Screening for osteoporosis reduced new fracture incidence by almost half

A 6-year follow-up of 592 fracture patients from an osteoporosis screening program

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Background and purpose **Fractures can be prevented if osteoporosis is identified and treated. In 2002, we initiated a screening program at our orthopedics department, in which patients between 50 and 75 years of age with a wrist, shoulder, vertebral, or hip fracture are assessed by DEXA of the hip and spine and encouraged to see their doctor for decision on treatment regarding osteoporosis. The patients receive written documents containing information, DEXA results, and a letter to their doctor with suggestions regarding blood tests and treatment. In this 6-year follow-up study, we compared the fracture recurrence in 2 groups: patients screened for osteoporosis after fracture as described, and a historical control group with fracture patients who presented at our department 1 year before we started the screening intervention.**

Methods **A questionnaire was sent to the 2 groups of fracture patients, those from before the time that we started the screening in 2002 and those who participated in the initial screening study in 2003. The questionnaire included questions on whether they had sustained further fractures, whether they had seen a doctor, and whether treatment had been initiated.**

Results **239 of the 306 unscreened patients (68%) and 219 of the 286 screened patients (77%) answered the questionnaire. In the unscreened group, 69 new fractures had occurred, in contrast to 39 in the screened group. The fracture risk was 42% lower in the screened group. Answers regarding treatment were incomplete in the unscreened group.**

Interpretation **Screening of fracture patients for osteoporosis reduced fracture recurrence, which indicates that the screening procedure has resulted in treatment that prevents fractures.**

Osteoporosis can be treated pharmacologically to reduce fracture risk (Black et al. 1996). Treatment involves agents that reduce bone resorption, such as bisphosphonates (Black et al. 2006), and bone anabolic agents (Mulder et al. 2006), with new treatment options entering the market. It is difficult to identify those in need of treatment before the first fracture since the early stages of osteoporosis give little or no symptoms. Dual-energy X-ray absorptiometry (DEXA) can measure bone mineral density (BMD), and low BMD is a strong risk factor for fracture (Blake and Fogelman 2007). However, low BMD provides limited information regarding bone quality or trabecular connectivity and this is a major reason why DEXA screening of the general population has not been considered effective. A recent report has challenged this opinion (Barr al. 2010), and in January 2011 the US Preventive Services Task Force issued a recommendation regarding osteoporosis screening (Nordin 2011). A fracture in itself signals reduced bone strength (Chevalley et al. 2002, Dalle and Giannini 2004, Genant et al. 2007) and a DEXA scan in the presence of a fracture might therefore improve prediction of future fracture risk.

It can be argued that the first adult fracture is an opportune time to identify patients with low BMD in order for them to get the maximum benefit of treatment (Mallmin et al. 1993, Edwards et al. 2005, Freedman et al. 2007). It seems logical to organize such an osteoporosis screening at orthopedics departments, where most fracture patients attend. We have previously reported the results of such a screening program at our department, where patients between 50 and 75 years of age presenting with a wrist, proximal humerus, vertebral, or hip fracture are referred for a DEXA scan (Astrand et al. 2006) and other authors have reported the results of similar screening programs (McLellan et al. 2003, Sander et al. 2008). In a second follow-up study of the participants in our screening, 90% of the patients with osteoporosis visited a doctor and about two-thirds of them received bisphosphonate treatment (Astrand et al. 2008). Our hypothesis was that our screening program results in reduced recurrence of fractures and the purpose of this follow-up study was to evaluate the validity of this hypothesis.

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Table 1. Analysis of study outcome. New fractures during the 6-year follow-up

Group	No. of patients	No. of deceased patients	No. of new fractures	Mean (SD) time to new fracture, years	No. of patients with 2 fractures
Unscreened	239	53 (17%)	69 (29%)	6.07 (0.30)	6 (2%)
Screened	219	34 (12%)	39 (18%)	6.09 (0.32)	4 (2%)

Patients and methods

We compared 2 populations of patients who were 50–75 years of age at the time of index fracture (wrist, proximal humerus, vertebral, or hip fracture) and who presented at the Department of Orthopedics, Lund University Hospital, which serves a population of 300,000. The first group presented between November 2001 and November 2002, before we started the screening and the second group presented between November 2002 and November 2003, after the screening had started. Thus, we had one group that was screened for osteoporosis and a historical, age-matched control group that was not screened. The screened group included 286 fracture patients (69 males) with a mean age 69 (SD 8) years at follow-up. The unscreened group consisted of 306 patients (87 males) with a mean age of 70 (SD 8) years at follow-up. The patients in this historical control group from the year before we started the screening were identified from our records, and those in both groups were sent the same follow-up questionnaire. Ethical approval (LU 826-03) was obtained from the Regional Ethical Review Board in Lund.

The osteoporosis screening service includes patients who are 50–75 years of age and who attend the Department of Orthopaedics, Lund University Hospital, Sweden with a fracture of the wrist, proximal humerus, vertebra, or hip. A nurse, a secretary, and a doctor run the screening service on a part-time basis. The nurse identifies the patients and interviews the inpatient cases. A telephone answering service is also required, which is split between the nurse and the secretary who takes care of correspondence. The doctor establishes diagnoses mostly based on the DEXA scan, but in some cases also based on records and questionnaires. The patients are referred for a DEXA scan and, based on the bone density measurement, we diagnose the patient as having normal bone mass, osteopenia, or osteoporosis. To assist treatment decisions, we also categorize osteopenia as being light/moderate or severe, the latter if the DEXA T-score is below –2.0 SD. The patient then receives an information letter and written copies of the results. If the diagnosis based on the DEXA results is osteoporosis or severe osteopenia (defined as BMD < –2.0 SD), the patients are encouraged to contact their own primary care physician or a doctor of their own choice for further evaluation, and to present the already enclosed letter of admission from us containing suggestions regarding blood tests and treatment according to current Swedish guidelines. Blood tests are recommended to check for secondary osteoporosis, such as parathyroid or kidney-related disease.

For this study, a follow-up questionnaire was sent out to the unscreened group in May 2008 and to the screened group in May 2009 (giving a mean follow-up time of 6 years). The patients were asked whether they had sustained subsequent fractures, when the fracture(s) had occurred, and if they had visited a doctor. They were also asked questions about risk factors: frequent falls, cortisone treatment, weight loss, length loss, early menopause, and smoking. If treatment had been prescribed, the patients were asked about the type of treatment and when it had started. The handwritten answers were collected in a file and analyzed manually.

Statistics

Statistical analysis included logistic regression analysis of group homogeneity, Andersen-Gill model for fracture risk, and robust standard errors for handling of multiple fractures. Logistic regression was used to analyze dropouts regarding age and sex. To determine the fracture risk in both groups, the Andersen-Gill model was used. Robust standard errors were used to include multiple fractures; thus, all new fractures were included.

Results

Response rate

In the screened group, 219 of the 286 patients answered the questionnaire with 67 (23%) lost to follow-up. In the control group, 239 of 306 answered, again with 67 (22%) lost to follow-up. In the screened group, 34 (12%) had died, 8 (3%) were too ill to participate, and 25 (9%) were non-responders. In the unscreened control group, 53 (17%) had died, 3 (1%) had moved abroad, and 11 (4%) were non-responders. 20–25% were lost to follow-up in each age group (Table 4).

Mortality

The mortality rate was 53 in the unscreened group and 34 in the screened group ($p = 0.06$).

New fractures

In the screened group there were 39 new fractures (18%), and in the unscreened control group there were 69 new fractures (29%). In both groups, the mean time to a new fracture was 6 years (Table 1). An age-stratified analysis as described above

Table 2. Distribution of risk factors. The numbers refer to patients who answered yes

Risk factors	Screened (n = 219)	Unscreened (n = 239)
New fractures	39	69
More than one fall in the previous year	63 (29%)	40 (17%)
Cortisone treatment for > 3 months	29 (13%)	28 (12%)
Weight loss of >10 kg since age 25	27 (12%)	30 (12%)
Loss of height >3 cm	63 (29%)	49 (20%)
Menopause before the age of 45	32 (15%)	36 (15%)
Smoking	29 (13%)	31 (13%)

Table 3. Type of treatment (first 4 rows) and known start of bisphosphonate treatment (last row)

	Screened (n = 219)	Unscreened (n = 239)
No treatment	93 (42%)	169 (71%)
Calcium + vitamin D	60 (27%)	29 (12%)
SERM	6 (3%)	1 (0%)
Bisphosphonates	60 (27%)	40 (17%) (15 (6%) [a])
Known start of bisphosphonate treatment	13 (6%)	13 (5%) [b]

[a] after second fracture screening
[b] most after second fracture

of the fracture distribution showed a gradual increase in fracture incidence in both groups. The rate of new fractures in the screened group was 42% less than in the unscreened controls; this effect was independent of age and sex. The effect of sex was on the borderline of being significant, which indicates that the rate of new fractures for men may have been lower.

Risk factors

The distribution of risk factors was similar in both groups (Table 2). There were more falls in the screened group (p = 0.006) and more patients lost more than 3 cm of their height (p = 0.04).

Treatment

No pharmacological treatment was prescribed to 93 patients (42%) in the screened group and to 169 patients (70%) in the unscreened group. In the screened group, 60 (27%) had been treated with bisphosphonates. In the unscreened control group, 40 (17%) had been treated with bisphosphonates, but it should be noted that of those 40, 15 (6%) had had a second fracture. After this, they had been screened for osteoporosis by us and as a result had received bisphosphonate treatment.

Thus, we compromised our own controls. Regarding pharmacological treatment for osteoporosis, the answers in the questionnaires were incomplete regarding when treatment was started. This prevented further statistical analysis of whether the effect on fracture incidence was treatment-related since no reliable calculations could be made regarding the duration of a pharmacological fracture-reducing effect (Table 3).

Risk of new fracture

There were significant differences between those who were followed up and those who were lost to follow-up regarding age and sex. The crude, unadjusted relative risk of a new fracture between the screened group and the unscreened control group was 0.58 (95% CI: 0.39–0.89). The relative risk of a new fracture between the screened group and the unscreened group, adjusted for age and sex, was 0.58 (CI: 0.40–0.87). The effect of sex was not significant (0.63 (CI: 0.38–1.03)) and the effect of age was 1 (CI: 1.03–1.09).

The effect of the dropouts on the estimate was difficult to evaluate, but an additional analysis weighted for non-response gave a similar result (data not shown). The model with age and sex as covariates could not explain most of the variance in the data.

Discussion

In this study, we found a 42% age- and gender-adjusted reduction in fracture incidence in a group that was screened for osteoporosis after a fracture compared to a historical control group that was not. There were fewer deaths in the screened group, 12% vs. 17% (p = 0.06). Notably, Nurmi-Lüthje et al. (2009) found lower mortality in patients who were given calcium-vitamin D supplements and concomitant anti-osteoporosis drugs (Nurmi-Luthje et al. 2009), which was confirmed in a nationwide analysis (Nurmi-Luthje et al. 2011). Whether lower mortality can be attributed to a reduced number of fractures or metabolic effects of vitamin D treatment is unclear.

There is growing realization that an "osteoporosis" fracture should not be perceived as an isolated event. Treatment should be twofold: treating the current fracture and preventing the next one. In our experience, this prevention is best organized separately from the actual fracture treatment since it is difficult to get consistent results in a crowded emergency room setting or if the screening is performed by many hands. Our screening service is organized with a coordinating "osteoporosis nurse" and has been in existence since 2002. The incidence of low BMD that we find in our fracture patients is consistent with similar programs—such as the fracture liaison service in Glasgow, which was early to report its results (McLellan et al. 2003). Like them, we leave the ultimate treatment decision to the patient and the GP, a model that is referred to by some authors as the coordinator model (Sander et al. 2008).

Apart from age, fracture and low BMD are among the strongest risk factors for osteoporosis. Low BMD can measure the mineral content of the bone, but it gives limited information on the structural orientation of bone, such as trabecular con-

Table 4. Fracture recurrence stratified according to age. 6-year follow-up; all patients were between 50 and 75 years at index fracture

Age group	Screened	Unscreened
50–59 years	6% (51)	16% (25)
60–69 years	11% (101)	20% (93)
70–79 years	14% (125)	35% (110)
> 80 years	50% (9)	63% (11)
Total	18% (286)	29% (239)

nectivity. This is one reason why a fracture together with low BMD improves prediction of fracture risk, since fracture can be said to signal poor structural quality of bone. This is also one of the reasons why DEXA screening of the general population is not recommended. Interestingly, a recent study from Scotland challenges this view, with results from a randomized controlled study showing fracture reduction after DEXA screening without fracture (Barr et al. 2010). However, a large proportion of the women who were treated in that study took hormone replacement therapy (HRT), which is not currently recommended for osteoporosis treatment (Rossouw et al. 2002). In addition, the results raise concerns over the cost-effectiveness of such a screening intervention.

Intuitively, fracture prevention at an early age is perhaps preferable, but its value remains to be proven. In the present study there was a substantial occurrence of fractures in the younger age groups also (Table 4), suggesting that screening for osteoporosis in the 50- to 60-year age group may be well advised. However, the effort to screen fracture patients at a younger age does raise concerns regarding selection bias, since the mean age of all fragility fracture patients at our orthopedics department is around 80. Our screening in the age group 50–75 years could be said to select fracture patients at lower risk of fracture instead of patients at an early stage of a sequence of fractures. Even so, some authors do suggest that wrist fractures can be seen not only as a result of a fall, but also as a warning sign of possibly low BMD and thus as a predictor of future fractures (Roux et al. 2011).

Our study does not allow conclusions to be made regarding what caused the lower fracture recurrence that we measured. A higher ratio of anti-resorptive treatment is a likely explanation for the lower fracture recurrence in the screened group, but we could not calculate treatment duration since most patients did not remember when treatment was initiated. Alternative explanations to a pharmacologically induced fracture reduction might include increased awareness of osteoporosis, increased propensity to seek medical help regarding osteoporosis, and patient initiatives such as fall-prevention measures that we counsel patients about in our correspondence. Barr et al. (2010) also speculated that the fracture reduction they could measure might be a result of other factors such as self-administered treatment. We have previously done a follow-up study on the screened group (Astrand et al. 2008), which gave us an indication of the state of treatment in a screened fracture patient group. It showed that most osteoporosis patients went to see a doctor, that two-thirds of those received bisphosphonate treatment, and that the remaining third received calcium and vitamin D treatment. Of the osteopenic patients, half of them received calcium and vitamin D treatment. In the present study, we have noted differences between the screened group and the unscreened controls regarding treatment (Table 3), which are possibly explained by our screening intervention.

It should be noted that 30 unscreened patients were caught in our screening program at the time of their subsequent fracture, which indicates that to some extent we compromised our own control group. Thus, the reduced fracture incidence we detected could in fact have been even higher if the study had been conducted as a prospective, randomized study with an intervention group and a control group. It can be argued that if you need such a setup to detect a difference, perhaps that difference is not substantial enough to be pursued. Furthermore, ethical considerations could be raised about conducting a randomized controlled trial where fracture patients serving as controls are not offered the treatment for osteoporosis that is recommended in current guidelines (Stein and Ray 2010).

We kept the questionnaire and the number of risk factors short in order to ensure maximum compliance, which is why we omitted other important risk factors such as weight or BMI at the time of fracture, previous low-energy fractures before the fracture that brought the patient to the study, low-energy fractures in close relatives, general patient fragility (measured for example by rising from a chair with or without using the arms), neuromuscular diseases, alcohol excess, chronic diseases such as rheumatoid arthritis, malabsorption diseases, diabetes, renal insufficiency, certain hormone disorders, and lack of dairy products or calcium use. Of the risk factors we considered, there was a higher number of falls and loss of height in the screened group, but there was still a lower number of fractures. Reasons for loss of patients to follow-up included dementia, psychiatric diseases, and alcohol abuse—and it can be argued that it is difficult for these patients to benefit from any screening program. Additional measures are needed.

An osteoporosis screening program for fracture patients is an uncomplicated, probably cost-effective service. The costs in our setting include a part-time nurse, a part-time secretary, a part-time doctor, the DEXA scans, and the eventual drug treatment. There is a need for constant updating of the routines of the screening service to maintain and improve effectiveness. Currently, we are addressing balance disorders by asking specific questions, such as “do you have impaired balance?”, which have shown a good correlation to falls (Wagner et al. 2009). A fragility fracture occurs not only as a result of low BMD but, in most cases, after a fall. Prevention of fractures must therefore include prevention of falls, where vertigo is one major contributing factor. In our screening service, we are

now cooperating with the Department of Otorhinolaryngology, Lund University Hospital, to include a self-administered physiotherapy program for improvement of balance, which we send to patients who have answered "yes" to questions regarding impaired balance. Another factor that increases the risk of vertigo in the older population is polypharmacy. This is also a consideration that we intend to address in our screening service in collaboration with the primary care physicians.

JÅ: study concept and design; acquisition, analysis, and interpretation of the data; and drafting of the manuscript. JN and KGT: critical review of the manuscript.

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