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Brief review

# Advances in the evaluation of bone health in kidney transplant patients☆

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ABSTRACT

Bone disease related to chronic kidney disease and, particularly, to kidney transplant patients is a common cause or morbidity and mortality, especially due to a higher risk of osteoporotic fractures. Despite the fact that this has been known for decades, to date, an appropriate diagnostic strategy has yet to be established. Apart from bone biopsy, which is invasive and scarcely used, no other technique is available to accurately establish the risk of fracture in kidney patients. Techniques applied to the general population, such as bone densitometry, have not been subjected to sufficient external validation and their use is not systematic. This means that the identification of patients at risk of fracture and therefore those who are candidates for preventive strategies is an unmet need.

Bone strength, defined as the ability of the bone to resist fracture, is determined by bone mineral density (measured by bone densitometry), trabecular architecture and bone tissue quality. The trabecular bone score estimates bone microarchitecture, and low values have been described as an independent predictor of increased fracture risk. Bone microindentation is a minimally invasive technique that measures resistance of the bone to micro-cracks (microscopic separation of mineralized collagen fibers), and therefore bone tissue biomechanical properties. The superiority over bone densitometry of the correlation between the parameters measured by trabecular bone score and microindentation with the risk of fracture in diverse populations led us to test its feasibility in chronic kidney disease and kidney transplant patients.



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## Avances en la valoración de la salud ósea en el trasplantado renal

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RESUMEN

La enfermedad ósea asociada a la enfermedad renal crónica, y en particular en el paciente trasplantado renal, representa una causa de frecuente morbimortalidad, sobre todo porque predispone a un mayor riesgo de fractura osteoporótica. Este hecho, bien conocido desde hace décadas, no ha estimulado lo suficiente hasta la fecha el desarrollo de una adecuada estrategia diagnóstica. Si dejamos aparte la biopsia ósea, técnica invasiva y escasamente utilizada, no disponemos de herramientas capaces de estimar de manera precisa el riesgo de fractura en el paciente renal. La escasa validación externa de técnicas aplicadas en la población general como la densitometría ósea hace que su uso tampoco sea sistemático. Por tanto, la identificación de qué pacientes tienen mayor riesgo de fractura y son susceptibles de intervención preventiva es una necesidad no cubierta.

La resistencia ósea, definida como la capacidad del hueso para resistir la fractura, viene determinada por la cantidad de material mineral (medida como densidad mineral ósea por densitometría ósea), la arquitectura trabecular y la calidad del tejido óseo. El score trabecular óseo estima la microarquitectura ósea y valores bajos se han demostrado como predictores independientes de mayor riesgo de fractura. La microindentación ósea es una técnica mínimamente invasiva capaz de medir la resistencia ósea que el hueso opone a la apertura de *micro-cracks* (separación microscópica de fibras de colágena mineralizada), y con ello, las propiedades biomecánicas del tejido óseo. La buena correlación con el riesgo de fractura de los parámetros medidos con el score trabecular óseo o la microindentación en diversas poblaciones, superior a la propia densitometría ósea, nos ha estimulado a desarrollar su potencial aplicación en los pacientes con enfermedad renal crónica y trasplantados renales.



## Introduction

Achieving bone health in the population with chronic kidney disease (CKD) is a unresolved issue. The guidelines suggest that bone health should be evaluated using spine Z-ray for screening of asymptomatic vertebral fractures or bone densitometry (dual X-ray absorptiometry, DXA) to determine of bone mineral density (BMD).[1–3] However, BMD is not the only feature that makes the bone able to absorb the energy of an impact and prevent a bone fracture. Other properties such as bone microarchitecture or the quality of bone tissue are determinants of bone resistance to fracture. Furthermore, although there is a good correlation between BMD and the risk of fracture in the general population, the validation of DXA as a reference diagnostic technique in the renal population has not been fully established, so it is not performed as a routine in clinical practice.[4]

We have reviewed the various diagnostic strategies to evaluate bone health in renal patients, with special interest in the kidney transplant (KT) recipient.

## Justification: bone disease and fractures after kidney transplantation

The bone mineral disease in CKD patients is characterized by abnormalities in bone turnover, mineralization and bone density, which cause bone fragility and an increased risk of fractures.[2] In the transplant patient, bone disease has its own peculiarities that are associated to the recovery of renal function, persistent hyperparathyroidism[5] and immunosuppressive treatment which is inherent in the transplant process.[6]

The main alteration in bone remodeling after renal transplantation is the reduction in bone formation and mineralization, with a persistent predominance of resorption. In fact, during the first 6 months after transplantation, there is a rapid decrease in BMD,[7] which is subsequently attenuated,[8] most likely related to the decrease in the dose of steroids. As a result, a high risk of fracture has been described in patients after KT (Tables 1 and 2),[9–23] which, initially, is even higher than that in dialysis patients.[12] In addition, it has been proven that this increase in risk persists in the late post-transplant period.[17]

## State of the art: diagnosis of bone disease in the kidney transplant patient

Evaluation of bone health in the renal patient is key to estimate the risk of fracture. Laboratory measurements such as bone remodeling markers, or invasive procedures such as bone biopsy are available for assessment of bone health, but it is not clear which diagnostic tests best predict the risk of fracture. Unlike in the general population, risk scales or DXA have a much more limited predictive power.