Alteration of Bone Mineral Density in Cystic Fibrosis Adults

To the Editor:

We read with interest the article by Stephenson and colleagues regarding the prevalence of vertebral fractures in adults with cystic fibrosis and their relationship to bone mineral density (BMD), and we would like to add some comments based on our clinical experience. In our cystic fibrosis center, 62 of 81 adult patients (76.5%) have undergone dual energy radiograph absorptiometry (DXA) at least once in the last 5 years; 25 of these patients are female and 37 are male (mean age, 27.1 years; SD, 3.2 years). At the time of DXA, none of the patients had been treated with drugs for osteoporosis before measuring bone density and none of them had received a lung transplant. BMD was measured using DXA (Delphi A S/N 70509; Hologic; Bedford, MA) in lumbar spine (L1-L4), and the results were expressed as an absolute value of BMD (grams per centimeter squared) and BMD T-score. Osteopenia was present in 45.1% of the patients (n = 28), and osteoporosis was present in 11.3% (n = 7) [World Health Organization diagnosing criteria]. In all examined patients, vertebral fractures were excluded by clinical history and by lateral chest radiographic imaging performed in occasion of follow-up visits.

In accordance with the findings of Stephenson and colleagues, in our patients BMD values correlated with body mass index (BMI) values (R = 0.34, p = 0.006) and with FEV1 expressed as percentage of the predicted value according to age and sex (R = 0.21, p < 0.05), but also with Chrispin-Norman radiographic score (R = −0.27, p = 0.03). Similarly, a correlation was found between the BMD T-score values and the BMI values (R = 0.27 p = 0.03) and Chrispin-Norman score (R = −0.32, p = 0.02).

The mean value of BMI was significantly different between subjects with normal BMD (22.2 kg/m²; SD, 2.1 kg/m²) and those with alterations in BMD (20.3 kg/m²; SD, 2.5 kg/m²); t test, p = 0.002). A statistically significant difference was also found in the mean value of FEV1 between those patients with normal BMD (70.6%; SD, 23.8%) and those with alterations in BMD (55.2%; SD, 25.6%; t test, p = 0.02).

Our data are consistent with the findings of Stephenson and colleagues, even though in our population we did not observe any case of fracture. However, knowing that patients with fractures have a higher mean BMD value is likely not to have clinical relevance; it would have been interesting to know the proportion of patients with osteopenia and osteoporosis in the fracture and no-fracture groups. This information would imply important consequences from a preventive point of view, as it would offer clinicians a tool to evaluate the risk of pathologic fractures in cystic fibrosis patients according to their mineral bone status. Also, the presence of symptomatic osteoporosis is a contraindication for lung transplantation, and the risk of chest fractures developing may exclude a patient from a possible vital therapeutic opportunity.

The authors have no conflicts of interest to disclose.

REFERENCES


Table 1—Response Frequencies for Modified AQ20 Items

<table>
<thead>
<tr>
<th>Item No.</th>
<th>Yes</th>
<th>No</th>
<th>Unable</th>
<th>NA</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>30.4</td>
<td>38.1</td>
<td>3.4</td>
<td>28.1</td>
</tr>
<tr>
<td>4</td>
<td>20.8</td>
<td>73.2</td>
<td>1.1</td>
<td>4.8</td>
</tr>
<tr>
<td>10</td>
<td>28.5</td>
<td>67.5</td>
<td>0.6</td>
<td>3.4</td>
</tr>
<tr>
<td>11</td>
<td>18.8</td>
<td>40.7</td>
<td>1.7</td>
<td>38.8</td>
</tr>
<tr>
<td>12</td>
<td>57.8</td>
<td>33.6</td>
<td>2.0</td>
<td>6.6</td>
</tr>
<tr>
<td>13</td>
<td>40.1</td>
<td>51.1</td>
<td>0.9</td>
<td>8.0</td>
</tr>
<tr>
<td>14</td>
<td>19.4</td>
<td>57.6</td>
<td>1.4</td>
<td>21.7</td>
</tr>
</tbody>
</table>

*NA = not applicable.

14 ("a night out"). The high frequency of “not applicable” responses to these items, despite the inclusion of the “unable” option, suggests that the activities queried by these items may in fact be less relevant to the study population. In a recent publication by Barley and Jones, Rasch analysis was used to assess the measurement properties of the AQ20 over time. Item 3 was found to be unstable due an increase in “not applicable” responses related to seasonal changes over the study period. The variable relevance of these items to subjects, rather than the inability to perform these activities, may explain the lack of correlation between “not applicable” responses and other health status measures noted by Blanco-Aparicio and Vázquez. Nonetheless, we believe that providing an “unable” response option further minimizes the potential for any misclassification, particularly among those subjects with a high degree of respiratory impairment.

We agree with the final conclusion of Blanco-Aparicio and Vázquez—that additional studies of this question are needed.
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Correspondence to: Filippo Festini, RN, BA, BSN, Department of Pediatrics, University of Florence, via L. Giordano 13, Florence, Italy 50132; e-mail: filippo.festini@unifi.it

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To the Editor:

We are grateful for the interest and comments by Neri et al1 on our article,2 and we appreciate the opportunity to respond. We agree with the authors that the finding of an association between fractures and higher bone mineral density (BMD) is not clinically useful. The importance of this finding is more to emphasize the point that the association between T scores and fracture risk is unclear in patients with cystic fibrosis (CF). It may be erroneous to assume that the data from postmenopausal women applies to those with CF. At our institution, the dual energy x-ray absorptiometry report states the fracture risk based on the T score, and that this may be misinterpreted, especially for caregivers who are unfamiliar with CF-related bone disease. Based on this report, bisphosphonates may be prescribed for CF patients with osteoporosis; however, the ability of these drugs to decrease fracture risk has not been studied. Bisphosphonates seem to increase BMD in CF patients,3,4 but whether this translates into fracture prevention is unclear. To initiate the long-term use of a drug in a population of young premenopausal patients, which potentially may have effects on fetal development, must be considered carefully.

Neri et al1 recognized the importance of developing a tool to evaluate the risk of fractures in CF patients, which, we agree, is much needed. Using World Health Organization criteria,3 36% of the subjects in our no-fracture group had osteopenia and 9% had osteoporosis. Within the fracture group, 25% had osteopenia and none had osteoporosis. However, it is unclear how knowing this breakdown helps clinicians assess fracture risk, given the paradoxical findings of our study. The more important question is whether or not a different modality for evaluating BMD in CF can identify those patients who are at high risk for fracture based on an abnormal test result. DEXA may not be the appropriate tool for this population. Hopefully, future studies will help to clarify these issues.

Anne Stephenson, MD
St. Michael’s Hospital
Toronto, ON, Canada

Cost Analysis of Intensive Glycemic Control in Critically Ill Adult Patients

To the Editor:

We congratulate Krinsley and Jones1,2 for their impressive improvement in patient survival, which was attributed to tight glucose regulation. Surprisingly, the intensification of therapy led to decreased costs, mainly due to shorter ICU and hospital stays. Fortunately, this finding has already been confirmed.3 However, they found1,2 a greater improvement in mortality than did van den Berghe et al4 in a key study. Moreover, in patients who were more comparable with the patients studied by Krinsley,1 and Krinsley and Jones,2 they found no significant improvement in mortality in the intention-to-treat analysis, although a tighter upper limit of 110 mg/dL was used instead of 140 mg/dL.5

We wonder whether other factors might have influenced the findings. In a before-and-after study; subtle changes in policy or patient characteristics can easily influence outcome without apparent changes in APACHE (acute physiology and chronic health evaluation) II score or diagnostic groups. The obviously very comprehensive database should allow further analyses. It might be worthwhile to check for factors known to influence patient outcome. We would suggest checking the following: medical staff availability; nursing staff availability; nurse/patient ratio; bed occupancy ratio; rate of referred patients; availability of daily rounds; hospital admission and discharge protocols; the introduction of ventilatory protocols; and the introduction of early goal-directed therapy. This might moderate the effect of glucose regulation, putting it more in line with the results of van den Berghe et al.6 Otherwise, the effect on mortality of a single measure seems incredibly high.

Jan G. Zijlstra, PhD
Anouk M. Corstjens, MD
Jaap E. Tulleken, PhD
John H.J.M. Meertens, MD
Jack J.M. Ligtemberg, PhD
University Medical Center Groningen
Groningen, the Netherlands

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