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● *Original Contribution*

PHALANGEAL QUANTITATIVE ULTRASOUND MEASUREMENTS IN CHRONIC HEMODIALYSIS PATIENTS: A 4-YEAR FOLLOW-UP

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Abstract—In the course of chronic kidney disease, bone metabolism disturbances occur and become aggravated simultaneously with the progression of renal disorder, worsening patients' quality of life. We conducted a 4-year follow-up to assess phalangeal quantitative ultrasound (QUS) measurements in 32 patients undergoing chronic hemodialysis (17 males and 15 females) whose mean ages were 56.3 ± 15.2 years. The QUSs of hand phalanges were performed using DBM 1200 (IGEA, Carpi, Italy) and are expressed as amplitude-dependent speed of sound (Ad-SoS), Z-scores, and T-scores. In comparison with the age-, sex-, and body mass index–adjusted control group, QUS parameters were significantly decreased in all patients undergoing dialysis. During the 4-year follow-up, Ad-SoS and T-scores in all study groups sloped significantly with time. The significant negative relationships between follow-up Ad-SoS results and both baseline and follow-up parathormone values were demonstrated. Our results confirm a high prevalence of bone disturbances in patients undergoing chronic hemodialysis, and they do not improve during renal replacement therapy. The parathormone level seems to be an important agent in influencing bone status, but further studies are needed to understand the other risk factors in kidney-related bone disease. (E-mail: jzywiec@sum.edu.pl) **© 2012 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Chronic kidney disease, Hemodialysis, Osteodystrophy, Phalangeal quantitative ultrasound, Parathormone.**

INTRODUCTION

Skeletal disturbances are common manifestations of many metabolic disorders. Chronic kidney disease (CKD), which is associated with morbidity rates of 11% to 33%, is a global social and medical problem (Palmer et al 2010; Shaheen et al. 2010; Cepoi et al. 2012; Nugent et al. 2011; Obrador et al. 2011; Raimundo and Lopes 2011; Stel et al. 2011). The skeletal damage in patients who have CKD is multifactorial (Gal-Moscovici and Sprague 2007; Sprague 2010). Psychosocial problems and various alimentary abnormalities (*i.e.*, lack of appetite, nausea, vomiting, diarrhea, malabsorption) induce malnutrition, hypoproteinemia, and mineral deficiency (Khalil et al. 2011). The decreased renal function changes both normal calcium-phosphorus balance and vitamin D metabolism, all of which finally result in inappropriate production of the parathyroid hormone (parathormone; PTH). Moreover, persistent low-grade inflammation secondary to comorbidities, frequent infections, and imperfect methods of renal replacement therapy (RRT) disturb mineral and bone homeostasis (McLean 2009; Dukkipati et al. 2010). In consequence, patients with CKD develop chronic renal osteoarthropathy (Rix et al. 1999; Sprague 2010). These pathologic processes become aggravated simultaneously with the progression of renal disorder, contribute to the worsening of the quality of life, and lead to disability. Numerous studies have shown a high prevalence of fractures, even spontaneous fractures, in patients with CKD (Marin et al. 2006; Toussaint et al. 2010; Nickolas et al. 2011). Moreover, pathogenic links between kidney-related bone disease and enhanced vascular calcification resulting in higher mortality rates in patients with CKD have been strongly suggested (Aoki 2009; Ambrus 2010; Dukkipati 2010; Eddington 2010; Raimundo and Lopes 2011). Early screening for and diagnosis of mineral and bone alterations allow for early therapeutic interventions and avoidance of severe disability or premature mortality (Gal-Moscovici and Sprague 2007). Therefore, it is

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important to screen for skeletal-status abnormalities in patients with CKD.

Based on the Clinical Practice Guidelines for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease–Mineral and Bone Disorder (CKD-MBD) (Kidney Disease: Improving Global Outcomes [KDIGO] 2009), the assessment of CKD-MBD in adults should begin at stage 3. This, in essence, is the monitoring of calcium, phosphorus, PTH, and alkaline phosphatase serum levels. The role of bone mineral density (BMD) measurements, by dual-energy x-ray absorptiometry (DXA) or quantitative computed tomography, as a diagnostic tool is not well-established. Although the essence of CKD-MBD is not only low mineral density but also abnormal bone microarchitecture and changes in bone matrix (caused by impaired bone turnover), the bone-mineral content does not correlate well with bone quality and strength. Moreover, arthritis, skeleton deformations, osteophytes, or arterial calcifications could potentially overestimate BMD. Patients with CKD have higher rates of fracture than the general population not only because of diminished bone quantity and quality, but also because of deteriorated general physical condition (low body weight, disturbed neuromuscular function, etc.). These combined causes of fractures, together with the technical limitations of BMD measurements, affect DXA performance in CKD, so it is not recommended routinely (because it could not predict either fracture risk or the type of osteodystrophy) (KDIGO 2009; Jamal et al 2010). The bone biopsy remains the gold standard diagnostic tool for the bone-component of CKD-MBD. However, as an invasive method, its common use is limited.

Starting in the 1990s, quantitative ultrasound (QUS) opened up new avenues for the evaluation of BMD and bone microarchitecture without the use of ionizing radiation and became an alternative method to DXA. This method allows the assessment of such skeletal sites as the calcaneus, radius, tibia, and phalanges and is easy to perform, mobile, relatively inexpensive, and radiation free. Its particular value is the ability to characterize bone-tissue changes in relation to strength and bone architecture. This allows estimation of changes in bone structure better than the standard densitometry studies (Guglielmi et al. 2006). Although DXA, according to the World Health Organization, remains the gold standard for the diagnosis of osteoporosis, QUS may be an alternative tool for predicting risk for future fractures in situations in which DXA availability is limited (Knapp 2009). The combining of clinical risk factors with QUS results improves detection of fracture risk (Durosier et al. 2007). Several studies that compared QUS measurements with DXA in differing populations showed the importance of the former in the analysis of bone status (Montagnani et al. 1999; Gonnelli et al. 2007; Krieg at al. 2008; Guglielmi et al. 2009). In a study by Albanese et al. (2009), phalangeal QUS parameter, amplitude-dependent speed of sound (Ad-SoS), showed high sensitivity to early changes in bone tissue after menopause and the same ability as lumbar-spine BMD in the prediction of fracture risk. Trimpou et al. (2010) examined 80 elderly women with osteoporosis over the 7-year period of the study and showed that QUS performed as well as DXA in all regions. The results of the Arici et al. (2000) study confirmed QUS as a useful substitute for DXA in assessing bone density in patients undergoing hemodialysis. One should also consider that QUS measurements not only express quantity of bone tissue but also reveal some qualitative bone tissue features, such as elasticity and microarchitecture (Njeh et al. 1997). In a study by Sakata at al. (2004), QUS phalangeal measurements were related to BMD and other skeletal properties (*e.g.*, cortical porosity and geometry of medulla). These findings suggest that phalanges may be valuable skeletal sites when assessing the bone status of patients with renal failure.

Whereas the development of skeletal changes begins during early stages of CKD, it is important to recognize the natural history of bone disturbances during the progression of chronic renal injury. Although abnormalities in biochemical and hormonal parameters accompanied by reduced BMD are commonly known, only few follow-up studies have been conducted in nonhomogeneous and small cohorts of patients with CKD (Pečovnik Balon et al. 2002; Pluskiewicz et al. 2003, 2006; Kuo et al. 2010). Our knowledge about bone changes during end-stage renal disease (ESRD) and RRT is also insufficient. Some authors found significant correlations between BMD and duration of dialysis (Pluskiewicz et al. 2002, 2006; Zayour 2004; Binici and Gunes 2010), but no connections were described by others (Arici et al. 2000; Kuo et al. 2010).

According to some studies, BMD decreased simultaneously with length of dialysis duration (Yücel et al. 2004), in contrast to earlier observations in which significant increase in bone density was noted during 3 years of hemodialysis (Eeckhout et al. 1989). In Pluskiewicz's 1-year follow-up study (Pluskiewicz et al. 2006) a decrease in ultrasound parameters was noted.

We conducted a 4-year follow-up study based on phalangeal QUS measurements in patients with ESRD who were undergoing chronic hemodialysis so we could estimate the influence of renal replacement therapy on bone status.

MATERIALS AND METHODS

Patients

We recruited 32 subjects (17 males and 15 females, of whom 5 were premenopausal and 10 were postmenopausal) and used 4-year follow-up QUS measurements