Arteriovenous Fistula Affects Bone Mineral Density Measurements in End-Stage Renal Failure Patients

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Background and objectives: Hemodialysis needs an arteriovenous fistula (AVF) that may influence the structure and growth of nearby bone and affect bone mass measurement. The study analyzed the effect of AVF in the assessment of forearm bone mineral density (BMD) measured by dual energy x-ray absorptiometry (DXA) and examined its influence on the final diagnosis of osteoporosis.

Design, setting, participants, & measurements: Forty patients (52 ± 18 yr) in hemodialysis program (12 ± 8 yr) with permeable AVF in forearm were included. Patients were divided in two groups (over and under 50 yr). BMD of both forearms (three areas), lumbar spine, and femur was measured by DXA. Forearm measurements in each arm were compared. Patients were diagnosed as normal only if all territories were considered nonpathologic and osteoporosis/osteopenia was determined by the lowest score found.

Results: Ten patients were excluded and 30 patients were analyzed. BMD in the forearm with AVF was significantly lower than that observed in the contralateral forearm in both groups of patients and in all forearm areas analyzed. When only lumbar spine and femur measurements were considered, 70% of patients were nonpathologic and 30% were osteoporotic. However, inclusion of AVF forearm classified 63% as osteoporotic and a further 27% as osteopenic, leaving only 10% as nonpathologic.

Conclusions: Forearm AVF affects BMD measurements by decreasing their values in patients with end-stage renal failure. This may produce an overdiagnosis of osteoporosis, which should be taken into account when evaluating patients of this type.


Metabolic bone disease is commonly seen in the course of chronic kidney disease (CKD), with nearly all patients affected by the time dialysis is initiated. Osteoporosis in end-stage CKD patients is only a part of a wider spectrum of metabolic bone problems, namely uremic osteodystrophy. Therefore, its diagnosis, management, and follow-up may differ from the general population. However, standard diagnostic tools such as dual energy x-ray absorptiometry (DXA) have been widely used for the assessment of bone mineral deficiency status in those patients. Patients with CKD with or without dialysis also run an increased risk of skeletal fractures (1–3). In the general population, the presence of osteoporosis is a strong predictor of increased risk of fractures, and the measurement of bone mineral density (BMD) by DXA is an important diagnostic tool to identify those patients most likely prone to fractures. But in dialysis patients a low BMD constitutes a multitude of other etiologies, including the spectrum of renal bone disease. Therefore, final diagnosis of osteoporosis in those patients is a pathologic diagnosis only really determined by bone histomorphology. Some studies with DXA in hemodialysis patients have shown unreliable results for routine measurement of BMD or highly variable findings in different measurement sites (4), whereas Atsumi et al. have reported the usefulness of lumbar spine DXA measurements in predicting vertebral fractures in hemodialysis patients (5). There is no consensus in this field, but it should be noted that the Clinical Practice Guidelines for Bone Metabolism and Disease in CKD, issued by the National Kidney Foundation, recommend the measurement of BMD by DXA in CKD patients with fractures or with known risk factors for osteoporosis (6) (e.g., severe hyperparathyroidism) and for kidney transplant recipients (7).

The low cost, short scan time, low radiation dose, and accuracy of DXA make it the most widely used method for BMD measurements. Although the diagnosis of osteoporosis is generally based on DXA measurements of the spine and hip, the T-score criteria developed by the World Health Organization refer to T-scores generated from DXA measurements of the spine, hip, or the forearm (33% radius, also called the one-third radius). The forearm is of special interest because some authors have said that radius values are more valuable than measurements from the lumbar spine for discriminating hemodialysis patients with all types of fractures from those without fractures (8). Moreover, the latest official position of the International
Society for Clinical Densitometry indicates that forearm BMD should be measured under particular circumstances, such as hyperparathyroidism (9–11). This indication is because of the predominant involvement of cortical bone found in this disorder, which coincides with the condition of most patients with end-stage renal failure (12). BMD at the distal radius is predictive of fracture risk and correlates with parathyroid hormone levels in these patients, yet another reason for measuring at this site (13).

Surgically created arteriovenous fistulas (AVFs) in the forearm are widely used in end-stage renal failure patients and are frequently located in the nondominant forearm (at the same place where the BMD measurement is made). Interestingly, experimental studies have shown that an AVF may influence the structure and growth of adjacent bone, which will in turn affect any bone mass measurement at this location (14). Although the assessment of BMD at the forearm in end-stage renal failure patients could be influenced by the presence of AVF, data related to this particular subject are scarce. This point is of special interest not only because of the AVF’s effect on bone mass, but because it could also interfere with diagnostic checks for osteoporosis in these patients. Our study set out to analyze the effect of AVF in the assessment of forearm BMD in patients with end-stage renal failure and examine how it influences the final diagnosis of osteoporosis in these patients.

Materials and Methods

Patients and Control Group

This prospective study included 40 consecutive patients with end-stage renal disease (13 women, 7 premenopausal) on hemodialysis between 24 and 89 yr of age (mean ± SD: 52 ± 18 yr). The study was done from June 2006 to June 2008. All patients had a radial fistula, had been undergoing hemodialysis for an average of 12 ± 8 yr (range 1 to 24 yr), and had a permeable or patent AVF in the forearm. The fistula was always at the same place throughout the dialysis period, although nearly 50% of patients had more than one transplant. The exclusion criteria were related to any possible cause of difference in BMD between the two forearms that could interfere with results (e.g., a previous fracture or previous AVF in the contralateral site). The fact that some patients had more than one transplant has not been considered as an exclusion criterion because although transplant patients are more likely to have glucocorticoid-induced osteoporosis and lower BMD, any possible effect is canceled out by our paired study design.

Patients were classified into two groups (15) on the basis of age: Group I, patients over 50 yr of age (17 patients, 12 men and 5 women); and Group II, patients under 50 yr (13 patients, 9 men, 4 women). A control group of 30 consecutive patients without an AVF was also included. All subjects gave informed consent to participation and the study was approved by the hospital ethics committee.

A control group for the short-term precision of DXA was assessed in vivo using 90 consecutive volunteers studied for diagnosis or control of low BMD. Volunteers were divided into three equal groups. On the same day, each group had a repeated measurement of one territory: lumbar spine, total hip, or nondominant forearm (total radius, 33% radius, and ultradistal radius). The volunteers were repositioned between the two measurements.

BMD Measurements

BMD was measured by DXA using a Lunar Prodigy device (instrument system n° 10233, software version 8.10.027) in accordance with the standardized method. Throughout the study, quality assurance scans were run on a daily basis and a weekly scan of the manufacturer-supplied spine phantom was carried out to confirm that no instrumental drift had occurred. All measurements were performed and reviewed by the same experienced operator.

Statistical Analyses

Precision error was expressed as the root mean square SD (SD of the group, RMS SD) and as a coefficient of variation (CV%). The CV% was calculated in the control group as $\text{CV\%} = \left( \frac{SD}{\text{mean}} \right) \times 100$, where mean is the mean of the results (17,18). The least significant change (LSC) was also calculated as $2.77 \times \text{RMS SD}$, where RMS SD is the largest precision error of the technique. For a BMD change to be considered statistically significant, it had to equal or exceed the LSC. A paired, matched control study was not done because of the paired data structure of the study.

Results were expressed as mean ± SD (SD of the mean) for all of the territories analyzed. Comparisons between forearm measurements (with and without forearm AVF) were done with the Wilcoxon signed rank nonparametric test. The mean of the difference between both sides was also reported for each forearm territory and expressed as absolute value and as a percentage $\left[ \text{contralateral forearm} \left( - \text{AVF forearm} \right) \right] / \text{contralateral forearm} \times 100 \%$. Finally, a coefficient of correlation was calculated between these percentages and the hemodialysis time. The analysis was performed using SPSS12 from the Windows statistical program package. Values of $P < 0.05$ were considered significant.

Results

Ten patients were excluded from the analysis because of additional factors or processes that could affect BMD assessment of the forearm (three patients previously had a AVF in the
contralateral forearm, one had forearm calcifications, one had a forearm fracture, three patients were excluded because of problems with positioning, and two because of a technical error during data storage). The remaining 30 patients were analyzed in two groups. Group I comprised the 17 (57%) who were over 50 (12 men and 5 women) with a mean age of 67 ± 12 yr (range 53 to 89 yr) and mean hemodialysis history of 9 ± 7 yr (range 1 to 18 yr). The remaining 13 patients (43%) (9 men and 4 women) were under 50 (Group II) with a mean age of 37 ± 7 yr (range 25 to 45 yr) and a mean hemodialysis history of 13 ± 9 yr (range 1 to 24 yr).

The RMS SD, CV%, and the LSC for the different territories can be seen in Table 1. The best precision and reproducibility results were obtained in hips, followed by lumbar spine and 33% radius.

BMD measurements and T- and Z-score values at the lumbar spine and hip are shown in Table 2. As expected, mean BMD values at total hip were lower in older patients (Group I), with mean T-score values indicating osteoporosis in these locations. Conversely, the lumbar spine mean value in younger patients was consistent with osteopenia (Z-score −1.4).

When we evaluated the effect of the AVF in forearm BMD measurement, we observed that BMD in the forearm with AVF was significantly lower than that observed in the contralateral forearm (Table 3). This was true in the younger and older groups of patients and in all forearm areas analyzed, with a mean decrease in BMD greater than the LSC in all territories except for the ultradistal radius in Group II (Table 3). This decrease, expressed as a percentage, was 7.5% at the 33% radius, 7.2% at the total radius, and 7.0% at the ultradistal radius. These results were not related to the number of years on hemodialysis. In contrast, the control group of patients without AVF showed no significant differences between forearms in any of the three territories.

When only lumbar spine and total hip measurements were used for diagnosis, 70% of patients showed a normal BMD and only 30% showed osteoporosis (Figure 1). However, because clinical guidelines recommend using the nondominant forearm (which coincides with the AVF forearm), when this was included, the number of normal BMD patients dropped to 10%; osteopenia was diagnosed in 27%; and osteoporosis was diagnosed more than double, at 63% of the group. Moreover, AVF territory proved to be the only territory affected in 24% of Group I patients (2 with osteopenia and 2 with osteoporosis) and in 30% of Group II patients (2 with osteopenia and 2 with osteoporosis).

### Discussion

Our reproducibility results were similar to those reported by different authors (1,19) and were in accordance with international clinical guidelines (8,9,18). The best reproducibility results obtained in our study were in hips, followed by lumbar spine and 33% radius, as has also been reported in the literature (20).

The results of this study show that for patients with end-stage renal failure, a forearm AVF lowers BMD measurements made in the same area, in particular in 33% radius (the forearm territory recommended for diagnosis) with a decrease that was greater than the LSC. As a result, osteoporosis or osteopenia can be greatly overdiagnosed when the international guidelines are followed and the nondominant forearm with an AVF is used for measurement (9).

In our study the decrease in BMD caused by AVF was seen to a similar degree in all patients, independent of age and in all forearm locations analyzed (i.e., the ultradistal radius, 33% radius, and total radius). The writers found no published results related to this particular finding except one previous study, where a higher percentage of fracture in the fistula forearm was reported but no significant differences were found between BMD in both forearms in relation to the presence of AVF (1). Although the reason for this difference in results is not known, a shorter history of dialysis therapy in the patients in this earlier study (60 ± 67 mo versus 12 ± 8 yr in our case) may partly explain the discrepancy.

Several experimental studies have analyzed the effects of AVF on bone, indicating that it can affect blood flow in the extremity by increasing the blood flow to adjacent bones (21–23). As a result, an increase in bone growth and a subsequent

### Table 1. Reproducibility and precision results

<table>
<thead>
<tr>
<th>Measurement</th>
<th>RMS SD</th>
<th>CV%</th>
<th>LSC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spine</td>
<td>0.008</td>
<td>0.80</td>
<td>0.016</td>
</tr>
<tr>
<td>Total hip</td>
<td>0.005</td>
<td>0.61</td>
<td>0.010</td>
</tr>
<tr>
<td>Forearm 33%</td>
<td>0.010</td>
<td>1.66</td>
<td>0.028</td>
</tr>
<tr>
<td>Forearm total</td>
<td>0.007</td>
<td>2.44</td>
<td>0.019</td>
</tr>
<tr>
<td>Forearm ultradistal</td>
<td>0.009</td>
<td>1.99</td>
<td>0.025</td>
</tr>
</tbody>
</table>

### Table 2. BMD and T- or Z-scores at the lumbar spine and femur

<table>
<thead>
<tr>
<th>Location</th>
<th>Measurement (g/cm²)</th>
<th>All Patients</th>
<th>Group 1 (n = 17)</th>
<th>Group 2 (n = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spine</td>
<td>BMD</td>
<td>1.071 ± 0.225</td>
<td>1.088 ± 0.266</td>
<td>1.062 ± 0.204</td>
</tr>
<tr>
<td></td>
<td>Z-score</td>
<td></td>
<td>−1.4 ± 1.7</td>
<td>−1.4 ± 1.1</td>
</tr>
<tr>
<td></td>
<td>T-score</td>
<td>−1.1 ± 2.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total hip</td>
<td>BMD</td>
<td>0.780 ± 0.080</td>
<td>0.713 ± 0.010</td>
<td>0.848 ± 0.095</td>
</tr>
<tr>
<td></td>
<td>Z-score</td>
<td></td>
<td>−2.7 ± 0.35</td>
<td>−1.0 ± 1.2</td>
</tr>
<tr>
<td></td>
<td>T-score</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 3. BMD and T- or Z-scores at both forearms

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Radius</th>
<th>AVF/Non-AVF Forearm</th>
<th>All Patients</th>
<th>Group I (n = 17)</th>
<th>Group II (n = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Value</td>
<td>Significance</td>
<td>Value</td>
<td>Significance</td>
</tr>
<tr>
<td>BMD (g/cm²)</td>
<td>33%</td>
<td>AVF</td>
<td>0.425 ± 0.080</td>
<td>P &lt; 0.05</td>
<td>0.435 ± 0.061</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Non-AVF</td>
<td>0.454 ± 0.087</td>
<td></td>
<td>0.466 ± 0.074</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean difference</td>
<td>0.029ᵃ</td>
<td>LSC = 0.028</td>
<td>0.031ᵃ</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total</td>
<td>0.429 ± 0.076</td>
<td>P &lt; 0.01</td>
<td>0.420 ± 0.071</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Normal</td>
<td>0.456 ± 0.083</td>
<td></td>
<td>0.453 ± 0.082</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean difference</td>
<td>0.027ᵃ</td>
<td>LSC = 0.019</td>
<td>0.033ᵃ</td>
</tr>
<tr>
<td>Ultradistal</td>
<td></td>
<td>AVF</td>
<td>0.234 ± 0.082</td>
<td>P &lt; 0.05</td>
<td>0.208 ± 0.083</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Normal</td>
<td>0.257 ± 0.090</td>
<td></td>
<td>0.242 ± 0.097</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean difference</td>
<td>0.023</td>
<td>LSC = 0.025</td>
<td>0.034ᵃ</td>
</tr>
<tr>
<td>T- or Z-score</td>
<td>33%</td>
<td>AVF</td>
<td>−2.5 ± 1.0</td>
<td>P &lt; 0.01</td>
<td>−2.3 ± 0.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Normal</td>
<td>−2.1 ± 1.0</td>
<td></td>
<td>−2.0 ± 0.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total</td>
<td>0.7 ± 1.8</td>
<td>P &lt; 0.01</td>
<td>0.0 ± 1.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Normal</td>
<td>1.2 ± 2.0</td>
<td></td>
<td>0.9 ± 2.0</td>
</tr>
<tr>
<td>Ultradistal</td>
<td></td>
<td>AVF</td>
<td>0.7 ± 1.8</td>
<td>P &lt; 0.01</td>
<td>0.0 ± 1.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Normal</td>
<td>1.2 ± 2.0</td>
<td></td>
<td>0.9 ± 2.0</td>
</tr>
</tbody>
</table>

LSC calculated in control group.

ᵃMean difference > LSC; therefore, a statistically significant change.
change in bone structure have been previously reported (14). However, these studies provided no data on the effect of these structural changes on bone mass measurements. Other factors such as immobilization (24), inactivity (25–27), or sympathetic tone (28) could have also had an influence on the AVF forearm BMD measurement.

Some authors reported that DXA cannot be used to make a diagnosis of osteoporosis in patients with end-stage renal failure because of its conflicting results. The reason for these reports may be the compounding effects of superimposed renal osteodystrophy, especially its components such as hyperparathyroid osteosclerosis or metastatic calcifications, both of which may interfere with bone mineral densitometric values or even other unknown factors. But, as previously mentioned, the Clinical Practice Guidelines for Bone Metabolism and Disease in CKD, issued by the National Kidney Foundation, recommend the measurement of BMD in specific patients (6,7) and in determining the response to therapy (12).

Our results have clinical implications, because, depending on the forearm used for BMD measurement, an overdiagnosis (false-positive) of osteoporosis/osteopenia can occur. Indeed, in the study presented here an additional 8 patients (27%) were diagnosed with osteoporosis (n = 4) or osteopenia (n = 4) on the basis of forearm measurement performed only on the AVF forearm. Moreover, in 16 of 19 patients diagnosed with osteoporosis and in all patients diagnosed with osteopenia, AVF forearm was involved. It is important to note that clinical guidelines recommend the nondominant-side forearm BMD assessment (9) in end-stage renal failure because of predominant cortical bone involvement due to associated secondary hyperparathyroidism, which can lead to skeletal fractures (7,29). Of the 63% osteoporotic patients in our group, a greater percentage of individuals was over 50 yr of age (13 patients (7,29). Of the 63% osteoporotic patients in our group, a greater

Figure 1. Pie chart showing the difference in diagnosis (normal, osteopenic, or osteoporotic) when the AVF forearm is included in the BMD result. (Left) Lumbar spine and femur total measurements. (Right) Lumbar spine, femur total radius, and femur 33% radius measurements.

This effect should be taken into account when evaluating patients of this type. Clearly, further studies and longer-term follow-up trials are necessary to confirm these results and to investigate the relationship between AVF forearm BMD and the risk of fractures in hemodialysis patients. If our results can be confirmed by other studies, an amendment to the clinical practice guidelines that specify that forearm DXA should be performed in the nondominant side, except in patients with AVF, needs to be added to prevent false-positive results in hemodialysis patients.

Disclosures
None.

References
10. Lewiecki EM, Watts NB, McClung MR, Petak SM, Bach...


