Bone Mineral Density and Serum Levels of Soluble Tumor Necrosis Factors, Estradiol, and Osteoprotegerin in Postmenopausal Women with Cirrhosis after Viral Hepatitis

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Context: Cirrhosis after viral hepatitis has been identified as a risk factor for osteoporosis in men. However, in postmenopausal women, most studies have evaluated the effect of primary biliary cirrhosis, but little is known about the effect of viral cirrhosis on bone mass (bone mineral density (BMD)) and bone metabolism.

Objective: Our objective was to assess the effect of viral cirrhosis on BMD and bone metabolism in postmenopausal women.

Design: We conducted a cross-sectional descriptive study.

Setting and Patients: We studied 84 postmenopausal female outpatients with viral cirrhosis and 96 healthy postmenopausal women from the general community. BMD was measured by dual-energy x-ray absorptiometry at lumbar spine (LS) and femoral neck (FN).

Results: The percentage with osteoporosis did not significantly differ between patients (LS, 43.1%; FN, 32.2%) and controls (LS, 41.2%; FN, 29.4%), and there was no difference in BMD (z-score) between groups. Serum concentrations of soluble TNF receptors, estradiol, and osteoprotegerin (OPG) were significantly higher in patients vs. controls ($P < 0.001$, $P < 0.05$, and $P < 0.05$, respectively). No significant difference was observed in urinary deoxypyridinoline. Serum OPG levels were positively correlated with soluble TNF receptors ($r = 0.35$; $P < 0.02$) and deoxypyridinoline ($r = 0.37$; $P < 0.05$).

Conclusions: This study shows that bone mass and bone resorption rates do not differ between postmenopausal women with viral cirrhosis and healthy postmenopausal controls and suggests that viral cirrhosis does not appear to increase the risk of osteoporosis in these women. High serum estradiol and OPG concentrations may contribute to preventing the bone loss associated with viral cirrhosis in postmenopausal women. (J Clin Endocrinol Metab 94: 4844–4850, 2009)
women (4, 8). The effects of liver cirrhosis on bone mineral density (BMD) may differ between men and postmenopausal women because there are important gender differences in endocrine function and bone metabolism. There are also likely to be differences between women with viral cirrhosis and women with PBC, a cholestatic disease with a distinct etiology and pathogenesis.

Male patients with viral cirrhosis were reported to have elevated serum levels of several potent bone-resorbing cytokines, such as IL-1, IL-6, and TNF and its soluble receptor sTNFR-55 (3, 9–11), and high serum sTNFR-55 levels have been related to increased bone resorption in these patients (3).

In postmenopausal women, liver disease and the subsequent cytokine secretion might exacerbate bone loss. There is also evidence that cytokines IL-1 and IL-6 and TNF are elevated after surgical or natural menopause and may be critical factors in postmenopausal osteoporosis (12). These cytokines increase bone resorption mainly by increasing the pool size of osteoclasts in bone marrow (12), whereas TNF-α also appears to exert a direct effect by increasing the expression of the receptor activator of nuclear factor-κB ligand (RANKL) in human osteoblastic cells (13) and has been reported to directly stimulate macrophages (14).

Although it is well established that estrogen deficiency is a major etiological factor of postmenopausal osteoporosis (12), the mechanism by which estrogen administration prevents bone loss in postmenopausal women is still not fully elucidated. Studies in laboratory animals have shown that the main mechanism is inhibition of osteoclastogenesis, because estrogen has been shown to induce osteoclast apoptosis (15) and inhibit osteoclast differentiation (16). It was recently proposed that estrogen may modulate the secretion of factors that are produced in the bone microenvironment and participate in bone remodeling. These factors include cytokines and the RANKL/RANK/osteoprotegerin (OPG) regulatory system (17). RANKL, expressed on the surface of preosteoblastic/stromal cells and osteoblasts, has been identified as the key mediator of osteoclastogenesis by binding to its receptor RANK, which is expressed on the surface of osteoclast-lineage cells (18). RANKL is critical for osteoclast differentiation and activation and for inhibition of osteoclast apoptosis (19). Its action is opposed by OPG, a soluble protein belonging to the TNF receptor superfamily, which is secreted by osteoblasts and marrow stromal cells, among others (20). The main biological action of OPG is to inhibit osteoclast differentiation and activity (18). The RANKL/RANK/OPG system participates in the antiresorptive action of estrogen mainly by increasing OPG production by osteoblastic and marrow stromal cells (20).

Liver cirrhosis raises estradiol levels in postmenopausal women with alcoholic or nonalcoholic liver disease (21), and it could be thought that these elevated serum estrogen levels might potentially help to protect the skeleton, at least in postmenopausal women, who have estrogen-deficient bone loss.

In the present study, we examined bone mass and bone metabolism changes in 84 postmenopausal women with viral cirrhosis and no history of alcohol intake and in 96 healthy postmenopausal women. We also investigated changes in serum levels of estradiol, sTNFR-55, sTNFR-75, OPG, and RANKL, analyzing their possible relationship with bone mass and bone turnover.

Patients and Methods

A total of 92 consecutive, Caucasian, postmenopausal female outpatients with viral cirrhosis (hepatitis C virus), diagnosed in the Department of Gastroenterology of the University Hospital of Granada in Spain between January 2002 and September 2006, were candidates for inclusion in the study. We excluded eight patients: two with abdominal malignancies, two who were taking T₄₅, one undergoing treatment with insulin for diabetes mellitus, one with renal failure, and two who were hospitalized for variceal bleeding. We finally enrolled 84 patients. The mean age was 65.1 yr (range, 55–80 yr). The diagnosis of cirrhosis was based on liver biopsy in 60 patients and on the following clinical findings and laboratory data in the other 24 patients: physical signs of chronic liver disease, hypoalbuminemia, reduced prothrombin activity, signs of liver cirrhosis on ultrasound examination, and esophageal varices on endoscopy. Exclusion criteria were less than 5 yr past menopause, consumption of more than 50 g alcohol per week, presence of endocrine, gastrointestinal, heart, or lung disease or malignancy, and a serum creatinine concentration higher than 0.15 mmol/liter. None had a family history of osteoporosis, and none had received corticosteroids, calcium, vitamin D supplements, hormone replacement therapy, thiazide, steroids, or any medication related to mineral metabolism. None of the patients had received interferon or ribavirin treatment, and there were no comorbidities of hepatitis. All 84 patients had a body mass index (BMI) higher than 20 kg/m². Our patients had the following genotypes: genotype 1b (n = 58), genotype 1a (n = 14), genotype 2a (n = 4), genotype 4a (n = 2), and genotype 3a (n = 6).

The patients were classified into two groups according to the Child-Pugh score of severity of liver disease (22): Child A group, 54 patients with well-compensated liver disease (mean age, 64.42 yr; range, 55–78 yr), and Child B+C group, 30 patients with moderate to severe liver disease (mean age, 66.4 yr; range, 55–80 yr). Child B and C patients were grouped together because patients with moderate or severe liver disease can change from one stage to another (e.g., Child B to Child C or vice versa), and the disease severity can be very similar between some Child B patients and Child C patients.

A control group was formed of 96 healthy postmenopausal women with a history of alcohol intake of less than 50 g ethanol per week. The mean age was 63.8 yr (range, 55–79 yr). They were recruited from among hospital staff, their friends and their fam-
ilies. All were Caucasian outpatients in good health. Detailed medical histories and biochemical studies were performed to identify any causes of low BMD. Their exclusion criteria were the same as those stated for patients. Patients and controls came from the same geographic area and gave their informed consent before enrollment in the study. The protocol was approved by the human ethical committee of the hospital.

**Laboratory analysis**

Blood and urine samples were collected in the morning after overnight fasting. Biochemical liver function parameters and serum urea, creatinine, and calcium (corrected for albumin concentration) were measured by means of a standard automated technique. Serum was analyzed using commercially available kits for sTNFR-55 and sTNFR-75, with enzyme-amplified immunocytometric assay from BioSource Europe (Nivelles, Belgium); OPG, with enzyme immunoassay from Biomedica Gruppe (Vienna, Austria); estradiol, using DSL-39100 third-generation estradiol RIA from Diagnostic Systems Laboratories Inc. (Webster, TX), with minimum detection limit of 0.6 pg/ml (23); RANKL, using ELISA from Biomedica Gruppe; bone alkaline phosphatase (b-AP), by Tandem-T, Ostase immunoradiometric assay from Hybritech Europe (Liege, Belgium); bone-Gla-protein (BGP) by RIA from Incstar Corp. (Stillwater, MN); 25-hydroxyvitamin D (25-OHD), by RIA from Incstar Corp.; IGF-I, by RIA from Nichols Institute (San Juan Capistrano, CA); intact PTH, by immunoradiometric assay (Incstar); urinary creatinine, using a standard automated technique, and urinary free deoxypyridinoline (D-Pyr), with a competitive ELISA test from Metra Biosystem (Mountain View, CA). Urinary D-Pyr excretion was expressed as the ratio of urinary D-Pyr to urinary creatinine. Intra- and interassay precision ranged from 4.5–12% for all biochemical tests.

**BMD measurements**

BMD was measured by dual x-ray absorptiometry (QDR1000; Hologic, Inc., Waltham, MA). Measurements were made at the lumbar spine (LS; L2–L4 area) and femoral neck (FN). Our laboratory has a long-term coefficient of variation (in vivo precision) lower than 2% at lumbar and femoral measurement sites (24). Values are expressed as z-score (number of SD adjusted by sex and age); 1303 females served to establish the mean in the healthy Spanish population (25). Osteoporosis was defined as BMD 2.5 SD or more below the young adult mean at LS or FN according to World Health Organization criteria (26).

**Statistical analysis**

Results are expressed as means ± SD. The normal distribution of values in different groups was verified with the Kolmogorov-Smirnov test. Mean values in groups were compared by one-way ANOVA, followed by the Tukey multiple-comparison test. The Pearson standard linear regression analysis (normal distribution) or Spearman test (nonnormal distribution) were used for correlation studies. To compare proportion of subjects with osteoporosis, we used χ² test. Backward step-wise multiple regression analysis was used, in cirrhotic patients, to establish the most significant determinants of BMD, expressed as z-score, in LS and FN. Variables entered into the equations were Child-Pugh score, BMI, and serum values of sTNFR-55, sTNFR-75, RANKL, OPG, estradiol, 25-OHD, IGF-I, and PTH. Only variables showing a P < 0.2 were retained in the final regression model. Because sTNFR-55 and sTNFR-75 were strongly correlated, with potential for collinearity that could create an unstable model, the multiple regression analysis was performed twice: 1) with all the variables entered except sTNFR-55 and 2) with all the variables entered except sTNFR-75. No differences between the two models were found.

**Results**

Results of liver function tests and BMI are shown in Table 1. The controls and cirrhotic patients had similar BMI values. None of the participants appeared malnourished. Nine of the patients had ascites, but none were jaundiced.

BMD values at LS and FN did not significantly differ between cirrhotic women and controls, between Child A and Child B+C patients (Table 2), or among different virus genotypes. The percentage with osteoporosis did not significantly differ between cirrhotic patients and controls (Fig. 1). Table 2 shows that serum concentrations of sTNFR-55 and sTNFR-75 were higher in patients than in controls (P < 0.0001 for both) and in Child B+C patients than in Child A patients (P < 0.001 for both). Serum OPG and serum estradiol concentrations were also significantly higher in patients than in controls (Child A, P < 0.03, and Child B+C, P < 0.02, for OPG; and Child A, P < 0.02, and Child B+C, P < 0.01, for estradiol). There was no significant difference in OPG between the two patient groups. Serum estradiol was higher in Child B+C group than in Child A group (P < 0.02). Serum PTH concentrations were lower in patients than in controls (P < 0.03 for Child A and P < 0.01 for Child B+C). Serum IGF-I concentrations were lower in Child B+C patients vs. controls (P < 0.02). Serum BGP concentrations were lower in Child A and Child B+C patients than in controls (P < 0.02 and P < 0.03, respectively). No significant differences

<p>| TABLE 1. BMI and liver function tests in postmenopausal control women and postmenopausal women with viral cirrhosis |
|---------------------------------------------------------------|-----------------------------|</p>
<table>
<thead>
<tr>
<th><strong>BMD (g/m²)</strong></th>
<th>Controls (n = 96)</th>
<th>Viral cirrhosis (n = 84)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum albumin (g/dl)</td>
<td>4.41 ± 0.67</td>
<td>3.71 ± 0.9³</td>
</tr>
<tr>
<td>Prothrombin activity (%)</td>
<td>99 ± 2.57</td>
<td>80.9 ± 1.65¹</td>
</tr>
<tr>
<td>Serum aspartate transaminase (U/liter)</td>
<td>26.2 ± 11.5</td>
<td>120.6 ± 142.87¹</td>
</tr>
<tr>
<td>Serum γ-glutamyl transferase (U/liter)</td>
<td>31.7 ± 18.86</td>
<td>79.6 ± 66.43³</td>
</tr>
<tr>
<td>Serum alkaline phosphatase (U/liter)</td>
<td>138.2 ± 6.9</td>
<td>288.8 ± 128.5²</td>
</tr>
<tr>
<td>Serum bilirubin (mg/dl)</td>
<td>0.77 ± 0.7</td>
<td>2.27 ± 2.18²</td>
</tr>
</tbody>
</table>

Values are the mean ± sd.

¹ P < 0.001 vs. controls.

² P < 0.01 vs. controls.
were found between cirrhotic patients and controls in serum b-AP or calcium or in urinary D-Pyr values.

A highly significant positive correlation was found between serum sTNFR-55 and sTNFR-75 (r = 0.8; P < 0.0001). Serum OPG was positively correlated with serum sTNFR-55 (r = 0.3; P < 0.02), serum sTNFR-75 (r = 0.30; P < 0.05), serum b-AP (r = 0.43; P < 0.001), and urinary D-Pyr (r = 0.39; P < 0.01). Serum estradiol was positively correlated with serum b-AP (r = 0.37; P < 0.01), Child-Pugh score (r = 0.49; P < 0.001), and serum albumin (r = 0.43; P < 0.003). No other significant correlations were found.

Results of the step-wise regression analysis show that OPG was the most important determinant of BMD (z-score) in postmenopausal women with viral cirrhosis at both LS (β-coefficient = 0.54; SE = 0.3; P < 0.01) and FN (β-coefficient = 0.43; SE = 0.2; P < 0.01). No other variable reached P < 0.05.

Discussion

In the present study, postmenopausal women with viral cirrhosis and healthy postmenopausal controls did not significantly differ in the percentage with osteoporosis or in BMD values at LS or FN. These findings suggest that viral cirrhosis may not increase the risk of osteoporosis in postmenopausal women. The prevalence of osteoporosis in our control postmenopausal women is similar to that previously reported for women in this age range from the same geographic area (27) and other countries (28). Nevertheless, the cross-sectional design of the study and the fact that our control women were neither family nor friends of patients may be study limitations. Our results contrast with previous reports of an association between bone mass loss and chronic liver disease in male patients (1–4) and in women with PBC (4–6). In fact, the reported prevalence of osteoporosis in patients with chronic liver disease varies (4, 7, 8), largely as a function of patient selection (age, gender, and years after menopause in women), etiology, and diagnostic criteria. PBC is a cholestatic disease that differs from viral cirrhosis in etiology, pathogenic mechanisms, prognosis, and treatment and may have distinct effects on bone mass and bone metabolism.

**TABLE 2.** BMD, serum concentrations of sTNFR and estradiol, and biochemical parameters of bone and mineral metabolism in postmenopausal control women, postmenopausal women with viral cirrhosis, and patients classified according to Child-Pugh score

<table>
<thead>
<tr>
<th></th>
<th>Controls (n = 96)</th>
<th>Cirrhotic patients (n = 84)</th>
<th>Child A (n = 54)</th>
<th>Child B+C (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMD-LS (z-score)</td>
<td>0.12 ± 1.45</td>
<td>−0.02 ± 1.18</td>
<td>−0.12 ± 0.8</td>
<td>0.08 ± 0.75</td>
</tr>
<tr>
<td>BMD-LS (g/cm²)</td>
<td>0.90 ± 0.15</td>
<td>0.87 ± 0.14</td>
<td>0.85 ± 0.16</td>
<td>0.86 ± 0.12</td>
</tr>
<tr>
<td>BMD-FN (z-score)</td>
<td>0.02 ± 0.97</td>
<td>0.11 ± 1.09</td>
<td>0.07 ± 1.16</td>
<td>0.15 ± 0.48</td>
</tr>
<tr>
<td>BMD-FN (g/cm²)</td>
<td>0.70 ± 0.11</td>
<td>0.71 ± 0.12</td>
<td>0.70 ± 0.13</td>
<td>0.73 ± 0.09</td>
</tr>
<tr>
<td>sTNFR-55 (ng/ml)</td>
<td>2.7 ± 0.8</td>
<td>5.5 ± 2.7</td>
<td>4.03 ± 0.73</td>
<td>6.7 ± 2.7</td>
</tr>
<tr>
<td>sTNFR-75 (ng/ml)</td>
<td>14.3 ± 2.9</td>
<td>36.4 ± 13.1</td>
<td>29.8 ± 12.5</td>
<td>43.2 ± 14.04d</td>
</tr>
<tr>
<td>Estradiol (pg/ml)</td>
<td>5.91 ± 4.85</td>
<td>15.7 ± 12.5</td>
<td>9.1 ± 6.9</td>
<td>22.3 ± 7.81c</td>
</tr>
<tr>
<td>OPG (pmol/liter)</td>
<td>5.7 ± 3.88</td>
<td>10.2 ± 4.05</td>
<td>9.7 ± 3.65c</td>
<td>10.9 ± 4.32c</td>
</tr>
<tr>
<td>RANKL (pg/ml)</td>
<td>3.9 ± 11.6</td>
<td>4.1 ± 10.56</td>
<td>3.7 ± 10.22</td>
<td>4.5 ± 9.18</td>
</tr>
<tr>
<td>25-OHD (ng/ml)</td>
<td>22 ± 13.58</td>
<td>16.8 ± 15.67</td>
<td>18.9 ± 8.76</td>
<td>14.4 ± 11.3c</td>
</tr>
<tr>
<td>PTH (pmol/ml)</td>
<td>69.5 ± 27.16</td>
<td>47.5 ± 17.75</td>
<td>55.1 ± 15.33c</td>
<td>39.8 ± 15.66b</td>
</tr>
<tr>
<td>IGF-I (ng/ml)</td>
<td>119.7 ± 9.6</td>
<td>85.8 ± 96.4</td>
<td>107 ± 88.33</td>
<td>63.8 ± 49.14c</td>
</tr>
<tr>
<td>b-AP (U/liter)</td>
<td>30.9 ± 10.67</td>
<td>31.3 ± 15.58</td>
<td>28.9 ± 10.22</td>
<td>33.8 ± 21.06</td>
</tr>
<tr>
<td>BGP (ng/liter)</td>
<td>3.6 ± 1.9</td>
<td>2.3 ± 2.03</td>
<td>2.5 ± 1.46c</td>
<td>2.1 ± 2.48c</td>
</tr>
<tr>
<td>Calcium (mg/dl)</td>
<td>9.2 ± 0.7</td>
<td>9.76 ± 0.9</td>
<td>9.39 ± 0.5</td>
<td>9.97 ± 0.94</td>
</tr>
<tr>
<td>Urinary D-Pyr/creatinine (mmol/mmol)</td>
<td>6.7 ± 1.94</td>
<td>7.23 ± 6.37</td>
<td>7.54 ± 5.03</td>
<td>6.93 ± 3.67</td>
</tr>
</tbody>
</table>

Data are the mean ± SD.

a P < 0.001 vs. all patients groups; b P < 0.01 vs. controls; c P < 0.05 vs. controls; d P < 0.01 vs. group A; e P < 0.05 vs. group A.

**FIG. 1.** Percentage of osteoporosis in LS (A) and FN (B) in healthy postmenopausal women (controls), postmenopausal women with viral cirrhosis (VC), and patients classified according to Child-Pugh score. NS, Not significant vs. controls.
Chronic alcohol consumption (with or without liver disease) and viral cirrhosis are independent risk factors for osteoporosis in men (1–4, 29–31). However, viral cirrhosis may not have the same effect on bone mass and bone metabolism in postmenopausal women because of endocrine and bone metabolism differences with men. Likewise, both moderate (32) and heavy (33) alcohol intake has been associated with an increase in bone mass in postmenopausal women but a decrease in men (29). Moderate alcohol consumption has been shown to increase serum estradiol levels in postmenopausal women (34), which may potentially help to protect bone mass against estrogen-deficient bone loss.

Serum sTNFR-55 and sTNFR-75 concentrations were higher in the patients than in the controls and were related to the severity of the liver disease, and these elevated levels may accelerate bone mass loss, as reported in men with viral cirrhosis (3). However, we found that postmenopausal women with viral cirrhosis also had elevated serum estradiol and OPG concentrations, which might prevent bone loss associated with viral cirrhosis. Although preliminary observations were described by our group in a letter to the editor (35), this is the first published study of the relationship of serum levels of estradiol, OPG, sTNFR-5 receptors, and RANKL with the development of osteoporosis in postmenopausal women with viral cirrhosis. We have no ready explanation for the high serum OPG concentrations found in our patients, but estrogen has been found to increase OPG production by human osteoblastic cells (20). On the other hand, although we acknowledge that elevated serum OPG levels do not reflect tissue OPG levels, the high serum OPG values in these patients may represent a homeostatic mechanism limiting the increase in bone loss produced by the high bone turnover and high sTNFR level associated with viral cirrhosis (3, 36).

We used D-Pyr urinary excretion as a biochemical marker of bone resorption, which is found almost exclusively in bone and dentine and not in human liver fibrosis. Only bone collagen appears to significantly contribute to urine D-Pyr (37). We found a significant positive correlation between serum OPG and D-Pyr urinary excretion and between urinary D-Pyr and both sTNFR. These results, alongside the known bone protector effect of OPG and our finding that serum OPG concentration was the most important determinant of bone mass at LS and FN, suggest that the high serum OPG levels in our patients may counteract the bone resorbing effect of high circulating levels of sTNFR in postmenopausal women with viral cirrhosis. Moreover, we found no significant differences in D-Pyr urinary excretion between patients and controls, indicating that there were no differences in bone resorption rates.

Serum RANKL concentrations were similar between patients and controls. Although a relationship between estrogen deficiency and the up-regulation of RANKL on bone marrow cells has been described (18), we cannot draw any conclusion from this finding, because circulating levels of RANKL may not predict its effect on marrow cells in the bone microenvironment (18).

Several other factors may be involved in bone metabolism and the development of osteoporosis in our patients. In our study, cirrhotic postmenopausal women had lower serum PTH levels than controls despite having lower 25-OHD concentrations, which could be a consequence of liver disease, as previously reported in male patients with viral cirrhosis (2, 3). In contrast, normal serum PTH concentrations have also been described in chronic liver disease (1), although male and female patients with different ages and etiologies were included in the study. The influence of PTH on bone mass loss in chronic liver disease remains unclear. Serum IGF-I and 25-OHD concentrations were only reduced in patients with advanced liver disease, which is consistent with previous studies in male patients with viral cirrhosis (2, 3). However, in disagreement with reports in male patients, we found no correlation between BMD and serum IGF-I or 25-OHD. Low serum 25-OHD and IGF-I concentrations appeared to have only a minor influence on bone mass loss in our patients.

Several studies have shown elevated serum b-AP concentrations in male patients with viral cirrhosis (2, 3), which were proposed to possibly reflect higher bone formation rates in response to high bone resorption rates. We found no differences in serum b-AP between postmenopausal women with viral cirrhosis and controls. This finding, together with similar urine D-Pyr values between patients and controls, supports the idea that bone resorption rates do not differ between postmenopausal women with viral cirrhosis and healthy postmenopausal controls.

Serum BGP values were lower in patients than in controls, and no parallelism was found between serum BGP and b-AP changes, as also found in studies of men (2, 3). The low BGP values and the lack of parallelism between BGP and b-AP changes may be at least in part due to liver failure and might also reflect reduced BGP synthesis due to a vitamin D deficit (38). Low serum IGF-I may also be implicated in low BGP synthesis (39). In conclusion, this study shows that bone mass and bone resorption rates do not differ between postmenopausal women with viral cirrhosis and healthy postmenopausal controls, suggesting that viral cirrhosis does not appear to increase the risk of osteoporosis in these women. High serum concentrations of estradiol and OPG may contribute to preventing the
bone loss associated with viral cirrhosis in postmeno-
pausal women.

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References

35. Gonzalez-Calvin JL, Mundi JL, Casado FJ, Olivares EG 2004 Bone mineral density and serum levels of estradiol and osteoprotegerin in postmenopausal women with viral cirrhosis. Gastroenterology 126: 1225–1226; author reply 1226