Outcomes of bone density measurements in coeliac disease

Mark J Bolland, Andrew Grey, David S Rowbotham

ABSTRACT

AIM: Some guidelines recommend that patients with newly diagnosed coeliac disease undergo bone density scanning. We assessed the bone density results in a cohort of patients with coeliac disease.

METHODS: We searched bone density reports over two 5-year periods in all patients from Auckland District Health Board (2008–12) and in patients under 65 years from Counties Manukau District Health Board (2009–13) for the term 'coeliac.'

RESULTS: Reports for 137 adults listed coeliac disease as an indication for bone densitometry. The average age was 47 years, body mass index (BMI) 25 kg/m², and 77% were female. The median time between coeliac disease diagnosis and bone densitometry was 261 days. The average bone density Z-score was slightly lower than expected (Z-score -0.3 to 0.4) at the lumbar spine, total hip and femoral neck, but 88–93% of Z-scores at each site lay within the normal range. Low bone density was strongly related to BMI: the proportions with Z-score <-2 for BMI <20, 20–25, 25–30, and >30 kg/m² were 28%, 15%, 6% and 0% respectively.

CONCLUSIONS: Average bone density was normal, suggesting that bone density measurement is not indicated routinely in coeliac disease, but could be considered on a case-by-case basis for individuals with strong risk factors for fracture.

Coeliac disease has been associated with an increased prevalence of low bone density and osteoporosis,1,2 and an increased risk of fracture,3,4 which has led to guidelines recommending that all patients with newly diagnosed coeliac disease undergo bone density scanning.5 We conducted a retrospective audit of bone density scans carried out over 5-year periods at Auckland District Health Board (ADHB) and Counties Manukau District Health Board (CMDHB) to assess the usefulness of bone density scans in individuals with coeliac disease.

Methods

We searched bone density reports over 5-year periods in all patients from ADHB (2008–12) and in patients under 65 years (for practical reasons relating to the reporting of bone densitometry at that institution) from CMDHB (2009–13) for the term ‘coeliac’. We extracted bone density raw data from the related bone density scan, and also searched electronic medical records for relevant medical information related to treatment of osteoporosis and diagnosis of coeliac disease. For individuals with more than one bone density scan, we used the first scan after the diagnosis of coeliac disease. This is an audit as defined by the New Zealand National Ethics Advisory Committee guidelines and therefore it did not require ethical approval.6

We present descriptive statistics for this cohort. Differences between patients from the two different sites for continuous variables were assessed using Student's t-test. We performed a one sample t-test to compare the observed mean with the expected population mean, and a test to compare the proportion with bone density above or below the normal range with the expected binomial proportion using the SAS software package (SAS Institute, Cary, NC version 9.4).

Results

We identified reports for 149 individuals that listed coeliac disease as an indication
for the bone density scan. Reports for 12 individuals were excluded: 8 because the scan was prior to the diagnosis of coeliac disease; 3 because the medical record indicated that the diagnosis of coeliac disease had been considered by the gastroenterology service and excluded; and 1 scan in a child. This left 137 adults over the 5-year periods with a bone density report stating an indication was coeliac disease, 61 from ADHB and 76 from CMDHB.

Selected clinical characteristics at the time of the bone density scan are shown in Table 1. The average age was 47 years, average body mass index (BMI) 25 kg/m², and 77% were female. Only 13% were underweight, with BMI <20 kg/m². Individuals from CMDHB were younger than those from ADHB (mean age 43 vs 52 years, P<0.001) but, otherwise, clinical characteristics of the two groups were similar (data not shown, P>0.24). From the electronic medical record search, 73% of individuals had elevated tissue transglutaminase antibodies and duodenal biopsy histology consistent with coeliac disease. The median time between first available duodenal biopsy, first measurement of tissue transglutaminase antibodies or, where these were not available, listed year of diagnosis of coeliac disease and the bone density scan was 261 days (0.7 years).

Bone density results are shown in Table 2. Because of the known relationship between bone density and age, and the spread of patient ages in the cohort, we have presented the results as Z-scores for each site. A bone density Z-score is the number of standard deviations from the mean bone density for an age and gender matched population. Thus, the average bone density Z-score for someone of the same age and gender is 0 and the normal range, containing 95% of people in the population of similar age and gender, is between -2.0 and 2.0. Bone density in the coeliac disease cohort was slightly low (Z-score -0.3 to -0.4, approximately corresponding to a 3–4% reduction) at all three sites. The Z-score for 88–93% of individuals at each site was within the normal range, with similar proportions of individuals with bone density Z-scores above or below the normal range.

Table 1: Clinical characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Entire cohort (n=137)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>47 (15)</td>
</tr>
<tr>
<td>Gender (% Female)</td>
<td>77</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>25 (5)</td>
</tr>
<tr>
<td>&lt; 20 (%)</td>
<td>13</td>
</tr>
<tr>
<td>20–25 (%)</td>
<td>45</td>
</tr>
<tr>
<td>25–30 (%)</td>
<td>23</td>
</tr>
<tr>
<td>≥ 30 (%)</td>
<td>18</td>
</tr>
<tr>
<td>Previous bone density scan (%)</td>
<td>6</td>
</tr>
<tr>
<td>Use of calcium or vitamin D supplements (%)</td>
<td>15</td>
</tr>
<tr>
<td>Current osteoporosis treatment (%)</td>
<td>2</td>
</tr>
<tr>
<td>Available diagnostic information for coeliac disease (%)</td>
<td></td>
</tr>
<tr>
<td>Suggestive biopsy and elevated antibodies</td>
<td>73</td>
</tr>
<tr>
<td>Suggestive biopsy but antibodies normal or not available</td>
<td>6</td>
</tr>
<tr>
<td>Elevated antibodies but biopsy normal or not available</td>
<td>4</td>
</tr>
<tr>
<td>Medical records listed coeliac disease as diagnosis</td>
<td>13</td>
</tr>
<tr>
<td>No confirmatory laboratory tests or medical records</td>
<td>4</td>
</tr>
</tbody>
</table>

Data are mean (SD) or percentage. Biopsy refers to duodenal biopsy histology, and antibodies to tissue transglutaminase antibodies.
Some individuals may have started treatment for coeliac disease before their bone density scan, and for other individuals, we did not have sufficient laboratory information available to confirm the diagnosis. Therefore, we repeated the analyses restricting the cohort to those individuals with elevated tissue transglutaminase antibodies and histology consistent with coeliac disease on duodenal biopsy who had a bone density measurement within 6 or 12 months of the biopsy. Thirty-six and 63 people, respectively, met these criteria. The mean bone density Z-scores at each site were similar to the results for the entire cohort (6 months: lumbar spine 0.4, total hip 0.5, and femoral neck -0.4; 12 months: lumbar spine -0.2, total hip -0.4, and femoral neck -0.3).

There was a strong relationship between BMI and both mean bone density Z-scores and the proportion of people with high or low Z-scores. Figure 1 shows that mean Z-scores increased and the proportion of individuals with bone density below the normal range decreased with increasing BMI. No individual with BMI ≥30 kg/m² had bone density below the normal range at any site, whereas more than 1 in 4 with body mass index <20 kg/m² had low bone density at any site (and none had high bone density). In those with BMI of 20–25 and 25–30 kg/m², the respective proportions were 15% and 6% for low bone density at any site, and 5% and 6% for high bone density at any site. No individual weighing >76 kg had bone density below the normal range.

Sixteen individuals had bone density below the normal range at any of the 3 sites. In the 12 months following the bone density scan, 3 were not prescribed any specific treatment, 4 were prescribed calcium and/or...
or vitamin D supplements, 4 etidronate, and 5 either alendronate or zoledronate. Eight of the 16 individuals had a follow-up bone density scan after a median of 3 years, with 7 showing improvements in bone density (6 treated with bisphosphonates, 1 no specific treatment), and 1 showing bone loss despite calcium and vitamin D supplements and etidronate.

**Discussion**

In this cohort of 137 adults with coeliac disease, the average bone density was slightly lower than expected, but still comfortably within the normal range. A 1 standard deviation decrease in bone density is associated with about a 1.5 fold increased fracture risk in older women, suggesting that a decrease in bone density of 0.3–0.4 standard deviations would be associated with a very small increase in fracture risk, if any. The changes in bone density we observed, therefore, are clinically unimportant. A greater proportion of people with coeliac disease had bone density below the normal range, but a similar proportion had bone density above the normal range. Taken together, these results suggest that routine measurement of bone density in newly diagnosed coeliac disease is unnecessary.

The study has limitations. In some patients, we were not able to confirm the diagnosis of coeliac disease because definitive test results were either not available or not done. Because of the nature of the study, bone density measurements were carried out at varying times after diagnosis of coeliac disease, and we had no information on adherence to a gluten-free diet. The strength of the study is its relevance to clinical practice. In all patients, coeliac disease was a stated indication for referral for bone densitometry. Thus, this cohort is a group of patients that clinicians felt would benefit from measurement of their bone density, presumably because they were believed to have a high risk of low bone density.

Guidelines recommending that all patients with newly diagnosed coeliac disease undergo bone density scanning were based on cross-sectional studies reporting an increased prevalence of low bone density and osteoporosis in coeliac disease. A further important point when considering whether to request a bone density scan is the natural history of bone density changes following diagnosis of coeliac disease. Longitudinal studies of individuals with treated coeliac disease showed that body weight and bone density increases. Thus, if body weight and bone density are likely to increase following diagnosis and institution of a gluten-free diet, and low bone density is both uncommon and unlikely to be clinically significant, the justification for routinely measuring bone density at diagnosis is weak. Low bone density has been reported in association with more severe villous atrophy. However, this association is confounded by body weight, because more severe villous atrophy was also associated with lower BMI, which is a recognised risk factor for low bone density. In our current study, low BMI was a strong predictor of the risk of low bone density.

A small proportion of individuals with coeliac disease have low bone density, 12% in this cohort. For younger individuals with no clinical risk factors for fracture whose bone density is likely to increase over time, the short-medium term fracture risk is low and knowledge of the bone density, even if it is low, is unlikely to lead to a change in management. For such people, measuring bone density is unnecessary. For older individuals, or those with strong clinical risk factors for fracture, the short-term risk of fracture is higher and measuring bone density could be considered on a case-by-case basis. For example, if bone density measurements in our cohort had been restricted to those with BMI <20 kg/m² or those aged >50 years with BMI <25 kg/m², 69% (11/16) of those with bone density below the normal range would have been identified, and 69% of the total number of scans would have been avoided.
ARTICLE

Competing interests:
Andrew Grey is a shareholder in Auckland Bone Density, a company that provides bone densitometry services.

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