The relationship between the OSTEODENT index and hip fracture risk assessment using FRAX

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Objectives. The OSTEODENT index is a predicted probability of osteoporosis derived from a combination of an automated analysis of a dental panoramic radiograph and clinical information. This index has been proposed as a suitable case-finding tool for identification of subjects with osteoporosis in primary dental care; however, no data exist on the relationship between OSTEODENT index and fracture risk. The aims of this study were to assess the relationship between the OSTEODENT index and hip fracture risk as determined by FRAX and to compare the performance of the OSTEODENT index and FRAX (without femoral BMD data), in determining the need for intervention as recommended in UK national treatment guidance.

Study design. The study was a retrospective analysis of data from 339 female subjects (mean age 55.3 years), from 2 centers: Manchester (UK) and Leuven (Belgium). Clinical information and femoral neck BMD were available for FRAX, and dental panoramic radiographic data and clinical information were available to calculate the OSTEODENT index. Subjects were classified into “treat” or “lifestyle advice and reassurance” categories using the National Osteoporosis Guideline Group (NOGG) threshold.

Results. The OSTEODENT index result was significantly related to the 10-year probability of hip fracture derived from the reference standard FRAX tool (Rs = 0.67, P < .0001); 84 patients (24.8%) were allocated to the “treat” category on the basis of FRAX and the UK national guidance. Using this “treatment/no treatment” classification as the reference standard, ROC analysis showed no significant difference between areas under the curves for the OSTEODENT index (0.815) and the 10-year probability of hip fracture derived from the FRAX index without BMD (0.825) when used as tests for determining therapeutic intervention.

Conclusion. The results suggest that the OSTEODENT index has value in prediction of hip fracture risk. Prospective trials are needed to confirm this finding and to examine the feasibility for its use in primary dental care. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2010;110:243-249)

A major challenge in managing osteoporosis is the difficulty in identifying affected individuals before the condition is established and fracture has occurred.1-3 Dental radiological examination can be used for osteoporosis risk assessment and a substantial number of patients undergo dental panoramic radiographic examinations each year.

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Diagnosis of osteoporosis relies on measurement of "areal" bone mineral density ($BMD_a$) at the hip and spine by dual energy x-ray absorptiometry (DXA), with classification being based on standard deviation (SD) scores (T score at or below $-2.5$). $BMD_a$ is, however, only one risk factor for fracture, with a doubling of risk for each SD reduction in $BMD_a$. Furthermore, some of the clinical risk factors used as indicators for $BMD_a$ measurement are themselves associated with a fracture risk greater than can be accounted for by $BMD_a$ alone. Factors such as a low body mass index, low milk consumption, lack of sunlight exposure, and low physical activity account for about half of hip fractures, and which are reversible by the patient.

In recent years, therefore, emphasis has shifted away from diagnosis of osteoporosis by $BMD_a$ toward assessment of clinical fracture risk. Early identification of risk factors for osteoporosis and fracture may facilitate access to appropriate medical intervention and fracture risk reduction. Such a "case-finding" approach, based on clinical risk factors, has been recommended rather than population screening. Using meta-analysis techniques applied to studies on population-based cohorts that identified clinical risk factors for fracture, algorithms (FRAX) have been developed that compute age-specific 10-year fracture probabilities. FRAX can be used without the availability of femoral neck $BMD_a$, or with its incorporation into the algorithm when available. In the United Kingdom, a management strategy guideline, based on an individual’s estimated fracture risk, has been devised by the National Osteoporosis Guideline Group (NOGG), providing a clear pathway from clinical fracture risk assessment using FRAX through to appropriate guidance on intervention.

Approximately 1 in 3 of all radiological examinations are made by dentists. Dental radiographs invariably show images of the bone of the jaws and there is evidence that jaw $BMD_a$ and radiomorphometric indices correlate significantly with $BMD_a$ of other skeletal sites, including the hip and spine. Subsequent work has demonstrated that various radiographic features of mandibular bone on panoramic radiographs have potential value in predicting $BMD_a$ at these important sites of fracture. The OSTEODENT study established that an “automatic” measurement of mandibular cortical bone thickness on panoramic radiographs was a valid test for diagnosis of osteoporosis in women aged 45 to 70 years, with a receiver operating characteristic (ROC) area exceeding 0.80. Subsequent data analysis showed that combining the radiographic mandibular cortical width data with clinical information, in the form of the Osteoporosis Index of Risk (OSIRIS) (age, weight, current estrogen therapy, and history of low trauma fracture), produced a test result (the “OSTEODENT index”) that was significantly better for prediction of $BMD_a$ than either test alone (ROC curve area $= 0.90$). The authors suggested that combining these clinical and radiographic tests had potential to be used in primary dental health care as a case-finding strategy for identification of patients at risk of osteoporosis.

Although the OSTEODENT index, along with other dental radiographic measurements, has been shown to have diagnostic validity in predicting $BMD_a$ and osteoporosis, there is no information on how the index relates to risk of fracture or to patient management decisions. If the OSTEODENT index is to be a tool for case finding in osteoporosis, then its performance should be comparable with that of the FRAX tool (without inclusion of $BMD_a$ data) in assessment of fracture risk and management recommendations.

The aims of this study, therefore, were to (1) assess the relationship between the OSTEODENT index and hip fracture risk as determined by the FRAX tool, and (2) compare the performance of 2 clinical tests, the OSTEODENT index and the FRAX tool (without $BMD_a$ data), to determine appropriate intervention as recommended by NOGG.

**MATERIALS AND METHODS**

This study was carried out by retrospective analysis of patient data from the OSTEODENT study (European Commission Fifth Framework Programme “Quality of Life and Management of Living Resources”; QLK6-2002-02243). The aim of that study was to identify the most valid and effective radiographic index, or combination of radiographic and clinical indices, for the diagnosis of osteoporosis applicable for use by dentists in a primary health care setting. Details of the study have been reported in full previously and a summary of pertinent aspects are reported here.

Women in the age range of 45 to 70 years were invited to participate in the study, recruited at 4 centers: Athens (Greece), Leuven (Belgium), Malmö (Sweden), and Manchester (UK). Local ethical approval for the study was obtained in each recruiting center and informed consent was obtained from all subjects. The racial origin of the patients, their menopausal status, and history of hysterectomy and hormone replacement therapy (HRT), if applicable, were noted. Weight (wt) and height (ht) were measured and body mass index (wt/ht$^2$; kg/m$^2$) calculated. Information about menopausal status, date of menarche, previous fracture history, tobacco-smoking habits, and alcohol intake were recorded. Recruitment was performed over a 24-month period extending from October 2003 to September 2005. For the study reported here, subjects from only 2 of the recruiting centers (Leuven and Manchester) are included in the analysis. Subjects from Athens and
Malmö were excluded because no record of glucocorticoid use (required for use of the FRAX tool) existed.

Bone densitometry

DXA of the left hip was carried out on each subject to determine femoral neck (FN) BMD. Scans were performed by experienced radiographers on the Hologic QDR 4500 (Hologic Inc., Bedford, MA) in Leuven and the Hologic Discovery (Hologic Inc.) in Manchester. T-scores were calculated using National Health and Nutrition Examination Survey (NHANES) reference data.21 The European spine phantom (ESP)22 was used to standardize measurements between different manufacturers using the method described by Pearson and colleagues.23 Standardization of BMD measurements was performed by one experienced scientist (E.M.). Scans and results from the 2 centers were reviewed and confirmed for good quality by one clinical radiologist (J.E.A.) with expertise in this field. Shewarts rules were used to monitor quality assurance throughout the study period.24

Clinical evaluation

All subjects were interviewed using a standard questionnaire covering a wide range of medical, social, and family history, including age, sex, weight, height, previous fractures, parental hip fracture, current smoking, glucocorticoid use, rheumatoid arthritis, secondary osteoporosis, and alcohol intake exceeding 3 units per day. In the absence of BMD data, subjects are classified into low risk (requiring reassurance), intermediate risk (requiring BMD to be ascertained), and high risk (requiring treatment be considered either with or without further BMD assessment).

We entered the femoral neck BMD and clinical data into the FRAX tool and, using the NOGG management guidance link (http://www.shef.ac.uk/NOGG) from the FRAX Web site, we calculated the 10-year hip fracture probability. Using the reference standard given there, subjects were classified into either “treat” or “lifestyle advice and reassurance” categories.

Radiographic/clinical test: OSTEODENT index assessment

The OSTEODENT index is the predicted probability of osteoporosis based on a combination of automatic measurement of mandibular cortical width on dental panoramic radiographs and OSIIRIS,18 calculated by a computer program.17 Briefly, the mandibular cortex was automatically detected on digitized panoramic radiographs using software based on an Active Shape Model search.25,26 The clinical data required to calculate OSIIRIS (age, body weight, current HRT use, and history of previous low-impact fracture) was then entered and combined with the radiographic data, producing the predicted probability (%) of osteoporosis. Each subject’s radiographic and clinical information was entered to give her OSTEODENT index.

Clinical test: 10-year probability of hip fracture derived from FRAX without FN BMD

Clinical information of subjects was used to calculate the 10-year probability of hip fracture using the FRAX tool (without inclusion of FN BMD).

Statistical analysis

The relationship between the OSTEODENT index and the 10-year probability of hip fracture derived from the FRAX tool (with FN BMD) was calculated using Spearman’s rank correlation. Similarly, the relationship between the 10-year probability of hip fracture derived from the FRAX tool (without FN BMD) and the 10-year probability of hip fracture derived from the FRAX tool (with FN BMD) was calculated.
The reference standard decision of “treat” or “lifestyle advice and reassurance” derived from 10-year hip fracture risk probability was calculated using FRAX (with FN BMDa) and NOGG management guidance link from the FRAX Web site and was used as a “gold reference standard” in our calculations. The abilities of FRAX (without FN BMDa) and the OSTEODENT index in categorizing subjects into the NOGG “treat” category were compared using ROC curve analysis. The areas under the ROC curves (AUC) and analysis for significant statistical differences between AUCs were calculated using the MedCalc programme (MedCalc Software bvba, Mariakerke, Belgium).

RESULTS
A total of 351 women were recruited to the study. It was not possible to record the mandibular cortical width for 7 subjects because these films were unusable for reasons including damage, accidental loss, lack of a ball-bearing image, and unacceptable image quality. Data on hip fracture probability (with FN BMDa) was not available for a further 5 subjects. Clinical information required to calculate FRAX was lacking in 3 subjects for whether they had a confirmed diagnosis of rheumatoid arthritis, the number of alcohol units consumed per day, and their exposure to oral glucocorticoids. Dentate and edentulous patients were included, as we have shown previously that the dental state of the patient was not significant in predicting mandibular bone mineral density.27 Several subjects had more than one missing item of data and complete datasets were available for 339 women. The mean age of this population was 55.3 years (SD = 6.32). From this study population, 62 (18%) were classified as having osteoporosis at the femoral neck.

The OSTEODENT index results (predicted probability of having osteoporosis) in the study population ranged from 0% to 99.4%. The data were not normally distributed, with most people having a low score and with a median result of 17.95%. Similarly, most subjects had low 10-year hip fracture probability using FRAX (with or without FN BMDa). For FRAX (without FN BMDa), median probability was 0.7%, with a range from 0.1% to 19.0%, whereas for FRAX (with FN BMDa) the median was 0.6% and the range extended from 0% to 49.0%.

Relationship between the OSTEODENT index and 10-year probability of hip fracture
A significant relationship was demonstrated between the OSTEODENT index and the 10-year probability of hip fracture derived from the standard reference FRAX tool (with FN BMDa), \( R_s = 0.67, P < .0001 \), indicating a strong relationship between the 2 variables (Fig. 1, A).

The relationship between the 10-year probabilities of hip fracture calculated using FRAX (without FN BMDa) and FRAX (with FN BMDa) was \( R_s = 0.77 \) \( (P < .0001; \) Fig. 1, B). The 2 independent correlation coefficients were significantly different from each other \( (z = -2.72, P = .007) \). All the indices were positively skewed. Most subjects had a low 10-year probability of hip fracture (Table I), measured using any of the indices, and the correlation coefficients may therefore have been influenced by outliers.28

Eighty-four patients (24.8%) were considered as requiring treatment by NOGG subsequent to their FRAX (with FN BMDa) assessment. Using this as the reference standard, ROC curve analysis (Fig. 2) showed that the AUC for the OSTEODENT index used as a means
of determining treatment need was 0.815 (SE = 0.030) and that for the 10-year probability of hip fracture derived from the FRAX index without BMD was 0.825 (SE = 0.029). There was no significant difference in AUC between these 2 curves (z = 0.36, P = .72).

**DISCUSSION**

Regular visits by patients to the dentist for check-ups and treatment provide an opportunity to address issues that may be of indirect relevance to dental health, but of great importance to general well-being. Thus, many dentists, at least in the United Kingdom, advise on smoking cessation, perform blood pressure checks, and carry out oral cancer screening. Bone health is of immediate importance to dentists, not least in the context of implant and periodontal therapies. The inclusion of opportunistic osteoporosis case-finding by dentists has, therefore, a reasonable prospect of adoption if a suitable test is available and if cost-effectiveness can be demonstrated. The OSTEODENT software, based on radiographic data supplemented by some simple clinical information, has been shown to have good diagnostic validity for identification of women with low BMD, but there was no information available about its relationship with fracture risk. This study aimed to address this deficiency.

The study design was retrospective, being a reevaluation of data obtained from a previous study, designed before the publication of the WHO FRAX fracture risk assessment tool. Such a design invariably introduces limitations. The number of women included was limited to those from only 2 of the original 4 recruiting centers because all items of data needed for FRAX had not been collected consistently. It should be recognized that the study did not measure actual fracture incidence in a longitudinal cohort study as the number of subjects was too small to provide statistically significant fracture data. Nonetheless, our study provides useful information that may help determine whether a larger, prospective study of the OSTEODENT index and fracture prediction is indicated.

The OSTEODENT index was significantly correlated with 10-year probability of hip fracture derived from FRAX (with FN BMD). The OSTEODENT index has previously been shown to have high diagnostic value in prediction of low BMD and osteoporosis. As BMD is a risk factor for hip fracture, such a finding is not surprising. The useful information, however, was the indication of the strength of the relationship between the OSTEODENT index and 10-year probability of hip fracture calculated using FRAX (with FN BMD). This significant association (Rs = 0.67) was weaker than that (Rs = 0.77) between FRAX (without FN BMD) and FRAX (with FN BMD), although the stronger relationship with the latter is not surprising in view of the shared elements contributing to their calculation.

Demonstration of a significant association between 2 variables does not address the potential value of the OSTEODENT index as a clinical case-finding test. Calculation of sensitivity and specificity and/or the use of ROC curve analysis do provide such information, but require a reference standard with which the test can be compared. In this study, in the absence of any “true” individual fracture data, we used the 10-year probability of hip fracture obtained from FRAX (with FN BMD). To perform ROC analysis, these reference standard data had to be dichotomized and this was achieved using the intervention threshold recommended by NOGG, which can be justified, as the FRAX Web site links directly through to the NOGG management recommendation. The FRAX tool provides an estimate of 10-year probability of both hip and “major” (clinical spine, forearm, hip, or shoulder) fracture. Similarly, when FN BMD is included, FRAX leads to NOGG guidance on intervention for both frac-

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**Table I.** The value of the different indices below which the stated percentage of subjects were classified

<table>
<thead>
<tr>
<th>Percentiles</th>
<th>OSTEODENT index, %</th>
<th>FRAX (without BMD), %</th>
<th>FRAX (with FN BMD), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median</td>
<td>17.9</td>
<td>0.7</td>
<td>0.6</td>
</tr>
<tr>
<td>20</td>
<td>3.3</td>
<td>0.3</td>
<td>0.2</td>
</tr>
<tr>
<td>30</td>
<td>6.4</td>
<td>0.4</td>
<td>0.3</td>
</tr>
<tr>
<td>40</td>
<td>10.2</td>
<td>0.5</td>
<td>0.4</td>
</tr>
<tr>
<td>60</td>
<td>28.2</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>70</td>
<td>37.9</td>
<td>1.4</td>
<td>1.7</td>
</tr>
<tr>
<td>80</td>
<td>62.6</td>
<td>2.6</td>
<td>3.0</td>
</tr>
<tr>
<td>90</td>
<td>83.3</td>
<td>4.7</td>
<td>6.8</td>
</tr>
</tbody>
</table>

**Fig. 2.** Receiver operating characteristic curves for the OSTEODENT index and FRAX (without FN BMD), demonstrating their value as diagnostic tests for allocating subjects into the NOGG “treat” category. There was no significant difference between areas under the curves.
ture probabilities. In this study, we chose to consider only hip, rather than major, fracture probabilities because the impact of hip fracture on the affected individual is greater.

Our ROC results indicate that the ability of the OSTEODENT index to predict patient management decisions according to NOGG is comparable with that of FRAX without FN BMD$_a$. The OSTEODENT index is a combination of clinical and radiographic information, whereas FRAX without FN BMD$_a$ is derived from clinical data alone, although there are more clinical items considered by FRAX than by the OSTEODENT index. It seems possible that the radiographic information provided by OSTEODENT is providing some indicator of BMD$_a$ status that compensates for the smaller number of clinical data items included. As such, it is interesting to consider whether adapting the OSTEODENT software to include the FRAX tool factors, rather than the more limited OSIRIS factors, might improve performance as a predictive tool. This should be considered in future research, although the advantage of the clinical data collection used in OSTEODENT (age, weight, current HRT, and history of low trauma fracture) is that it is quick and easy to collect and more feasible for application in dental practice.

Although there are limitations in this study, the OSTEODENT index has potential as a case-finding tool for osteoporosis and as an indicator of hip fracture risk, and a larger prospective trial in primary care seems justified. Such a study should also address the important issues of stakeholder acceptability, possible interprofessional barriers, and an essential economic evaluation.

REFERENCES


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