

SUPPLEMENTAL DATA

Mild hyponatremia is not associated with degradation of trabecular bone microarchitecture despite bone mass loss

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Supplementary Table 1. Multivariable ordered logistic regression analysis for the prediction of normal bone density (T-score > -1), osteopenia (T-score > -2.5 and ≤ -1) or osteoporosis (T-score ≤ -2.5) as ordered categorical outcomes at lumbar spine, total hip and femoral neck. Effect sizes are reported in terms of proportional odds ratio. Significant p-values are highlighted in bold. Abbreviations: 25OH-VitD, 25-hydroxyvitamin D; BMI, body mass index; CI, confidence interval; CKD G4-G5, chronic kidney disease stage G4-G5; GC, glucocorticoid; pOR, proportional odds ratio; ref, reference.

Parameter	Lumbar spine T-score category			Total hip T-score category			Femoral neck T-score category		
	pOR	95%CI	p-value	pOR	95%CI	p-value	pOR	95%CI	p-value
Hyponatremia	0.64	(0.37, 1.10)	0.101	1.59	(1.06, 2.37)	0.025	1.30	(0.78, 2.16)	0.300
Age (per 10 years increase)	1.39	(1.27, 1.53)	<0.001	1.92	(1.66, 2.23)	<0.001	2.02	(1.80, 2.28)	<0.001
Female sex	3.51	(2.92, 4.22)	<0.001	6.98	(5.79, 8.40)	<0.001	3.41	(2.83, 4.10)	<0.001
Race/ethnicity									
Non-Hispanic White	1 (ref)			1 (ref)			1 (ref)		
Non-Hispanic Black	0.51	(0.39, 0.66)	<0.001	0.56	(0.39, 0.82)	0.004	0.37	(0.28, 0.48)	<0.001
Hispanic	1.93	(1.41, 2.63)	<0.001	0.88	(0.63, 1.23)	0.456	0.86	(0.62, 1.21)	0.375
Other	2.01	(1.27, 3.19)	0.004	0.82	(0.41, 1.65)	0.572	0.98	(0.50, 1.94)	0.959
Current smoking	1.32	(1.02, 1.71)	0.038	1.97	(1.49, 2.60)	<0.001	1.37	(1.14, 1.63)	0.001
BMI category									
Normal weight	1 (ref)			1 (ref)			1 (ref)		
Overweight	0.54	(0.41, 0.72)	<0.001	0.31	(0.26, 0.37)	<0.001	0.39	(0.32, 0.47)	<0.001
Obesity	0.33	(0.27, 0.41)	<0.001	0.17	(0.12, 0.24)	<0.001	0.17	(0.13, 0.23)	<0.001
Underweight	3.42	(1.55, 7.52)	0.003	4.84	(1.92, 12.21)	0.002	2.43	(1.11, 5.31)	0.028
25OH-VitD (per 10 ng/mL increase)	0.86	(0.77, 0.96)	0.008	0.83	(0.70, 0.98)	0.027	0.77	(0.68, 0.87)	<0.001
Diabetes mellitus	0.85	(0.64, 1.13)	0.253	0.96	(0.67, 1.37)	0.814	0.88	(0.73, 1.06)	0.168
CKD G4-G5	1.08	(0.68, 1.70)	0.733	1.90	(1.01, 3.56)	0.046	2.14	(1.12, 4.07)	0.022
Loop diuretics	1.22	(0.80, 1.87)	0.346	1.66	(1.08, 2.56)	0.022	1.26	(0.77, 2.07)	0.344
Thiazide diuretics	0.81	(0.63, 1.04)	0.100	0.88	(0.68, 1.13)	0.307	0.79	(0.61, 1.02)	0.064
Potassium-sparing diuretics	0.77	(0.49, 1.21)	0.247	0.77	(0.46, 1.29)	0.313	0.73	(0.46, 1.16)	0.176
History of chronic GC treatment	0.84	(0.48, 1.48)	0.538	0.97	(0.56, 1.68)	0.916	1.19	(0.85, 1.67)	0.308

Supplementary Table 2. Sensitivity analyses for the prediction of T-score at lumbar spine, total hip and femoral neck. In Model 1, patients actively treated with anti-osteoporotic drugs (n=243) were excluded. In Model 2, patients were reclassified as hyponatremic or normonatremic according to glucose-corrected sodium values (maintaining <135 mmol/L as the threshold for the definition of hyponatremia). In Model 3, low plasma osmolality (<275 mOsm/kg) was considered as a predictor instead of hyponatremia. All models are adjusted for the same set of covariates as the primary analysis. Significant p-values are highlighted in bold. Abbreviations: CI, confidence interval; β -coeff, β -coefficient.

Parameter	Lumbar spine T-score			Total hip T-score			Femoral neck T-score		
	β -coeff.	95%CI	p-value	β -coeff.	95%CI	p-value	β -coeff.	95%CI	p-value
Model 1									
Hyponatremia	+0.15	(-0.14, +0.43)	0.303	-0.22	(-0.41, -0.02)	0.030	-0.11	(-0.33, +0.11)	0.299
Model 2									
Hyponatremia (glucose-corrected)	+0.24	(-0.09, +0.57)	0.146	-0.12	(-0.31, +0.07)	0.215	+0.02	(-0.19, +0.24)	0.835
Model 3									
Low plasma osmolality	+0.09	(-0.07, +0.26)	0.261	-0.01	(-0.13, +0.11)	0.824	+0.05	(-0.07, +0.16)	0.424

Supplementary Table 3. Sensitivity analyses for the prediction of TBS. In Model 1, patients actively treated with anti-osteoporotic drugs (n=243) were excluded. In Model 2, patients were reclassified as hyponatremic or normonatremic according to glucose-corrected sodium values (maintaining <135 mmol/L as the threshold for the definition of hyponatremia). In Model 3, low plasma osmolality (<275 mOsm/kg) was considered as a predictor instead of hyponatremia. All models are adjusted for the same set of covariates as the primary analysis. Significant p-values are highlighted in bold. Abbreviations: CI, confidence interval; TBS, trabecular bone score; β -coeff, β -coefficient.

Parameter	Lumbar spine TBS		
	β -coeff.	95%CI	p-value
Model 1			
Hyponatremia	+0.016	(-0.011, +0.042)	0.242
Model 2			
Hyponatremia (glucose-corrected)	+0.017	(-0.010, +0.044)	0.211
Model 3			
Low plasma osmolality	+0.005	(-0.004, +0.015)	0.266