Mineral and Electrolyte Metabolism
Editor-in-Chief: S.G. Massry, Los Angeles, Calif.

Reprint
Publisher: S. Karger AG, Basel
Printed in Switzerland

Original Paper

Miner Electrolyte Metab 1994;20:287–293

Osteoporosis in a Largely Self-Referred Population: High Prevalence but Low Medical Priority: Why?

Wayne Perry
Monique Andersson
Christopher Mortimer†

The Endocrine Centre, London, UK

Key Words
Bone mineral density
Hormone replacement therapy
Oral contraceptive
Osteoporosis
Risk questionnaire

Abstract
Dual photon bone density screening for osteoporosis (OP) and osteopenia of the lumbar spine was performed in 108 women aged 34–75 years of whom 91% were self-referred in a cross-sectional study. OP was present in 18.6% when defined as greater than 2 SD bone mineral density (BMD) reduction compared to young normals and in 41.6% with osteopenia (1 SD BMD reduction). Twelve percent gave an actual history of previous fractures. In those who showed reduced BMD (60%), 69.5% had a family history and 54% scalp hair loss although this was not a good prognostic sign. An Osteoporosis Risk Questionnaire was not an accurate predictor of BMD, thus bone density screening remains essential for early and accurate diagnosis. Previous oral contraceptive use appears to be protective ($p = 0.004$). Sex hormone replacement therapy (sHRT) taken by 20% of the postmenopausal patients had not yet provided significant protection ($p = 0.15$) probably due to its late introduction, short exposure and failure to optimise dose levels. Despite detailed information and questionnaires provided to their doctors, of 53 patients with OP or osteopenia 15 (28%) started sHRT without additional investigation, 19 (36%) remained untreated, while the outcome in the rest, 19 (36%), was unknown. A disturbing indifference by doctors and patients continues to the prevention and treatment of OP and low BMD, a potentially preventable and reversible condition, which signals a higher risk of future fragility fracture.

Introduction

Public awareness and concern about the current epidemic of primary osteoporosis (OP) has been raised by recent publications [1] and the work of the National Osteoporosis Society. However, patient access to NHS services is severely limited in relation to the potential size of the problem. There are 9.6 million women over the age of 45 years in the United Kingdom of whom at the most conservative estimate a third will develop OP-related fractures, if judged from the American experience [2]. We have presented our views previously [3, 4] on the contentious issue of screening for OP [5], and in our opinion there is a perceived and justifiable need for

Received:
June 22, 1994
Accepted:
August 29, 1994

Dr. Wayne Perry
The Endocrine Centre
69 Wimpole Street
London W1M 7DE (UK)

0378–0392/94/0205–0287
$ 8.00/0

such facilities. To meet this requirement the centre offered the first self-referral service in the United Kingdom from June 1987 using the modern technique of dual photon absorptiometry of the lumbar spine. We felt that patients who were concerned about the possibility of having OP should have the opportunity of referring themselves to a specialist clinic for diagnosis and counselling. Their medical advisers were informed of the results and recommendations for further evaluation, treatment and follow-up were made either under their own care or at the centre on receipt of a formal letter of referral.

This unique group of patients gave us the opportunity of analysing the prevalence of OP and osteopenia in women who are probably more orientated to self care than most and to assess the subsequent response of both patients and doctors to its prevention, detection and treatment. We believe the presence of low bone mineral density (BMD) indicates a disease (inherited or acquired) which may or may not express itself as fracture in the same category as hypertension which may or may not express itself as stroke or other complications.

Patients and Methods

A population of 108 Caucasian women aged 34–75 years (mean 53.2, SD 7.6) from throughout the United Kingdom were serially screened between January 1988 and January 1989. There were no exclusion criteria. The reasons for self-referral included: availability of direct access to bone density screening, presence of a family history of OP, menopausal symptoms and the desire for specialist information on the value of sex hormone replacement therapy (sHRT), as well as general health concerns. They were mainly drawn from social class I and II with a high rate of private health insurance (60%) and reimbursable costs.

Clinical Assessment

Clinical Assessment of 105 women comprised a medical history, completion of an Osteoporosis Risk Questionnaire with the physician (Appendix 1), with the measurement of height, span and weight. The risk questionnaire was weighted in relation to existing evidence for risk factors.

The recording of scalp hair loss was introduced as an effect of oestrogen-progesterone (the endogenous anti-androgens) deficiency [6] and 12 points were given to menopausal patients to ensure their inclusion as a high risk group. Twenty patients were pre- or perimenopausal and 85 were postmenopausal, defined as an absence of periods for longer than 6 months. Three patients, of only 10 referred, were scanned with a minimum of clinical information by request of their medical practitioners.

Bone Density Screening

This was performed by dual photon absorptiometry using a Lunar DP3 (Lunar Radiation) incorporating a gadolinium-153 source with 13 mm detector collimation. Calibration using a bone mineral phantom measured at three different densities was performed each day prior to screening. No source change was made during the study.

Lumbar Spine Measurement and Normal Values

Bone density between L1 and L4 was calculated by computer and expressed in g/cm^2 using a standard procedure [7]. OP was defined as a reduction of BMD exceeding 2 SD (or 20% in this context) in one or more vertebrae compared to young normal white American females aged 20–40. Their mean values are identical to English normals using the same instrumentation [8]. Comparison with age-related controls may be misleading as the postmenopausal population is already abnormal showing varying degrees of accelerated bone loss in the early years. Fracture risk for peripheral, spine and hip sites becomes significant for each 1 SD decline below young normal levels [9–12] and confirms the need for a higher index of suspicion of early OP and osteopenia before fracture occurs.

OP Recall Service

This comprised the posting of a recall service letter to 53 patients with OP or osteopenia who had not returned for full evaluation and a Recall Service Questionnaire (Appendix II) to their respective medical advisers. These were sent twice to non-responders. One patient subsequently returned to the centre for full evaluation.

Statistical Analysis

For the 85 postmenopausal women in the sample, the mean BMD values for lumbar vertebrae 2–4 were analysed using a multiple regression model. The following factors were included in the regression: (1) age at menopause (years), (2) current age (years), (3) oral contraceptive pill (OCP) (0 = no, 1 = yes), (4) sHRT (0 = no, 1 = yes), (5) hysterectomy (0 = no, 1 = yes), (6) other secondary cause present (0 = no, 1 = yes) and (7) family history (0 = no, 1 = yes).

Criteria for OCP and sHRT use are shown in table 1, based on patient recall and conclusions should be viewed in that light. Variables were selected for the model using a backwards stepwise elimination procedure, with maximisation of the percentage variance accounted for being the inclusion criterion. Visual inspection of residuals was used to confirm the appropriateness of the linearity assumption.

Results

Of the 108 patients screened 20 (18.6%) met the criteria for lumbar spine OP. The absolute bone mass calculated for lumbar vertebrae L2 to 4 for those without OP or osteopenia was 1.304 ± 0.101 g/cm^2 (mean ± SD), low BMD with mild fracture risk (1 SD or 10–20% reduction) 1.097 ± 0.055 (n = 45), low BMD with moderate fracture risk (2 SD or 20–30% reduction) 0.963 ± 0.037 (n = 18), and low BMD with marked risk (3 SD or 30–40% reduction) 0.801 ± 0.065 (n = 3). Each 10% bone loss is approximately 1 SD below the young normal mean and represents a doubling of fracture risk for each 10% loss [12]. Besides risks attributed to life-style, 8 patients had possible contributory secondary causes to

Table 1. Criteria for OCP, sHRT and clinical analysis

Characteristics of population	Number of patients (total 105)	Patients with OP/osteopania	
		n	%
Family history of OP	46	32	69.5
Personal fracture history from minor trauma	13	–	12
Current or past history of calcium and/or vitamin D supplements	8	–	7.6
History of OCP 1–20 years	25	15	60
Premenopausal and perimenopausal group	20	8	40
Postmenopausal patients	85	57	67
Current or past history of sHRT > 6 months in postmenopausal group	17	9	53
Current users of sHRT	15	–	12.8
Postmenopausal patients known to have stopped sHRT within 3 months (ever use = 22)	5	–	22.7
Patients returning for full evaluation following a diagnosis of OP/osteopenia	12	–	18

When no figure is given in the central column % refers to the total number of patients (n = 105).

low BMD: coeliac disease for 30 years in 1, long-term Questran treatment in 1, diabetes mellitus in 1, prednisolone in 2, *L*-thyroxine replacement in 3 [13]. The characteristics of the 105 patients completing a full history are shown in table 1. Of those patients having received some form of treatment sHRT 20%, calcium and/or vitamin D 7.6%, none were being monitored for the beneficial effect or otherwise on the progress of their BMD, no measurement of oestradiol-17B levels in the postmenopausal women on sHRT was carried out and no patient had been instructed in specific 'bone builder exercises'. Twenty-four patients complained of scalp hair loss of whom 13 (54%) had OP or osteopenia.

Of the factors included in the multiple regression model, hysterectomy and other secondary causes were found not to improve the fit of the model. The best-fitting model, excluding these factors, accounted for 26% of the variation in BMD score. The regression coefficients for this model are shown in table 2. No improvement in fit was obtained if the OCP and sHRT factors represented in the model by a simple presence/absence code were replaced with the number of years exposure. The multiple R^2 value for the regression is 0.26. The multiple regression analysis seeks to measure the association between a number of (posibly interrelated) factors, listed in the statistical methods section, and the BMD score. The regression coefficients given in table 2 can be used to predict the average score that a postmenopausal woman will have. To use the model in this way, start with the constant term (1.277), add the age at menopause times its coefficient, and subtract (since its sign is negative) the current age times its coefficient. Finally, add or subtract the coefficients for OCP, sHRT or family history if any of these are present. The result is an estimate of the average score that would be expected for a woman with these attributes (or prognostic factors).

Table 2. Estimated regression coefficients for postmenopausal patients accounting for the principal variations in BMD

Factor	Estimate	SE	t	p
Constant	1.277	0.152	8.40	
Age at menopause	0.00562	0.00284	1.98	0.051
Current age	−0.00711	0.00246	−2.89	0.005
OCP	0.1187	0.0398	2.98	0.004
sHRT	0.0558	0.0378	1.47	0.15
Family history	−0.0752	0.0304	−2.47	0.016

sHRT was with Premarin in 5, Prempak C in 4, Harmogen in 2, Implants in 2 and one each with Cyclo-Progynova, Duphaston, Estraderm patches and oestradial injections weekly. SE = Standard error of estimate of regression coefficient; t = t value for test of estimated coefficient against zero; p = p value for two-tailed test of estimated coefficient against zero; OCP = oral contraceptive therapy.

From table 2, it can be seen that the BMD ($g \cdot cm^2$) value is higher for women with a late menopause (about 0.006 per year 95% limits 0.000 and 0.011), and decreases by about 0.007 for every year of age (95% limits 0.002 and 0.012), making this a highly significant indicator.

A history of sHRT use in 20% of the patients was associated with an increase in the score of about 0.056,

Table 3. Specificity and sensitivity error rates (%) of the Osteoporosis Risk Questionnaire compared with actual BMD results on lumbar spine screen

Error rates	Premenopausal	Postmenopausal	Combined
False-negative	62.5	5.4	12.5
sensitivity	37.5	94.6	87.5
False-positive	83.3	72.4	75.6
specificity	16.7	27.6	24.4

Score > 12 points indicates risk of OP (see Appendix 1).

but this was not statistically significant (95% limits −0.019 and 0.131). Of these, 9 patients had started sHRT between 5 and 14 years after the menopause. A family history of OP was associated with a reduction in the value of about 0.075 (95% limits 0.015 and 0.135) making this a significant risk factor in having a low BMD.

Five postmenopausal patients were known to have started sHRT in the past but stopped within 3 months because of side effects which included the discovery of a breast lump, non-specific symptoms of feeling unwell or intolerance and one who was put on as a 'trial'. Three patients out of 15 who had begun sHRT as a result of the finding of OP on screening had treatment stopped within 3 months of starting by their general practitioners for which no clear reason was available.

The sensitivity and specificity of the Osteoporosis Risk Questionnaire was compared to the actual findings on lumbar spine dual photon bone densitometry scanning (table 3). The questionnaire failed to reliably predict the prevalence of OP or osteopenia in the premenopausal group (false-negative 62.5%) although it was more sensitive in the postmenopausal group (false-negative 5.4%).

Of the 53 recall service questionnaires sent to the medical advisers of those patients diagnosed as having OP or osteopenia 34 (66%) were returned. Fifteen patients (28%) were started on sHRT without further investigations; 19 (36%) were left untreated and a further patient already receiving sHRT with OP was not further advised. The outcome of the remaining 19 (36%) was unknown since no replies were received although 2 were known to be on sHRT. Seven were prescribed calcium supplements, either Sandocal from 1 to 5/day or Ossopan (830 mg) 2–4/day as a consequence of their bone density screening but without further evaluation or follow-up measurement of bone density or measurement of circulating oestrogen levels on treatment and no patient had been instructed in specific 'bone builder exercises'.

Discussion

The high prevalence of lumbar spine OP and osteopenia (60%) in our self-referred cross-sectional study indicates that the overall prevalence in the Caucasian community which has been variously estimated to be between 30- and 32% based on actual fracture rates [14, 15] may have seriously underestimated the premorbid rate. Our figures, however, are influenced by the family history which led to considerable self-referral. Mild (10–20%) low BMD compared to young normals is defined here as unpathological osteopenia probably related to inherited low peak bone mass, but we believe this does represent the first sign of the same disease process with increased risk fracture even though many are in the low normal range for their age and weight group. Those with low peak bone mass are more susceptible to fracture later [11]. Furthermore, it is likely that the prevalence of OP and osteopenia for a critical fracture site would probably be higher, by 15% [our unpublished observations from 45 women aged 47–66 years in whom both lumbar spine and right hip were scanned], if the proximal femurs were also routinely scanned since pure trabecular bone in Ward's triangle may be more metabolically sensitive to postmenopausal oestrogen deficiency. While there are clearly selective biases operating in our population it is not surprising to find twice as many patients with detectable low BMD (60%) as will fracture in their lifetime (30%).

On the other hand, our patients were from social class I and II; as such they might have been expected to have a lower prevalence of OP and osteopenia because of presumed advantages in health awareness and nutrition. Thus the prevalence in the general population could be higher, particularly if associated with other adverse lifestyle factors including smoking [16] and alcohol [17]. Up to 20% of the postmenopausal group had received sHRT but this is still less than in the United States. Despite this OP or osteopenia was present in 53% of them probably because the duration of treatment was too short, begun too late and oestrogen levels not optimised with any additional therapy. By implication, if 80% of our social group had not received sHRT for the postmenopausal syndrome and OP it is likely that the remainder of the population are even less well provided for. A disturbing fact to emerge was that 20% of women on sHRT

had given up within 3 months of starting. This was confirmed from analysis of the recall service letters and questionnaires when 23% who had begun sHRT failed to continue beyond 3 months. We believe this reflects a failure of the patients medical advisers to establish optimal therapy [18] and explain the benefits of long-term treatment while providing a critical analysis of any contra-indications.

We confirm previous work [8] that exposure to the oral contraceptive pill appears to protect against low BMD and may indicate that the ethinyl oestradiol component is particularly potent in maintaining peak bone mass premenopausally. Among the group of premenstrual patients (aged 34–51 years) who still had regular periods the incidence of OP and osteopenia was high at 40%. This emphasizes the importance of early bone density screening since bone loss may proceed for several years before oestrogen and progesterone levels decline sufficiently for periods to cease and classical menopausal symptoms to occur.

Consequently, it is our recommendation that bone density screening should begin at the age of 30 years to identify those patients already with a low peak bone mass. At this time advice can be given to correct adverse life-style factors with the introduction of calcium 1,500 mg/day, vitamin D 400 IU/day and 'bone builder exercises' but without sHRT if oestrogen levels appear adequate during the menstrual cycle. Bone density screening on an annual basis will then determine rates of bone loss and the need for additional treatment.

We found the Osteoporosis Risk Questionnaire underestimated the prevalence of the condition in the premenopausal group while overpredicting it in postmenopausal women. However, it does have value in alerting patients to their potential risk. The recent evidence for the importance of family history [19], suspected clinically for a long time and confirmed in 69.5% of patients screened in this study, indicates that a higher risk weighting should be given to this factor to reduce the false-negative rate in premenopausal patients in a future questionnaire. A history of mother or relatives shrinking, bending, with multiple fractures or fractures of the hip was the most compelling reason why women requested OP screening. This clearly identifies a group of patients to whom resources should be directed to reduce the morbidity and mortality from OP. The finding that 54% of women with scalp hair loss had OP or osteopenia provides a visually recordable sign that the condition may be present but is not a prognostic sign. Despite such refinements which may be made to the questionnaires, bone density scanning remains the only simple non-invasive, quantitative, precise and reliable method of detecting OP early when treatment is likely to be most effective and to monitor future progress.

After screening, patients had the option of returning to their medical advisers for further evaluation and treatment or to the centre (the latter 18%). The non-return rate of the Osteoporosis Recall Service Questionnaires (36%), failure to establish effective treatment by their medical advisers, together with the fact that all the patients themselves with OP and osteopenia were sent a letter reminding them to contact their doctors for advice appears to indicate that in many cases both doctors and patients did not regard the diagnosis of sufficient importance to be acted upon. A major factor may be that most patients with osteopenia had a 'mild fracture risk', i.e. between 10- and 20% BMD loss recorded upon their scan. It is probable that such a term instead of alerting patient and doctor to the need for the early institution of preventive measures was considered a reason to do nothing and hope for the best despite being associated with a 2- to 3-fold increase in fracture rates [12] and continued deterioration. Patients with greater than 20% bone loss were more likely to receive sHRT or be referred for further evaluation.

Patient and doctor compliance to programmes of prevention, detection and treatment of OP and osteopenia may be enhanced as international consensus conferences, the lay press, national societies and the improving health consciousness of women continue to highlight the problem. However, for the present in the UK we are far from the implementation of such an integrated approach. There is an absence of state funding [pers. commun] for the provision of OP and bone density scanning clinics in the general hospital system, while the health insurance companies both in the UK and the USA appear reluctant to provide recoverable costs for the early detection of the disease. Thus the outlook in the face of a rising incidence of OP looks bleak even at the historically accepted morbidity and mortality rates [20, 21] for the condition, while the prevalence by our definition may approach 6 million women in the UK. Of the small population of those who will ever have a bone scan at least one third and possibly half may not be treated at all despite OP and osteopenia being a potentially preventable even reversible disease if detected early.

Acknowledgements

We wish to acknowledge the support of Imperial Pharmaceutical Services Ltd during this study, Dr. D.O. Chanter for the statistical analyses and Shirley Jones for the preparation of the manuscript.

Following completion of this study, Dr. Mortimer died and the authors wish to dedicate this work to him as a small testimony to the help he has given them in recent years.

Appendix 1: Osteoporosis Risk Questionnaire

SECTION I

Give yourself 1 point for every YES answer: SCORE

- Do you have gum disease or excessive tooth decay? _____
- Do you drink five or more cups of tea, coffee, or fizzy drinks or other caffeine containing drinks daily? _____
- Do you or have ever smoked cigarettes? _____
- Do you drink alcohol? _____
- Is it true that you have never been pregnant? (women only) _____
- TOTAL SCORE FOR SECTION I _____

SECTION II

Give yourself 2 points for every YES answer:

- Are you female? _____
- Are you Caucasion (white), Asian or Oriental? _____
- Do you have a pale complexion? _____
- Are you slender or have small bone structure? _____
- Have any of your relatives suffered a broken hip or wrist at the age of 45 years or older, lost height or developed Dowager's hump? _____
- Do you exercise infrequently or not at all? _____
- Have you avoided milk and dairy products? _____
- Have you got thin skin and bruise more easily than before? _____
- Have you notices thinning of scalp hair or increased body hair growth? (women only) _____
- TOTAL SCORE FOR SECTION II _____

SECTION III

Give yourself 3 points for every YES answer: SCORE

- Do you have thyroid problems, epilepsy, rheumatoid arthritis, insulin-dependent diabetes mellitus or chronix liver problems? _____
- Have you taken steroids or anticonvulsants for a long time? _____
- Have you had operations for stomach, duodenal ulcers or removal of part of the bowel? _____
- Have your menstrual periods become irregular, infrequent or scanty? (women only) _____
- Have you had undescended testes, impaired beard growth or impotence? (men only) _____
- TOTAL SCORE FOR SECTION III _____

SECTION IV

Give yourself 12 points for every YES answer:

- Did your menstrual periods stop naturally before the age of 46 years? _____
- Did you have both ovaries removed before the age of 46 years? _____
- If you are menopausal (whether naturally or following surgery) have you avoided taking female (sex) hormone replacement therapy (sHRT)? _____
- TOTAL SCORE FOR SECTION IV _____

Add your scores from Sections I, II, III, IV to give the overall OSTEOPOROSIS RISK TOTAL _____

If your score totals 12 points or more you are now at risk of having osteoporosis: the higher your score the greater the risk.

Appendix 2: Osteoporosis Recall Service Questionnaire (including Osteopenia)

Please tick the correct box and return the questionnaire in the SAE provided.

	YES	NO
(1) Has the patient been further evaluated?	☐	☐
(2) Have you started the patient on treatment?	☐	☐
(3) Have you prescribed sex hormone replacement therapy (sHRT)?	☐	☐
(4) Have you checked the serum oestradiol level on sHRT?	☐	☐
What was the result: _____ pmol/l		
Please show here the formulation of sHRT and the dosage: Type _____ Dose _____		
(5) Have you prescribed calcium tablets?	☐	☐
Please show the formulation of calcium and the dosage: Type _____ Dose _____ mg/day		
(6) Have you prescribed vitamin D tablets?	☐	☐
Have you checked the serum 25 OH vitamin D level on treatment?	☐	☐
What was the result: _____ nmol/l		
Please show here the formulation of vitamin D and the dosage: Type _____ Dose _____ IU/day		
(7) Have you prescribed physiotherapy instruction for bone builder exercises?	☐	☐
(8) Would you like your patient to return to EDC for full evaluation?	☐	☐

If YES we would request a short letter of referral.
An appointment can be made by telephone or by writing to the above address.

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