

Associations of Impaired Sensation with Bone Turnover Markers in Patients Undergoing Surgical Repair for Hip Fracture

Jan M. Hughes-Austin¹, Lauren Claravall¹, William T. Kent¹, Paul Girard¹, Alexandra Schwartz¹, Renata Pereira², Isidro Salusky², Ronit Katz³, Sameer B. Shah¹ and Joachim H. Ix⁴

1. Department of Orthopaedic Surgery, University of California, San Diego, 2. Department of Pediatric Nephrology, University of California Los Angeles, 3. Department of Obstetrics and Gynecology, University of Washington 4. Department of Medicine, University of California, San Diego

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INTRODUCTION: The peripheral nervous system contributes to the regulation of bone turnover. However, clinical evidence in support of such association as well as insight into biological pathways underlying this association is sparse. We therefore sought to determine whether bone turnover markers at the hip differed in patients with impaired sensation compared to those with intact sensation in the distal lower extremity. Considering additional influences of chronic kidney disease (CKD) and diabetes on peripheral nerve function and bone turnover, we also evaluated whether these conditions modulated associations between sensory function and bone turnover.

METHODS: This cross-sectional study included patients ages 18 years or older who were admitted to our institution for surgical repair of hip fracture from January 2021 to present. Of 55 patients recruited thus far, 29 had complete measures of bone turnover and results for testing sensation to light touch along the sural/saphenous/superficial peroneal nerve/deep peroneal nerve/tibial nerve distributions. Impaired sensation was determined based on surgeon testing and reporting of 'sensation intact to light touch' or 'SILT.' Static bone turnover parameters were determined by histomorphometry with bone biopsies from the femoral head (n=22) or greater trochanter (n=7). We used nomenclature in accordance with recommendations from the ASBMR Histomorphometric Nomenclature Committee for bone turnover markers (Table 1 legend). We log transformed bone turnover markers to approximate a normal distribution and used analysis of covariance to evaluate associations between intact vs impaired sensation and bone turnover markers, adjusting individually for estimated glomerular filtration rate for kidney function (as defined by the CKD-EPI Creatinine Equation 2021) and diabetes status (defined by use of insulin or diabetes diagnosis) in distinct models. This study was approved by the Institutional Review Board and all patients provided written consent.

RESULTS: Average age was 78 ± 12, 62% were women, 72% were white, 7% were Asian, and 21% were another or more than one race; 28% were of Hispanic/Latino ethnicity, 55% had CKD, and 48% had diabetes. Among the 24% with impaired sensation, median values for static bone turnover markers were lower, whereas OV/BV was higher (Table 1). Even after adjusting for kidney function and diabetes, static bone turnover markers were lower in patients with impaired sensation, although this difference was not statistically significant (Table 2). Sclerostin expression by tissue area was approximately 23% lower in those with impaired sensation. This relative difference varied from 27% lower when adjusted for kidney function to 9% lower when adjusted for diabetes. (Table 2).

DISCUSSION: In this pilot study, patients who have experienced hip fracture and have impaired sensation demonstrate lower concentrations of static bone turnover markers and sclerostin. Kidney function may affect the magnitude of these associations.

SIGNIFICANCE/CLINICAL RELEVANCE: Impaired sensation may affect bone turnover. Earlier screening of sensory function may guide therapeutic intervention.

Table 1.

	Intact Sensation	Impaired Sensation
N	22	7
OV/BV, %	0.08 [0.04, 0.30]	0.30 [0.03, 0.60]
BV/TV, %	17.60 [10.51, 21.80]	14.50 [8.76, 14.71]
Ob.S/BS, %	0.05 [0, 0.16]	0 [0, 0.63]
Oc.S/BS, %	0.02 [0, 0.06]	0.005 [0, 0.06]
Sclerostin/T.Ar, %	6.05 [1.99, 16.78]	2.89 [1.24, 7.68]
Sclerostin/B.Ar, %	39.05 [21.57, 87.99]	25.25 [14.22, 46.66]

median [25th, 75th percentile]

OV/BV = Osteoid volume, BV/TV = bone volume, Ob.S/BS = osteoblast surface, Oc.S/BS = osteoclast surface, Sclerostin/T.Ar. = sclerostin expressed by tissue area, Sclerostin/B.Ar. = sclerostin expressed by bone area

Table 2.

	Unadjusted			Adjusted for Kidney Function			Adjusted for Diabetes		
	RD	95% CI		RD	95% CI		RD	95% CI	
OV/BV	1.23	[0.67, 2.09]		1.34	[0.71, 2.30]		1.2	[0.65, 2.04]	
BV/TV	0.89	[0.54, 1.39]		0.86	[0.51, 1.36]		0.9	[0.54, 1.41]	
Ob.S/BS	0.88	[0.43, 1.60]		0.93	[0.44, 1.74]		0.87	[0.42, 1.59]	
Oc.S/BS	0.91	[0.72, 1.14]		0.95	[0.47, 1.19]		0.92	[0.72, 1.15]	
Sclerostin/T.Ar.	0.77	[0.25, 1.85]		0.73	[0.22, 1.81]		0.81	[0.25, 1.99]	
Sclerostin/B.Ar.	1.04	[0.26, 2.87]		0.97	[0.23, 2.78]		1.08	[0.26, 3.06]	

RD=Relative Difference for patients with impaired sensation. For example, OV/BV RD=1.23 is interpreted as a 23% higher OV/BV for patients with impaired sensation.