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Maximising the cost effectiveness of BMD referral for DXA using ultrasound as a selective population pre-screen

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Abstract. Bone mineral density (BMD) referral for dual energy X-ray absorptiometry (DXA) is generally based upon agreed clinical referral criteria (CRC). The aim of this study was to determine whether ultrasound measurements of Broadband Ultrasound Attenuation (BUA) and velocity (VOS) provide a superior selective pre-screen referral method for BMD assessment by DXA. 107 women aged 60–69 years (64.2 ± 2.8) had BMD measurements at lumbar spine and right femoral neck along with ultrasound BUA and VOS measurements of the left calcaneus. Each subject completed an extensive clinical and social questionnaire to ascertain those who would have met one or more of the five general clinical referral criteria adopted by our Centre. Each subject was classified by DXA using the WHO criteria as normal, osteopenic or osteoporotic at lumbar spine or femoral neck. The cost per osteoporotic subject correctly identified was calculated. As a reference, based upon DXA measurements alone on all 107 subjects, the cost per osteoporotic subject identified would be £185. If subjects had been referred using the clinical referral criteria the cost is £171. For assessment of referral by BUA or VOS, an additional charge for ultrasound measurement of all subjects was incorporated. At a BUA of 60 dB MHz^{-1} the cost per osteoporotic subject is £107. Ultrasound velocity or a combination of BUA or VOS with clinical referral criteria did not provide a significantly reduced cost than the current clinical referral criteria alone. This study has demonstrated that BUA provides an improved referral procedure to that currently achieved with clinical referral criteria and supports the concept of BUA being used as a selective pre-screen for DXA in 7th decade subjects.

1. Introduction

Although there has been a rapid proliferation of calcaneal ultrasound bone densitometers in clinical research centres, there lacks a consensus on how ultrasound measurements should be incorporated in the management of osteoporosis. There is a concern that due to the lower unit cost, ultrasound may be used inappropriately in an independent strategy rather than being complementary to the current technical and clinical resources based around dual energy X-ray absorptiometry (DXA).

Several studies have shown that the *exact* DXA measurement in $g\,cm^{-2}$ at the hip or spine cannot be predicted by measurements of Broadband Ultrasound Attenuation (BUA) or velocity (VOS), concluding that ultrasound cannot be used as a direct surrogate for DXA [1]. BMD referral for DXA is generally based upon agreed clinical referral criteria (CRC) such as those suggested in the WHO [3] and AGO [2] reports. The Centre for Metabolic Bone Disease in Hull UK, has a contract with East Riding Health Authority for referral for BMD by DXA, with or without a clinical consultation, based upon eight clinical referral criteria (Table 1). Category 1 is broad, considering any oestrogen

Table 1
The clinical referral criteria adopted by our centre. Note that categories 1, 7 and 8 were excluded for this study

1.	Any oestrogen deficient woman who would want to be treated or would want to continue treatment if found to be osteopenic or osteoporotic.
2.	Patients suspected to be osteoporotic from radiological and clinical findings.
3.	Patients who have a medical condition predisposing to osteoporosis if effective treatment is available, e.g., metabolic bone disease, liver disease, anorexia nervosa, malabsorption syndromes and other rarer causes of osteoporosis.
4.	Patients receiving corticosteroids at a dose of $\geqslant$5 mg Prednisolone or equivalent.
5.	Women who experience primary amenorrhoea or secondary amenorrhoea (including hysterectomy) below the age of 45 years.
6.	Patients with a positive family history of osteoporosis in at least one first degree relative.
Monitoring	
7.	Patients prior to starting management with oral corticosteroids of a prolonged duration of six months or more.
8.	To monitor response to treatment in patients with established osteopenia or osteoporosis.

deficient woman. Categories 7 and 8 consider monitoring of treatment, leaving Categories 2–6 related to general clinical referral.

The concept behind this pilot study was simply to determine whether ultrasound measurements of BUA and VOS provide a superior pre-screen referral method for BMD assessment by DXA than the presently accepted clinical referral criteria.

2. Methods

107 women aged 60–69 years (64.2 $\pm$ 2.8) were investigated as part of a study examining the prevalence of osteoporosis. Lumbar spine and right femoral neck BMD were determined by DXA (Lunar DPX-L), along with ultrasound BUA and VOS measurements of the left calcaneus (McCue CUBAclinical II). Each subject completed an extensive clinical and social questionnaire from which a Clinical Research Fellow (PAB) ascertained whether or not each individual would have met one or more of the five general (2–6) clinical referral criteria. All subjects, being postmenopausal, would have met Category 1 and hence it is considered inappropriate for this particular study. Subjects who would be eligible under the monitoring Categories 7 and 8 were previously excluded. Each subject was defined by DXA as being normal, osteopenic or osteoporotic at femoral neck or lumbar spine using the WHO criteria for BMD values.

3. Results

3.1. ROC analysis

Receiver–operator characteristic (ROC) analysis provides a means of comparing the sensitivity (true positive ratio) and specificity (true negative ratio) over a range of measurement threshold values. In this case, subjects with BUA and VOS measurements above a particular threshold are considered to be normal, those below are considered to have a positive test. When comparing ROC analyses it should be noted that the CRC provide a discreet value for sensitivity and specificity whereas the ultrasound parameters provide a continuous measure of sensitivity and specificity. ROC analysis was undertaken using a Microsoft Excel Macro. Ultrasound BUA and VOS results were entered for control and disease (osteopenic or osteoporotic defined by DXA) populations. The programme automatically sorted the

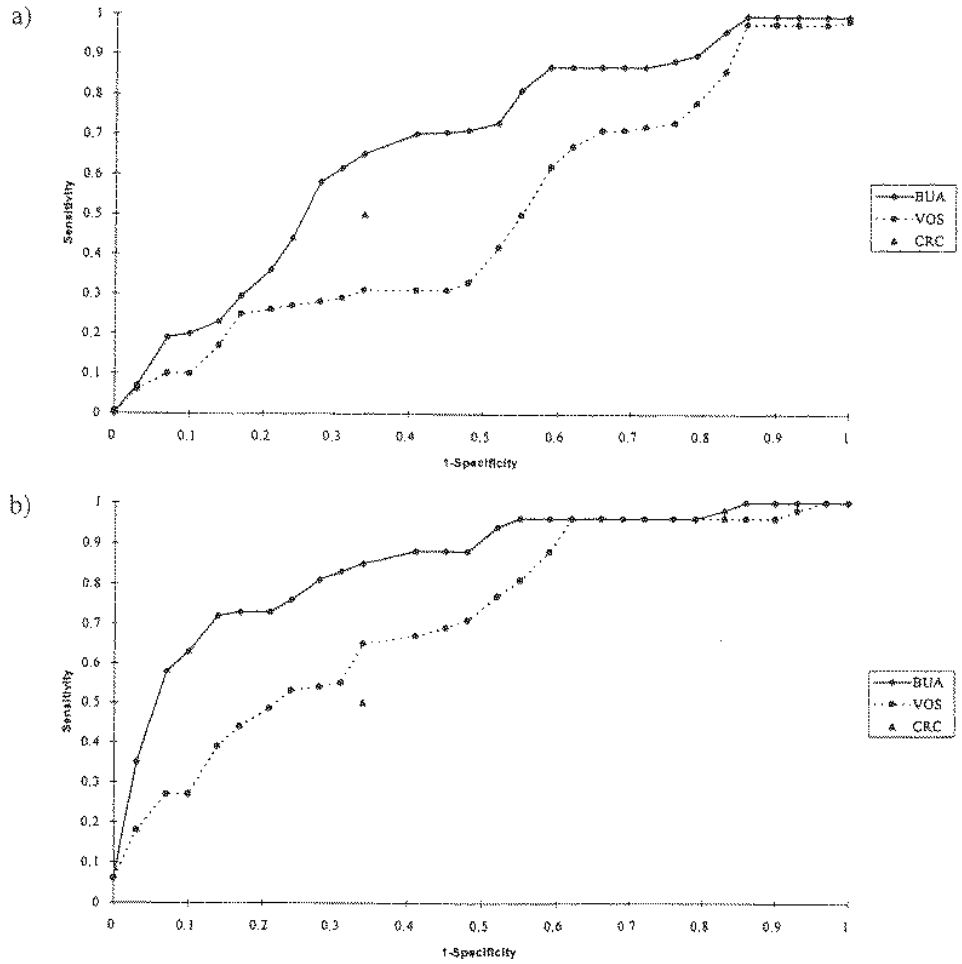

Fig. 1. (a) Receiver operator characteristic (ROC) for osteopenic and normal subjects assessed by broadband ultrasound attenuation (BUA), velocity (VOS) and the clinical referral criteria (CRC). Note that the CRC provide a discreet point whereas the ultrasound parameters provide continuous data. (b) Receiver operator characteristic (ROC) for osteoporotic and normal subjects assessed by BUA, VOS and CRC.

data and calculated the sensitivity and specificity at each ultrasound threshold level. The ROC analysis for BUA and VOS measurements is shown in Figs 1a and 1b for osteopenic and osteoporotic subjects, respectively, compared to normal subjects. The discreet sensitivity and specificity data for the clinical referral criteria is also indicated.

3.2. Cost analysis

The cost analysis model is based upon the concept of patients being referred for DXA by (a) meeting one or more clinical criteria or (b) having ultrasound readings below a defined threshold. In both cases, the number of patients referred for BMD by DXA will be the true positive and false positive subjects. The cost per osteoporotic subject correctly identified using solely the CRC is the cost for all referred DXA scans divided by the number of true positive osteoporotic subjects identified. For the ultrasound

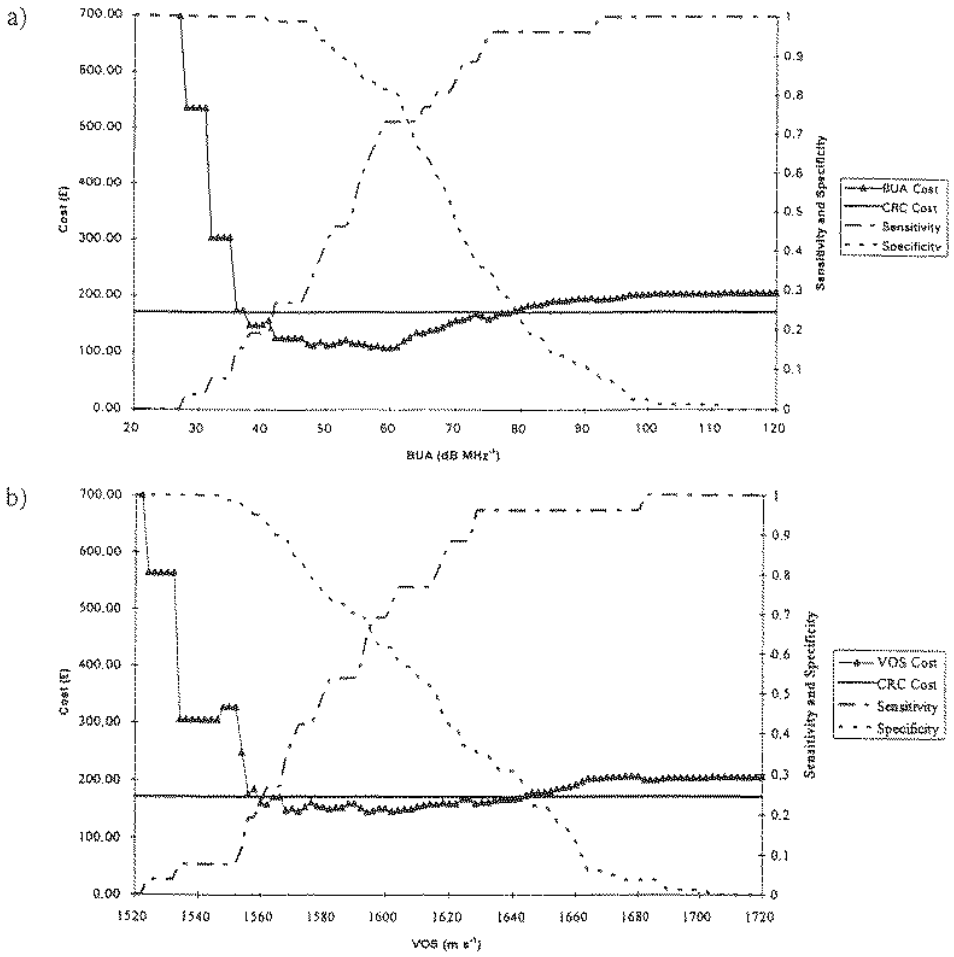

Fig. 2. (a) Sensitivity, specificity and cost per osteoporotic subject identified with respect to BUA threshold value. The cost based upon the clinical referral criteria is indicated as a constant value. (b) Sensitivity, specificity and cost per osteoporotic subject identified with respect to VOS threshold value.

analysis, there is an additional cost associated with all subjects being measured by ultrasound. We have incorporated into the model a typical cost of £45 per DXA scan, this being the figure adopted by East Riding Health, our local Health Authority. For the ultrasound measurement we have calculated the proposed cost to be £4.85 per subject based upon four subjects measured per hour, for 6.5 hours per day, totalling 5,460 subjects per year. In both cases the costs incorporate system depreciation over five years, along with Clinical Scientist, Medical Technical Officer and Clerical staffing costs incorporated. For the ultrasound measurements an additional transportation cost is incorporated to reflect their community basis.

For the cost analysis, the control subjects consisted of both normal and osteopenic subjects defined by DXA, the diseased subjects being osteoporotic defined by DXA. This provides a realistic comparative evaluation for ultrasound and clinical referral criteria to identify those osteoporotic subjects requiring therapeutic intervention from the remainder of the population.

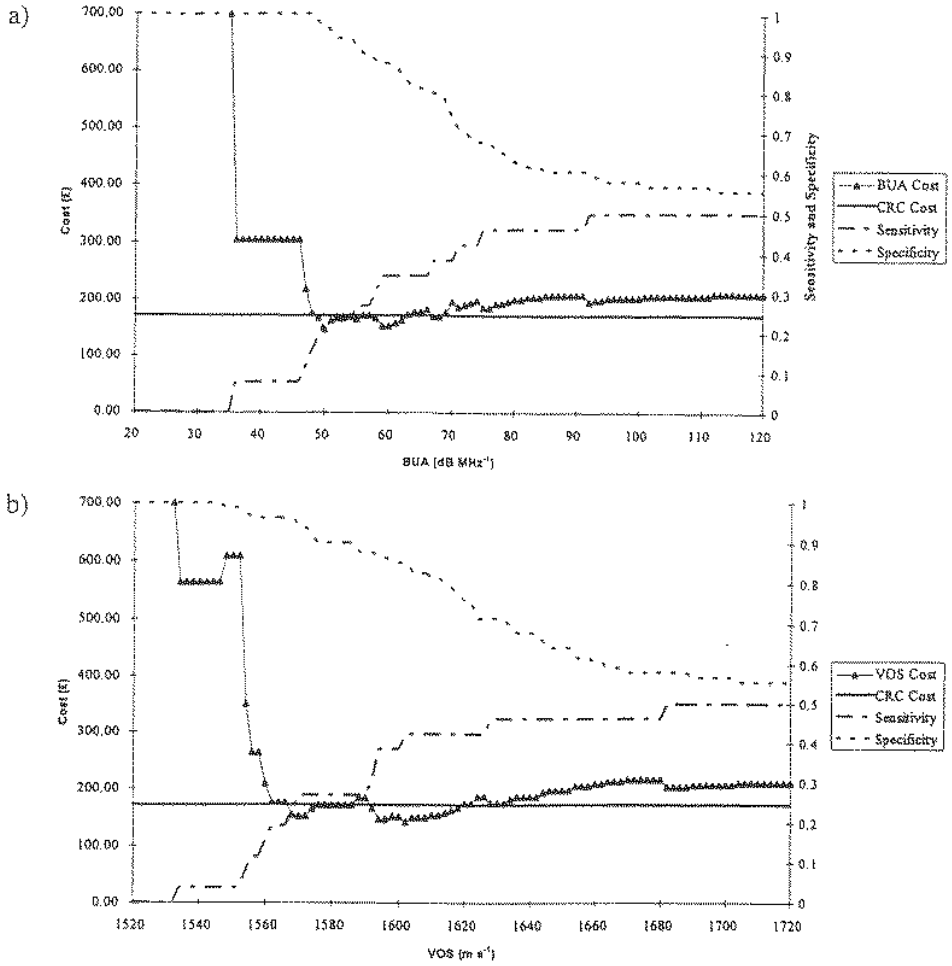

Fig. 3. (a) Sensitivity, specificity and cost per osteoporotic subject identified who met one or more of the clinical referral criteria with respect to BUA threshold value. (b) Sensitivity, specificity and cost per osteoporotic subject identified who met one or more of the clinical referral criteria with respect to VOS threshold value.

Since the clinical referral criteria provide a discreet sensitivity and specificity, the cost per osteoporotic subject will be a single value. By comparison, however, the threshold value for the ultrasound measurements of BUA and VOS may be continuously varied over the range of values observed within the population studied, namely, 20–120 dB MHz^{-1} for BUA and 1520–1720 $m\,s^{-1}$ for VOS. The cost per osteoporotic subject identified by BUA and VOS is shown in Figs 2a and 2b, respectively. In both cases sensitivity and specificity data is provided along with the discreet cost per osteoporotic subject defined using the clinical referral criteria. It is interesting to note that for BUA and VOS threshold values below the lowest osteopenic or osteoporotic subject, the cost per subject identified is infinite since no subject would, in fact, have been identified. The cost reduces to a minimum value and then steadily increases. As the BUA or VOS threshold increases above the highest ultrasound value for osteopenic (or osteoporotic) subjects identified, we are simply measuring more false positive subjects without identifying any additional osteopenic (or osteoporotic) subjects.

Clearly, if the cost associated with an ultrasound measurement is below the fixed CRC cost then ultrasound is providing a cost effective alternative for identifying subjects requiring further evaluation by DXA. It is envisaged that the choice of an ultrasound threshold value would be one with a low cost but also an associated compromise between sensitivity and specificity.

As an illustrative exercise for an alternative protocol for the incorporation of ultrasound in clinical management, we have studied the cost effectiveness of identifying subjects who had an ultrasound value below a particular threshold *and* met one or more of the clinical referral criteria. This analysis is shown in Figs 3a and 3b for BUA and VOS, respectively.

4. Discussion

For the ROC analysis, BUA provides superior performance over VOS and CRC for both osteopenic and osteoporotic subjects compared to normal controls. VOS has a particularly poor ROC performance for osteopenic subjects with the CRC providing the same sensitivity and specificity for both osteopenia and osteoporosis.

Upon analysis of the cost per osteoporotic subject correctly identified BUA, again as expected from the ROC analysis, provides a superior performance over VOS and CRC. At a BUA of 60 dB MHz^{-1}, the cost per osteoporotic subject identified is £107 compared to £171 for CRC. The corresponding sensitivity and specificity for a BUA of 60 dB MHz^{-1} is 73% and 81%, respectively, compared to 50% and 55%, respectively, for the CRC. For VOS, with a threshold of 1590 $m\,s^{-1}$ the cost is £159 with a sensitivity and specificity of 54% and 70%, respectively. As a reference, based upon DXA measurement alone, the cost per osteoporotic subject identified would be £185. This is based upon all 107 subjects having a DXA scan costing £45 each and identifying, by definition, all 26 osteoporotic subjects.

The analysis incorporating subjects who had met one or more of the clinical criteria and were below a particular ultrasound threshold provides quite interesting data, different to that normally observed for sensitivity and specificity analysis. Due to the 50% sensitivity of the CRC, this predetermines the maximum sensitivity achievable using the additional ultrasound parameters. The cost per osteoporotic subject is extremely similar to the CRC cost, at £171, for BUA and VOS subjects in the region 50–70 dB MHz^{-1} and 1560–1640 $m\,s^{-1}$, respectively.

The data analysis is implicitly dependent upon the charges for DXA and ultrasound. We believe that the calculated charges incorporate all direct costs associated with a Health Authority based service and hence represents an accurate cost effectiveness assessment.

5. Conclusion

This study has demonstrated that the incorporation of ultrasound, particularly BUA, as a pre-screen for all female subjects in the age range 60–70 years, provides an improved referral procedure to that currently achieved by clinical referral criteria, both in terms of sensitivity and specificity for identifying osteoporotic subjects and also in the cost per osteoporotic subject correctly identified. We believe these to be the first data to support the concept of BUA being used as a selective pre-screen for DXA, thus operating in a complementary rather than alternative role.

Future work based upon a larger cohort is required to confirm these findings and should also consider different age ranges and populations.

Acknowledgement

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