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Impact of Systematic Implementation of a Clinical Case Finding Strategy on Diagnosis and Therapy of Postmenopausal Osteoporosis

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Micro-abstract

Systematic implementation of an osteoporosis case finding strategy based on age, weight and fracture history, in 41 478 postmenopausal women nearly tripled referrals for bone densitometry, with a significant shift towards referring women at highest risk. Of newly referred patients 37% had osteoporosis, most of whom were prescribed treatment.

Introduction. Case finding for osteoporosis in postmenopausal women is advocated in guidelines of osteoporosis, but implementation is unsatisfactory. We studied, in daily practice, the impact of systematic implementation of a previously validated clinical decision rule and fracture history on referral for bone densitometry (DXA) and drug prescription for osteoporosis.

Methods. Before-after impact analysis in 41 478 consecutive consulting postmenopausal women, included by 1080 general practitioners (GPs) during 2 months, using the osteoporosis self-assessment (OST) index [based on age and weight, indicating women at low (LR), moderate (MR), and high risk (HR) for having osteoporosis (T-score <-2.5 in spine and/or hip] and fracture history. Relative risks (RR) and 95% confidence intervals were calculated between referrals before (n=6 580) and after intervention (n=10 379) and between risk subgroups.

Results. Post-intervention RR for referral for DXA was 1.9 (1.8-2.0). Compared to LR women with prior DXA, the RR was 6.3 (6.0-6.6) in MR and 10.7 (10.0-11.4) in HR women without fracture, but similar in MR and HR women with fracture (11.4 and 11.6, respectively). New cases of osteoporosis were diagnosed in 3 811 women, 96% of whom were prescribed drug treatment. Of HR women,

79% were referred for DXA. The sensitivity of a low OST index to predict osteoporosis was 92% and specificity was 16%.

Conclusions. The impact of temporary systematic implementation of this case finding strategy on GP practice was high: it nearly tripled referrals for DXA and 96% of patients found to have osteoporosis had treatment. The impact depended on OST index and fracture history. Only 79% of HR women were referred for DXA. Specificity of a low OST index to predict osteoporosis was low. This indicates the need in the GP population for case finding strategies with fewer barriers for referral for DXA and with higher accuracy for predicting osteoporosis.

Introduction

Clinical case finding for the risk of osteoporosis and fractures in postmenopausal women is advocated in all guidelines of osteoporosis⁽¹⁻³⁾ in order to 1/ select patients for bone densitometry;⁽⁴⁻⁶⁾ 2/ calculate the absolute fracture risk;^(4,5) and 3/ decide about therapy.⁽⁴⁻⁶⁾ However, implementation of case finding remains unsatisfactory,⁽⁷⁻¹⁸⁾ resulting in under diagnosis and under treatment of osteoporosis.⁽⁶⁾

Validation studies have shown evidence for reproducible accuracy of clinical case finding strategies for identifying patients at risk for low bone mineral density (BMD)^(4,5,19-32) and for fractures^(20,29,33,34) in various settings and populations.

The reasons for low implementation of validated case finding strategies are not well documented. Barriers for implementing case finding have been described in doctors and patients.^(10,16,17) In addition, only scarce data are available about implementation of case finding in daily practice and the resulting treatment.^(7,8,25,35) The available impact studies on implementation were of limited size or concentrated on patients suffering from a recent fracture.^(7,8,16,25,35-39) No studies are available on the impact of systematic implementation of clinical case finding for osteoporosis on referral for DXA in postmenopausal women in daily practice. Impact studies on implementation of clinical strategies in daily practice are available in other specialties, such as cardiology. In patients with suspected acute cardiac ischemia, the use of a clinical decision rule that had been previously validated in different settings and populations, had favourable impact on physician's hospital triage decisions within four months of implementation.⁽⁴⁰⁾ In patients hospitalised because of coronary artery disease, a pilot study on systematic implementation of a Web-based quality improvement reporting showed an enhanced adherence to secondary prevention guidelines within one year of use.⁽⁴¹⁾

The simplest screening tool to identify candidates for BMD testing, and therefore the most appealing for use in large populations, is the Osteoporosis Self-Assessment (OST) index, based only on age and weight.^(22,28,32) In a

previous validation study, the OST Index has been shown to have modest positive and high negative predictive value for osteoporosis defined by bone mineral density (BMD) criteria in a population of women already selected for bone mineral density (BMD) measurement.⁽²²⁾ In addition, a history of fracture after menopause was used in the clinical decision rule in this study, because such patients are advocated in all available guidelines to have a bone densitometry to make decisions about treatment.⁽²⁾

We therefore studied in daily practice the impact of systematic implementation of a clinical decision rule for clinical case finding (using the OST index and fracture history) on referral for DXA in postmenopausal women that consecutively consulted their general practitioner (GP). We examined differences in referral for DXA between pre- and post-intervention and between risk groups and evaluated drug initiation in patients with diagnosed osteoporosis after the intervention. We based our analysis on guidelines for interpretation of trials on clinical decision rules.⁽⁴²⁾

Methods

In total, 1 080 GPs were invited to include 50 consecutively consulting postmenopausal women over a period of 2 months. The GPs were informed about the clinical significance of the OST index and fracture history in case finding for patients at high risk for osteoporosis and fractures.

The OST index was calculated from age and weight as integer of $(0.2 \times \text{self-reported weight}) - (0.2 \times \text{age})$.^(21,22) An OST of >1 indicated low risk (LR), -3 to 1 moderate risk (MR) and <-3 high risk (HR).⁽²²⁾ The OST was calculated by the GP using a chart indicating the level of OST according to age and body weight.⁽²²⁾

GPs questioned their patients about history of fractures after menopause, without specifying location or timing.^(43,44) The GPs noted if women had already had a prior DXA (yes/no). If the women had no prior DXA, the GPs did refer women following their clinical judgement based on the presence of the clinical risk factors (OST and fracture history). GPs did send their patients to the bone densitometry unit of their choice. Most devices

were from Hologic or Lunar. The type of instrument was not specified because in Belgium, all units have quality control according to governmental regulations.

The FRACTURE index, which is based on age, weight, fracture history and BMD, was calculated after the end of the study.⁽²⁰⁾ Hence, the FRACTURE index was not used by the GPs, but was used in a post-hoc analysis to verify the number of women who had a 5-year absolute risk for non-vertebral fractures of more than 20%.

The medical ethical committee approved this project, patients signed an informed consent and documents were made anonymous.

Statistics

The impact of systematic implementation was calculated by analysing the relative risk (RR) with 95% confidence interval (CI) for differences 1/ between risk groups (based on OST and fracture history and its combinations) before and after intervention and 2/ between pre- and post-intervention.

In order to test the validity of the OST index in this population, we determined the sensitivity, specificity and positive predictive value (PPV) of an OST index of <2.0 to identify women with osteoporosis and compared these results with the published data in the validation study on the performance of the OST-index by Caderette et al. in a population of women already referred for DXA.⁽²²⁾

SPSS software (version 12.0; SPSS Inc. Chicago, IL, USA) was used for the statistical analysis.

Results

Most GPs included more than 50 women (829 GPs, 77%), 125 between 20 and 50 women (11%) and 126 less than 20 women (12%). Of the 46 511 participating women, all data were available in 42 082 women, of whom 41 478 were older than 50 years and were included in the analysis (**Figure 1**). These 41 478 women had full registration of age, weight, fracture history, information about prior referral for DXA, results of DXA of women referred during the study and information on newly started drug therapy in women in whom osteoporosis was diagnosed after referral for DXA during the study.

First we assessed the impact of the OST index, fracture history and both combined on clinical behaviour, i.e. on referral for DXA, before and after the intervention (**Table 1**). Next we analysed the impact of the systematic implementation, i.e. the change in referral for DXA after intervention as compared to before intervention, in the total group and in subgroups according to the presence of OST index and fracture history.

Implementation before intervention

Before intervention, a DXA had been performed in 6 580 (16%) women, in 1 368 (7%) of the LR, 4 375 (23%) of the MR and 837 (27%) of the HR women (**Table 1**). Compared to LR women, the RR was 3.0 (CI: 2.8-3.1) in MR and 3.4 (CI: 3.2-3.7) in HR women. A prior DXA had been performed in 4 756 (14%) of women without a fracture and in 1 822 (27%) of women with a fracture (RR versus women without fracture: 2.0, CI: 1.9-2.1). The RR in HR women without fracture was slightly higher than in all MR women (3.4, CI: 3.2-3.7 and 3.0, CI: 2.8-3.1, respectively). The RR was similar between HR and MR women without fracture history (3.4, CI: 3.1-3.8 and 3.1, CI: 2.9-3.3, respectively) and between HR and MR women with fracture history (4.7, CI: 4.3-5.2 and 4.6, CI: 4.2-4.9, respectively).

Implementation after the intervention

After intervention, a DXA was performed in 10 379 women (30% of the 34 898 women without prior DXA), in 1 384 (8%) of LR, 7241 (47%) of MR and 1

754 (72%) of HR women (**Table 1**). Compared to LR women with prior DXA, the RR was 1.1 (1.0-1.2) in LR, 6.3 (CI: 6.0-6.6) in MR and 10.4 (CI: 9.8-11.0) in HR women. A DXA was performed in 7 332 (24%) of the women without fracture and in 3 047 (63%) of the women with fracture (RR versus prior DXA without fracture: 1.8 (1.7-1.9) and 4.6 (4.4-4.8), respectively). The RR in HR women without fracture was higher than in all MR women (RR:10.7, CI:10.0-11.4 and 6.3, CI: 6.0-6.6, respectively). This RR was also higher in HR without fracture than in MR women without fracture (10.7, CI: 10.0-11.4 and 6.4, CI: 6.0-6.8, respectively), but was similar in HR women with fracture as compared to MR women with fracture (11.6, CI: 10.9-12.5 and 11.4, CI: 10.4-11.8, respectively).

Impact of systematic implementation

Next we analysed the impact of the systematic implementation by comparing referrals for DXA before and after the intervention in the total group and in subgroups according to the presence of OST index and fracture history (**Table 1**). The intervention nearly doubled RR for DXA referral (RR:1.9, CI: 1.8-2.0), resulting in tripling of referrals for DXA in the total group. The RR remained unchanged in LR women without fracture (RR:1.0, CI:0.9-1.1), but was significantly higher in the MR (RR:2.1, CI:2.0-2.2) and HR women (RR:2.8, CI:2.6-3.0) and in women with a fracture (RR: 2.3, CI:2.2-2.4). The impact was higher in MR women (RR: 2.1, CI: 2.0-2.2) than in LR women (RR: 1.1, CI:1.0-1.2). The impact was higher in HR women without fracture (RR:3.2, CI: 2.9-3.5) than in MR women without fracture (RR: 2.0, CI: 1.9-2.1), but similar in HR women with fracture (RR:2.5, CI:2.3-2.7) and MR women with fracture (RR:2.4, CI:2.3-2.6). In HR women, the RR was significantly lower in women with fracture (RR:2.5) than without fracture (RR:3.2).

At the end of the study, the percentage of women who had a DXA before and after intervention achieved 80% in the MR group with a fracture and 79% in all HR women (**Figure 2**). The number of new cases of osteoporosis (T-score <-2.5 in the spine and/or hip) in women who were referred for DXA during the study was 3 811 (37% of those referred during the study). More than

90% of the patients with newly diagnosed osteoporosis were prescribed drug treatment, mainly bisphosphonates (89%).

In the context of this publication we analyzed the validity of the OST index in this population, as reported by Caderette.⁽²²⁾ The sensitivity for an OST score of <2.0 for detecting osteoporosis was 92%, specificity was 16% and the PPV was 21% in LR, 35% in MR and 58% in HR women. The PPV was lowest in LR women without fracture (18%) and highest in HR women with a fracture history (65%).

We further analysed the absolute risk of fractures based on the FRACTURE index in patients with referral for DXA during the study (24). The number of women with a high 5-year risk for non-vertebral fractures ($>20\%$) could be calculated based on age, weight, fracture history and T-score.⁽²⁰⁾ Such high fracture risk was found in 91% of the women with a T-score <-2.5 .

Discussion

The results of this impact study indicate a high influence on clinical behaviour in daily practice. The GPs had already sent many patients for DXA prior to the study according to OST and fracture history, but clearly not in the desirable numbers. Our study is the first to show a high impact of implementation of systematic evaluation by using a simple screening tool based on the OST index and fracture history: it contributed to the nearly tripling of the proportion of women referred for DXA with a significant shift towards referring more women with high risk of osteoporosis and future fractures. 3 811 patients had newly diagnosed osteoporosis and high risk for fractures, representing more than one third of new referrals for DXA, and most of them were prescribed bisphosphonates to prevent fractures.

The impact of implementing case finding strategies has only been studied scarcely. Pre-specified clinical pathways in patients with a recent fracture^(8,25) and electronic medical record reminders after a fracture⁽³⁵⁾ were most effective, while simple reminder letters and offering free bone densitometry after a fracture were not.^(7,37,39) One of the reasons of the high impact of the implementation in this study could be that this case finding strategy was GP-driven: it was the GP who took the initiative for case-finding with a personal contact with the patient during a medical consultation. Such clinical situation is quite different from less personal methods of communication, such as letters or posters about osteoporosis.^(10,16,17) Indeed, in spite of many such efforts, osteoporosis is still under diagnosed and under treated.⁽⁶⁾ However, we lack impact studies analyzing to what degree GP-versus patient-driven initiatives would make a difference for implementing DXA referral.

The impact of implementation varied between subgroups based on OST index and fracture history. In real world practice, the OST score discriminated well between LR and MR patients and between HR and MR in the absence of fracture history, but not any more between MR and HR in the presence of fracture history. After intervention, fracture history was a significant positive discriminator for referral to DXA in LR and MR women.

However, after intervention, HR women with a fracture were significantly less referred for DXA than those without fracture. This indicates that a fracture history positively contributes to referral for DXA in all but HR women. This finding is quite surprising as GPs were advocated to refer patients with a fracture history for DXA and as PPV was highest in HR women with a fracture. It suggests that in HR women with a fracture barriers exist for referral for DXA, such as physical or mental limitations as the result of a fracture⁽³⁾ or in the context of co-morbidities that are frequently present in fracture patients.⁽³⁾

It was not the aim of this study to evaluate the validity of the OST index, as no BMD data were available in women with a prior DXA. However in women referred for DXA during the implementation study BMD results were available. Caderette et al. reported a sensitivity of OST score <2 for detecting osteoporosis of 92% and specificity of 46%.⁽²²⁾ The PPV for detecting osteoporosis was 19% in MR and 56% in HR women.⁽²²⁾ We found similar sensitivity for OST score <2 (92%) and similar PPVs (35% in MR and 58% in HR women). In contrast, the specificity was lower in our sample (16%). The reason was the still high prevalence of osteoporosis in the LR group (PPV of 21%), which is much higher than reported by Caderette (PPV of 2.3%).⁽²²⁾ This could be explained by differences between the study populations. First, the background prevalence of osteoporosis in our total sample was double that of Caderette (37% versus 18%, respectively).⁽²²⁾ Second, Caderette et al. excluded women with a prior fragility fracture.⁽²²⁾ In LR women, we found that the RR was 1.7 (1.5-2.0) in women with a fracture history as compared to LR women without fracture, indicating that in LR women, additional risk factors contribute to the risk of having osteoporosis. Third, Caderette et al. also excluded women with major risk factors for secondary osteoporosis (e.g. menopause before age 45, malabsorption syndromes, hyperthyroidism, long-term glucocorticoid use) while our sample was based on women consulting their GPs at for other reasons than osteoporosis. All these women had co-morbidities for which they consulted their GP, the nature of which was however not recorded in this study. The high prevalence of osteoporosis in the LR group without fracture (18%) suggests that this is indeed the case. This also

suggests that case finding strategies with higher accuracy are needed in the LR risk population, such as proposed by the WHO.⁽⁵⁾

In a post-hoc analysis in the context of this publication patients referred for DXA had a high risk for fractures and 91% of those with osteoporosis had a >20% 5-year risk of non-vertebral fractures, the most common type of fracture that is seen in traumatology and orthopaedic emergency departments.⁽⁴⁵⁾ Thus, even using a limited number of risk factors, a large group of patients with high risk for fractures could be identified.

This study has several limitations. First, the intent of this study was to show that this tool makes a difference in general use. A follow-up study has not been performed, but future studies are needed to determine whether any of the GPs learned from this and integrated it in their practice. The results of a follow-up study might show why a risk-assessment tool like this is not more widely and systematically used.

Second, only 79% of HR women were referred for a BMD which indicates that there are other barriers to referral that persist despite objective evidence of being at high risk of fracture and therefore in high need of a BMD. As mentioned above, co-morbidities could have limited referral for DXA in HR women. We have however no data collected about the reasons for refusal, but also in other studies many patients do not participate in further examinations, even in more acute situations, such as after a recent fracture.^(7,8,22,27) Future studies on implementation are indicated about the patient-related factors that contribute to implementation, such as socioeconomic status, educational level and inequalities in health care provisions and reasons for this and about GP-related factors.

Third, this study was mainly aimed towards referral for DXA. In the absence of a prevalent vertebral fracture, low BMD is still a necessary variable in order to start drug treatment according to the principles of Evidence-Based Medicine and according guidelines of osteoporosis and, in many countries, to get reimbursement of drug treatment.⁽¹⁻⁴⁾ If, as suggested in several guidelines,⁽¹⁻³⁾ the treatment thresholds of T-scores were increased in the presence of history of fracture, the number of women that could be treated

was increased by 414 when the treatment threshold was a T-score < -2.0) and by an additional 439 when the treatment threshold was a T-score < -1.0.

Finally, a potential bias is the patient's recall of all fractures after the menopause.⁽⁴⁴⁾ Ismail et al. have shown that using a questionnaire, 9% of all clinical fractures were not recalled, but this percentage was lower for forearm and hip fractures (3%).⁽⁴⁶⁾ However, we can assume that this percentage was lower in this study, as fracture history was performed by the GP who knew most of the patients since years and could have helped in recalling the fracture history according to his medical registration files.

The WHO is currently on its way to construct a case finding strategy, based on clinical risks that are independent of low BMD.⁽⁵⁾ This strategy is aimed to refine 5- and 10-year fracture prediction in the individual patient. However, it will be based on more clinical risk factors than used in our study, such as family history, smoking, alcohol abuse, rheumatoid arthritis and immobility. In view of the higher complexity of such case finding and decision strategies, further studies are warranted to evaluate its implementation in case finding and initiation of treatment in daily clinical practice.

This study leads to several conclusions. First, the impact of temporary implementation in the total group was high, tripling of referrals for DXA, of which 96% of those patients found subsequently to have osteoporosis were started on treatment for the condition. Second, the OST index was the best discriminator in LR and MR women, and fracture history in HR women. Still, the impact of implementation remained insufficient in HR women (only 79% of HR women received a BMD). This indicates that there are other barriers to referral that persist despite objective evidence of being at high risk of fracture and therefore in high need of a BMD measurement and the need for case finding with less barriers for referral for DXA in GP practice. Third, the validation analysis of the OST index showed that still 18% of LR women had osteoporosis, indicating the need for case finding with higher accuracy.

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None of the authors have conflicts of interest in this study

All authors had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis

Table 1. Relative risks (RR) for referral for DXA in women with prior and current DXA according to OST index, fracture history and combination of OST and fracture history.

Group	All women n	Prior DXA n	RR Prior DXA vs. reference	Current DXA n	RR current DXA vs. reference of prior DXA	RR current vs. prior DXA
All	41478	6580		10379		1,9 (1,8-2,0)
OST index						
			1,0 (reference)			
Low risk	18374	1368		1384		1,1 (1,0-1,2)
Medium risk	19824	4375	3,0 (2,8-3,1)	7241	6,3 (6,0-6,6)	2,1 (2,0-2,2)
High risk	3280	837	3,4 (3,2-3,7)	1754	10,4 (9,8-11,0)	2,8 (2,6-3,0)
Fracture						
			1,0 (reference)			
No	34822	4758		7332		1,8 (1,7-1,9)
Yes	6656	1822	2,0 (1,9-2,1)	3047	4,6 (4,4-4,8)	2,3 (2,2-2,4)
Fracture history						
			1,0 (reference)			
LR, no fracture	16929	1098		1003		1,0 (0,9-1,1)
LR + fracture	1445	270	2,9 (2,6-3,3)	381	5,0 (4,5-5,5)	1,7 (1,5-2,0)
MR, no fracture	15982	3240	3,1 (2,9-3,3)	5294	6,4 (6,0-6,8)	2,0 (1,9-2,1)
MR + fracture	3842	1135	4,6 (4,2-4,9)	1947	11,4 (10,4-11,8)	2,4 (2,3-2,6)
HR, no fracture	1911	420	3,4 (3,1-3,8)	1035	10,7 (10,0-11,4)	3,2 (2,9-3,5)
HR + fracture	1369	417	4,7 (4,3-5,2)	719	11,6 (10,9-12,5)	2,5 (2,3-2,7)

LR= low risk, MR=medium risk, HR=high risk, all according to OST index

Figure 1. Flow diagram of participating and analysed women.

Figure 2. Figure 2. Percent of women referred for prior DXA (% of all), current DXA (% of women without prior DXA) and having had any DXA (prior or current) according to subgroups based on OST index and fracture history.

LR: low risk, MR: medium risk, HR: high risk based on OST index

Frac: fracture history after age of 50 yrs

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