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## Increased osteoclastic activity as shown by increased sRANK-L/OPG ratio in boys with hemophilia

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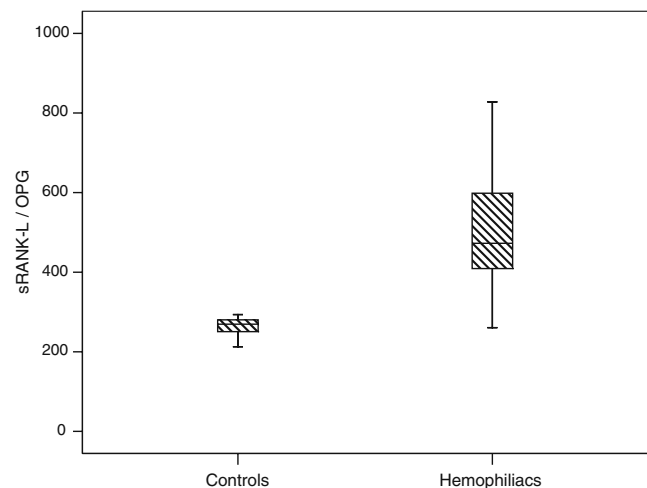
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Dear Editor,

We read with interest the report by Katsarou et al. that originally assessed biochemical bone markers in patients with hemophilia and correlated these results to clinical and laboratory parameters [1]. As we have recently measured, bone markers in our hemophilic patients and our results differ significantly with those already released; we would like to report our experience. In 27 hemophilic boys with a mean decimal age of  $11.63 \pm 4.66$  years (range: 4–17 years) and 25 age-matched male controls (mean decimal age:  $11.45 \pm 5.26$  years), levels of soluble receptor activator of nuclear factor  $\kappa$ B ligand (sRANK-L), osteoprotegerin (OPG) and osteocalcin (OC) were measured in serum. All samples were deep frozen after immediate centrifugation until the day of measurement. Enzyme-linked immunosorbent assays were used for the determination of bone markers: sRANK-L (total), Biovendor Laboratorni Medicina, Modrice, Czech Republic; OPG, Biomedica Medizinprodukte GmbH & Go, Vienna, Austria; OC, Bender MedSystems GmbH, Vienna, Austria. Our results demonstrate that, compared to controls, patients with hemophilia have significant higher serum levels of sRANK-L ( $395.86 \pm 90.60$  vs.  $297.25 \pm 36.46$  pmol/l,  $p=0.001$ ) and of OC ( $5.31 \pm 2.26$  vs.  $3.09 \pm 0.61$  ng/ml,  $p=0.001$ ) and significantly decreased levels of OPG ( $0.78 \pm 0.13$  vs.  $1.19 \pm 0.22$  pmol/l,  $p<0.001$ ). These result to an even more striking difference of the ratio sRANK-L/OPG between patients and controls ( $527.27 \pm 181.51$  vs.  $256.24 \pm 45.01$ ,  $p<0.001$ , Fig. 1).

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Our results indicate an increased osteoclastic activity followed by a compensatory up-regulated osteoblastic function and further substantiate the common pathogenetic mechanism that both hemophilic and rheumatoid arthritis share [2, 3]. In the study by Katsarou et al. [1], serum sRANK-L and OPG levels did not differ significantly between patients and controls, whereas OC levels were significantly decreased in hemophiliacs, in contrast to our results. In that study, an up-regulated osteoclastic activity in hemophiliacs was shown by the increased levels of N-terminal and C-terminal cross-linking telopeptide of collagen type I (NTX and CTX); the latter was also found in the recent study by Jansen et al. [4]. Further studies are warranted to elucidate the exact mechanism of the hemophilic arthropathy and translate this knowledge into potential therapeutic options.



**Fig. 1** Significantly increased sRANK-L/OPG ratio on patients with hemophilia compared to controls ( $527.27 \pm 181.51$  vs.  $256.24 \pm 45.01$ ,  $p<0.001$ )

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