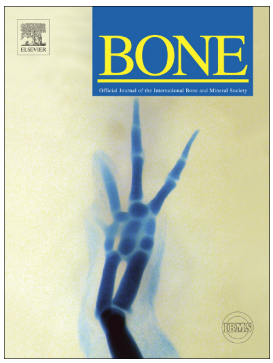

The 24-hour serum profiles of bone markers in healthy older men and women

Evie van der Spoel, Nicole Oei, Ricardo Cachucho, Ferdinand Roelfsema, Jimmy F.P. Berbée, Gerard J. Blauw, Hanno Pijl, Natasha M. Appelman-Dijkstra, Diana van Heemst

PII:	S8756-3282(18)30366-1
DOI:	doi:10.1016/j.bone.2018.10.002
Reference:	BON 11768
To appear in:	*Bone*
Received date:	1 June 2018
Revised date:	28 September 2018
Accepted date:	3 October 2018

Please cite this article as: Evie van der Spoel, Nicole Oei, Ricardo Cachucho, Ferdinand Roelfsema, Jimmy F.P. Berbée, Gerard J. Blauw, Hanno Pijl, Natasha M. Appelman-Dijkstra, Diana van Heemst , The 24-hour serum profiles of bone markers in healthy older men and women. Bon (2018), doi:10.1016/j.bone.2018.10.002

The 24-hour serum profiles of bone markers in healthy older men and women

Evie van der Spoel[1], Nicole Oei[2,3], Ricardo Cachucho[1,4], Ferdinand Roelfsema[5], Jimmy F.P. Berbée[5], Gerard J. Blauw[1], Hanno Pijl[5], Natasha M. Appelman-Dijkstra[5], Diana van Heemst[1]

[1]Section Gerontology and Geriatrics, Department of Internal Medicine, Leiden University Medical Center, Leiden, The Netherlands
[2]Department of Developmental Psychology (ADAPT-lab), Institute of Psychology, University of Amsterdam, Amsterdam, The Netherlands
[3]Amsterdam Brain and Cognition, University of Amsterdam, Amsterdam, The Netherlands
[4]Section Molecular Epidemiology, Department of Biomedical Data Sciences, Leiden University Medical Center, Leiden, The Netherlands
[5]Section Endocrinology, Department of Internal Medicine, Leiden University Medical Center, Leiden, The Netherlands

Correspondence: Evie van der Spoel, Section Gerontology and Geriatrics, Department of Internal Medicine, Leiden University Medical Center, PO Box 9600, 2300 RC, Leiden, The Netherlands. Tel.: +31(0)71 5266640; fax: +31(0)71 5248159; e-mail: e.van_der_spoel@lumc.nl

Abstract
The process of bone turnover displays variations over 24 hours, with C-terminal cross-linked telopeptide of type 1 collagen (CTX) and osteocalcin exhibiting a nadir in the afternoon and a peak in the night. In contrast, N-terminal propeptide of type 1 procollagen (P1NP) did not display an apparent 24-hour rhythm. Other emerging novel biomarkers of bone, sclerostin and Dickkopf-related protein 1 (DKK1), are markers of osteocyte activity with limited data available regarding their 24-hour profiles. In this study, we aimed to extend available data on 24-hour profiles of CTX, osteocalcin, and P1NP and to assess the 24-hour profiles of sclerostin and DKK1 in healthy older men and women and to compare these between men and women. We measured these five bone markers in EDTA plasma collected every 4 hours during 24 hours in 37 healthy older men and women (range 52–76 years). Differences between time points were determined using repeated measures ANOVA and cosinor analyses were performed to determine circadian rhythmicity. The circadian rhythm of CTX was confirmed by the cosinor model, with women showing larger amplitude compared to men. Osteocalcin showed higher levels during night-time compared to daytime in both men and women. For P1NP levels we observed a small but significant increase in the night in men. Sclerostin and DKK1 did not show a circadian rhythm, but sclerostin levels differed between time points. Because of the large intraindividual variation, DKK1 as measured in this study cannot be considered a reliable marker for diagnostic or research purposes. In conclusion, when measuring CTX, osteocalcin, P1NP, or sclerostin either in clinical practice or in a research setting, one should consider the 24-hour profiles of these bone markers.

Key words
Bone markers; circadian rhythm; 24-hour profile; cosinor analysis; sex differences