 0.01
Femoral neck <i>n</i> = 143	0.17	0.00 to 0.33	0.05	0.17	0.03 to 0.30	0.02	0.15	0.02 to 0.29	0.03
Total hip <i>n</i> = 143	0.14	-0.01 to 0.30	0.07	0.12	-0.16 to 0.40	0.41	0.06	-0.20 to 0.33	0.65

^a Adjusted for age and sex^b Adjusted for age, sex, and T-score at baseline

over a 3-year period [28]. These savings are primarily due to the prevention of subsequent fractures and related costs.

To our knowledge, the present study is the largest to evaluate a planned investigation strategy addressing osteoporosis in patients with hip fractures. However, several limitations apply to our study. We were unable to access the electronic medical journal of subjects included in the study. Therefore, we could not assess any secondary causes of osteoporosis, i.e., comorbidities or medical history of the participants. Unfortunately, we did not have access to the hospitals' data in regard to the number of patients receiving osteoporosis investigation prior to the implementation of the OIP and therefore, we were not able to assess the effect of the program. We might have underestimated the prevalence of osteoporosis, due to 14% of patients lacking BMD measurement at the hip due to previous hip surgery. Finally, we have no information on long-term outcome and no records of compliance or adherence to the initiated treatment. However, if patients in our study had a low compliance, this would underestimate the increase in T-score seen in patients initiated in treatment.

It is surprising that, even with a fairly intensive secondary prevention program, 40% of eligible patients were not investigated for osteoporosis. The biggest barrier against having a DXA-scan performed was patients not showing up at the date of the DXA scan. One way to address this issue could be an electronic medical reminder sent out to the general physician of patients with fragility fractures, reminding them to refer these patients to osteoporosis investigation. This could help increase the number of patients receiving a DXA-scan and consequently osteoporosis treatment, as reported by Feldstein et al. [29].

Even more surprising is the fact that only 57.7% of patients received adequate osteoporosis treatment, when in fact almost all patients with hip fractures warranted the diagnosis of osteoporosis. One way of overcoming this problem would be to initiate treatment, while the patients are still under admission due to their fractures.

In conclusion, this study should serve as an example of the difficulties in investigating and treating osteoporosis following hip fractures. Even with a fairly intensive outreach osteoporosis screening strategy, only a minority of patients were investigated and treated. However, these patients reached a significant increase in T-score after 1 year and a half.

Compliance with ethical standards

Conflict of interest Anas Ould Si Amar, Lars Hyldstrup, and Jette Nielsen declare that they have no conflict of interest. Henrik Palm is an advisor for UCB and Amgen, salary to departmental research account, sum below 5.000 euros, and a board member at the Copenhagen Medical Society.

Jens-Erik Beck Jensen has received consulting fees from Eli Lilly, Amgen, Gilliad, and MSD and is an advisory board member at Eli Lilly, Amgen, and UCB.

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