

Table S1: Baseline characteristics of beta-1 selective blockers versus non-selective beta-blocker users

Characteristics	Beta-1 selective blockers (N=23)	Non-selective beta-blocker users (N=48)	<i>p</i> -Value
Age, years, mean (SD)	66.6 (11.0)	62.7 (17.5)	0.34
Female, <i>n</i> (%)	13 (56.5)	29 (60.4)	0.80
BMI, kg/m ² , mean (SD)	23.6 (4.6)	25.0 (5.3)	0.26
Alcohol, <i>n</i> (%)			0.76
• Never	18 (78.3)	33 (68.8)	
• Current	1 (4.3)	4 (8.3)	
• Former	4 (17.4)	11 (22.9)	
Former Smoking, <i>n</i> (%)	4 (17.4)	6 (12.5)	0.72
Underlying disease, <i>n</i> (%)			
• Dyslipidemia	12 (52.2)	28 (58.3)	0.80
• Ischemic stroke	0 (0)	6 (12.5)	0.17
• Ischemic heart disease	7 (30.4)	10 (20.8)	0.40
• Gout	3 (13.0)	7 (14.6)	1.00
• Hypertension	23 (100.0)	43 (89.6)	0.17
• Diabetes mellitus	8 (34.8)	27 (56.2)	0.13
• Atrial fibrillation	2 (8.7)	2 (10.4)	1.00
Dialysis vintage, months, median (IQR)	38.0 (22.0-67.0)	28.5 (16.0-64.5)	0.28
Antihypertensive drugs, <i>n</i> (%)			
• ACEi	1 (4.3)	2 (4.2)	1.00
• ARB	8 (34.8)	21 (43.8)	0.61
• Alpha - 1 blocker	5 (21.7)	14 (29.2)	0.58
• CCB	18 (78.3)	35 (72.9)	0.77
• Vasodilator	9 (39.1)	12 (25.0)	0.27
Statin, <i>n</i> (%)	16 (69.3)	32 (66.7)	1.00
Non-calcium-based phosphate binder, <i>n</i> (%)	3 (13.0)	7 (14.6)	1.00
Active vitamin D, <i>n</i> (%)	13 (56.5)	20 (41.7)	0.31
Laboratory			
• Calcium, mg/dL, median (IQR)	9.0 (8.25-9.46)	9.0 (8.5-9.4)	0.89
• Phosphate, mg/dL, median (IQR)	4.7 (3.85-5.6)	4.5 (3.85-5.17)	0.64
• PTH, pg/mL, median (IQR)	457.0 (327.0-782.4)	457.9 (300.9-624.0)	0.66
• PTH level, <i>n</i> (%)			0.054
PTH < 120 pg/mL	2 (8.7)	0 (0)	
PTH 120-585 pg/mL	12 (52.2)	37 (70.8)	
PTH > 585 pg/mL	9 (39.1)	14 (29.2)	
• ALP, U/L, median (IQR)	96.0 (69.0-154.0)	82 (65.7-113.5)	0.14
• ALP level, <i>n</i> (%)			1.00
ALP ≤ 120 U/L	40(70.18)	50(70.42)	
ALP > 120 U/L	17(29.82)	21(29.58)	
• Vitamin D, ng/mL, median (IQR)	41.8 (30.1-51.2)	34.8 (24.8-48.4)	0.25

• Bicarbonate, mEq/L, median (IQR)	24.0 (23.3-24.7)	25.0 (23.8-26.5)	0.03
• nPCR, g/kg/day, median (IQR)	1.1 (1.0-1.2)	1.1 (0.9-1.3)	0.90
• URR, %, median (IQR)	80.7 (79.0-84.0)	80.2 (78.0-83.6)	0.45
• Albumin, g/dL, median (IQR)	3.6 (3.4-3.8)	3.7 (3.5-3.9)	0.34
Bone turnover*, <i>n</i> (%)			0.18
• High turnover	4 (17.4)	8 (16.7)	
• Low turnover	2 (8.7)	0 (0)	
• Undetermined	17 (73.9)	40 (83.3)	

Abbreviation: ACEi, angiotensin-converting enzyme inhibitor; ALP, alkaline phosphatase; ARB, angiotensin II receptor blocker; BMI, body mass index; CCB, calcium channel blockers; nPCR, normalized protein catabolic rate; PTH, parathyroid hormone; URR, urea reduction ratio

*high turnover defined as high PTH and ALP, low turnover defined as low PTH and ALP, undetermined defined as high PTH with low ALP or low PTH with high ALP

Table S2: Comparison of BMD and incidence of osteoporosis between beta-blocker and control group

BMD	Total (N=128)	Control group (N=57)	Beta-blocker group (N=71)	<i>p</i>-Value (Control VS BB)
Total Lumbar spine				
BMD, median [IQR]	0.92 [0.78-1.08]	0.93 [0.79-1.05]	0.91 [0.77-1.10]	0.88
T-score, median [IQR]	-0.85 [-2.00 to 0.55]	-0.7 [-1.90 to 0.30]	-0.90 [-2.10 to 0.80]	0.91
Osteoporosis, <i>n</i> (%)	21 (16.4)	9 (15.8)	12 (16.9)	1.00
Femoral neck				
BMD, median [IQR]	0.59 [0.49-0.70]	0.59 [0.50-0.70]	0.57 [0.46-0.67]	0.21
T-score, median [IQR]	-2.05 [-2.90 to -1.10]	-2.0 [-2.80 to -1.00]	-2.20 [-3.00 to -1.20]	0.39
Osteoporosis, <i>n</i> (%)	46 (35.94)	18 (31.6)	26 (36.6)	0.58
Total hip				
BMD, median [IQR]	0.71 [0.60-0.84]	0.73 [0.61-0.85]	0.70 [0.58-0.83]	0.38
T-score, median [IQR]	-1.40 [-2.20 to -0.30]	-1.40 [-2.10 to -0.50]	-1.50 [-2.30 to -0.20]	0.59
Osteoporosis, <i>n</i> (%)	23 (17.97)	9 (15.8)	14 (19.7)	0.65
1/3 Radius				
BMD, median [IQR]	0.65[0.51-0.71]	0.68[0.51-0.72]	0.64[0.52-0.71]	0.40
T-score, median [IQR]	-2.00 [-2.95 to -0.75]	-2.00 [-2.90 to -0.70]	-2.1 [-3.10 to -0.80]	0.74
Osteoporosis, <i>n</i> (%)	45 (35.16)	19(33.33)	26(36.62)	0.71
Osteoporosis				
Osteoporosis any, <i>n</i> (%)	64 (50.00)	27 (47.37)	37 (52.11)	0.72

BB, beta-blocker users; BMD, bone mineral density

Table S3: Association of BMD with beta-blocker subtypes

Site of BMD	Multivariate analyses			
	Beta-1 selective blocker		Non-selective beta-blocker	
	Model A	Model B	Model A	Model B
	Coefficient (95%CI) <i>p</i>-Value	Coefficient (95%CI) <i>p</i>-Value	Coefficient (95%CI) <i>p</i>-Value	Coefficient (95%CI) <i>p</i>-Value
Total Spine	-0.04 (-0.79 to 0.71) 0.92	0.01 (-0.75 to 0.75) 0.997	0.06 (-0.54 to 0.66) 0.84	0.08 (-0.53 to 0.69) 0.80
Femoral Neck	-0.17 (-0.33 to -0.005) 0.04	-0.16 (-0.33 to 0.003) 0.054	-0.01 (-0.014 to 0.12) 0.83	-0.01 (-0.15 to 0.12) 0.83
Total Hip	-0.003 (-0.10 to 0.10) 0.95	-0.003 (-0.10 to 0.10) 0.95	0.0009 (-0.08 to 0.08) 0.98	0.001 (-0.08 to 0.8) 0.98
1/3 Radius	0.009 (-0.04 to 0.06) 0.72	0.01 (-0.04 to 0.06) 0.65	0.02 (-0.04 to 0.04) 0.92	0.002 (-0.04 to 0.04) 0.92

BMD, bone mineral density

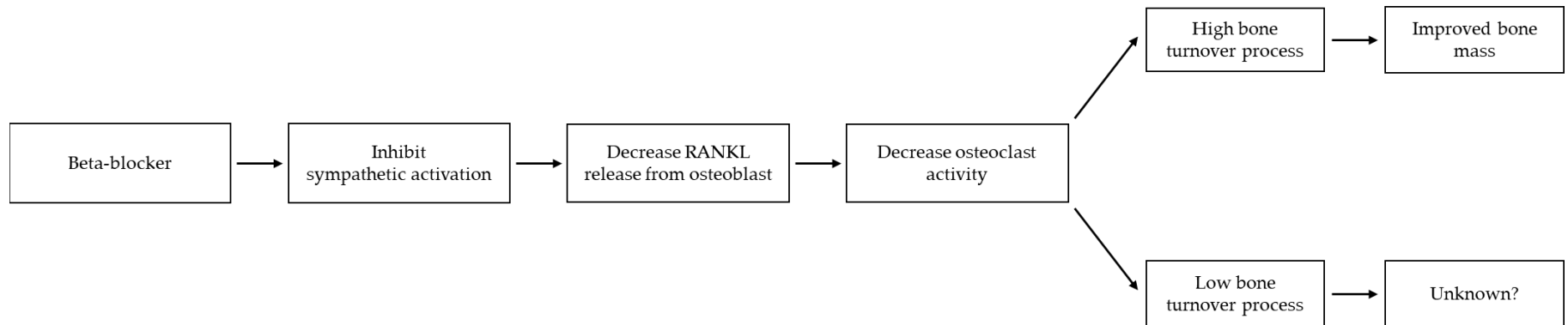


Figure S1: Potential mechanism of beta-blocker use and bone remodeling in hemodialysis patients.

Beta-blocker decreases bone remodeling via inhibition of sympathetic activation and decrease RANKL releasing from osteoblast which results in decreasing osteoclast activity. This mechanism potentially has beneficial effect in patients with high bone turnover, however the exact effect is still unknown in patients with low bone turnover. RANKL, the Receptor Activator of Nuclear factor Kappa-B Ligand