



## Original article

# Feasibility of measurement of bone turnover markers in female patients with systemic lupus erythematosus



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## ABSTRACT

**Objective:** To investigate the feasibility of bone turnover markers for the assessment of bone metabolism in patients with systemic lupus erythematosus, according to the guidelines of the International Osteoporosis Foundation and the International Federation of Clinical Chemistry and Laboratory Medicine.

**Methods:** The study included 43 female systemic lupus erythematosus patients. Serum procollagen type I N propeptide, C-terminal telopeptide of type I collagen, osteocalcin, parathyroid hormone, 25-hydroxyvitamin D2 and 25-hydroxyvitamin D3, anti-cardiolipin, anti-dsDNA, and anti-nucleosome levels were measured.

**Results:** Procollagen type I N propeptide and C-terminal telopeptide of type I collagen levels were elevated in systemic lupus erythematosus patients aged >45 in comparison to those aged <45, although with borderline significance ( $p=0.05$ , respectively). Correlations were found between bone turnover markers: the strongest being between procollagen type I N propeptide and osteocalcin ( $r=0.69$ ,  $p<0.05$ ). Procyclagen type I N propeptide and osteocalcin were found to be associated with parathyroid hormone ( $r=0.3$ ,  $r=0.29$ , respectively,  $p<0.05$ ). Age correlated with procollagen type I N propeptide ( $r=0.23$ ,  $p<0.05$ ). Elevated procollagen type I N propeptide was found more frequently than elevated osteocalcin or C-terminal telopeptide of type I collagen, both in patients aged <45 ( $p=0.001$ ) and >45 ( $p<0.001$ ). No significant difference in procollagen type I N propeptide, osteocalcin or C-terminal telopeptide of type I collagen levels was found with respect to season, neither in the entire systemic lupus erythematosus group nor in the under-45 or over-45 groups. Previous glucocorticoid treatment was not associated with difference in bone turnover markers.

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**Conclusions:** Increased bone turnover markers in systemic lupus erythematosus appear to predominantly reflect the pattern of bone remodeling related to age. Increased procollagen type I N propeptide is expected to be the most frequent outcome among bone turnover markers. Better diagnoses of bone disturbances with bone turnover markers performed in accordance with international reference standards need to be included in the approach to systemic lupus erythematosus patients, in addition to bone mineral density assessment.

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## Viabilidade da mensuração de marcadores de remodelação óssea em mulheres com lúpus eritematoso sistêmico

### RESUMO

#### Palavras-chave:

Remodelação óssea  
Lúpus eritematoso sistêmico  
Procolágeno  
Osteocalcina  
Vitamina D

**Objetivo:** Investigar a viabilidade dos marcadores de remodelação óssea (MRO) na avaliação do metabolismo ósseo em pacientes com lúpus eritematoso sistêmico (LES), de acordo com as diretrizes da International Osteoporosis Foundation e da International Federation of Clinical Chemistry and Laboratory Medicine.

**Métodos:** O estudo incluiu 43 pacientes do sexo feminino com LES. Foram medidos os níveis séricos de propeptídeo N-terminal do procolágeno tipo I (PINP), telopeptídeo C-terminal do colágeno tipo I (CTX), osteocalcina, HPT, 25(OH)D, anticorpos anticardiolipina, antidsDNA e antinucleossomo.

**Resultados:** Os níveis de PINP e CTX estavam elevados em pacientes com LES com idade >45, em comparação com aqueles com idade <45 anos, embora com significância estatística limítrofe ( $p=0,05$ ). Foram encontradas correlações entre os MRO: a mais forte foi entre o PINP e a osteocalcina ( $r=0,69$ ,  $p<0,05$ ). Encontrou-se que o PINP e a osteocalcina estão correlacionados com o HPT ( $r=0,3$ ,  $r=0,29$ , respectivamente,  $p<0,05$ ). A idade estava correlacionada com o PINP ( $r=0,23$ ,  $p<0,05$ ). Valores elevados de PINP foram encontrados em maior frequência do que valores elevados de osteocalcina ou CTX, tanto em pacientes com idade <45 ( $p=0,001$ ) quanto >45 ( $p<0,001$ ). Não houve diferença estatisticamente significativa nos níveis de PINP, osteocalcina ou CTX com relação à estação do ano, nem em todo o grupo de pacientes com LES, nem naqueles com mais ou menos de 45 anos. O uso prévio de glucocorticoides não esteve associado a diferenças nos MRO.

**Conclusões:** O aumento nos MRO no LES parece refletir predominantemente o padrão de remodelação óssea relacionado com a idade. Pode-se esperar que o PINP aumentado seja o desfecho mais comumente encontrado entre os MRO. É necessário incluir melhores diagnósticos de distúrbios ósseos com MRO, feitos de acordo com as normas internacionais de referência, na abordagem de pacientes com LES, além de avaliar a densidade mineral óssea.

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## Introduction

In 2011, the International Osteoporosis Foundation (IOF) and the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) stated that assessment of a marker of bone formation, serum procollagen type I N propeptide (PINP), and a marker of bone resorption, serum C-terminal telopeptide of type I collagen (CTX), provided reference parameters for bone turnover markers (BTMs) in clinical studies.<sup>1</sup> Increased serum concentration of BTMs may predict fracture risk in postmenopausal women, independent of bone mineral density (BMD) measurements.<sup>1</sup> High bone turnover may be associated not only with bone loss, resulting in a low BMD, but also with the deterioration of bone architecture not detected in bone mass assessment.<sup>1</sup> Bone strength is determined by both BMD and bone quality.<sup>2</sup> Apart from BMD, bone quality depends mainly on micro-architecture and bone turnover.<sup>2</sup>

Osteoporosis, and consequently indication for treatment, is diagnosed either clinically on the basis of fractures following low energy trauma, or in the pre-fracture stage by assessment of clinical risk factors associated with densitometry and bone metabolism.<sup>3</sup>

In a recent study of Mak et al. conducted on 45 patients with systemic lupus erythematosus (SLE), a high 10-year fracture risk was found in 16% of patients and in 2% of healthy controls.<sup>4</sup> Demonstration of a high (>20%) individual 10-year absolute fracture risk is the criterion for initiation of pharmacological treatment.<sup>3</sup> As pregnancy is an absolute contraindication to dual X-ray absorptiometry (DXA) in the assessment of BMD, and female SLE patients of child-bearing age may be apprehensive of densitometry, compliance might be limited. Under such circumstances, BTM analysis would appear to be a practical alternative, as samples of blood are easily collected and the procedure is relatively noninvasive.<sup>1</sup> BTMs have been used in clinical researches for many years,

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