Supplementary Material

Association of circulating osteoprotegerin level with blood pressure variability in patients with chronic kidney disease

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Table of contents

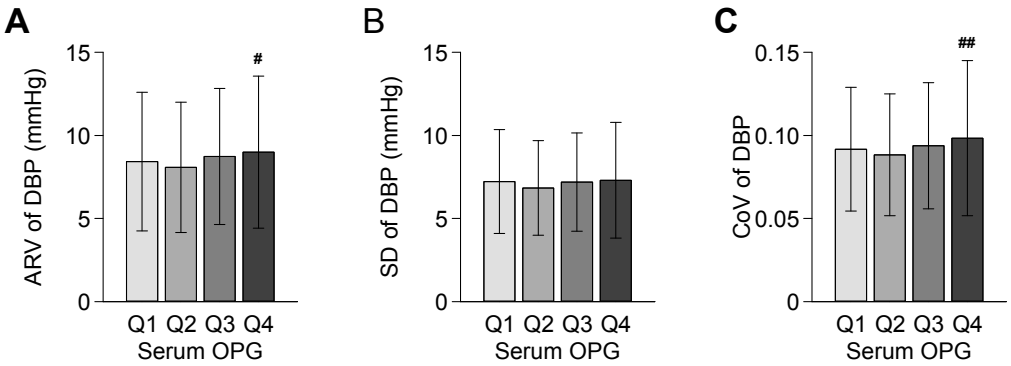

Figure S1. Comparisons of diastolic BPV by serum OPG level

Note: Diastolic BPV, represented by ARV (A), SD (B), and CoV (C), is compared by the quartile of serum OPG level. Error bars indicate standard deviation. **P* < 0.05, ***P* < 0.01 vs. Q1; ##*P* < 0.01 vs. Q2; †*P* <0.05, ‡*P* <0.01 vs. Q3 by one-way ANOVA with Scheffe test. Abbreviations: ARV, average real variability; CoV, coefficient of variation; OPG, osteoprotegerin; Q1, 1st quartile; Q2, 2nd quartile; Q3, 3rd quartile; Q4, 4th quartile; SBP, systolic blood pressure; SD, standard deviation.

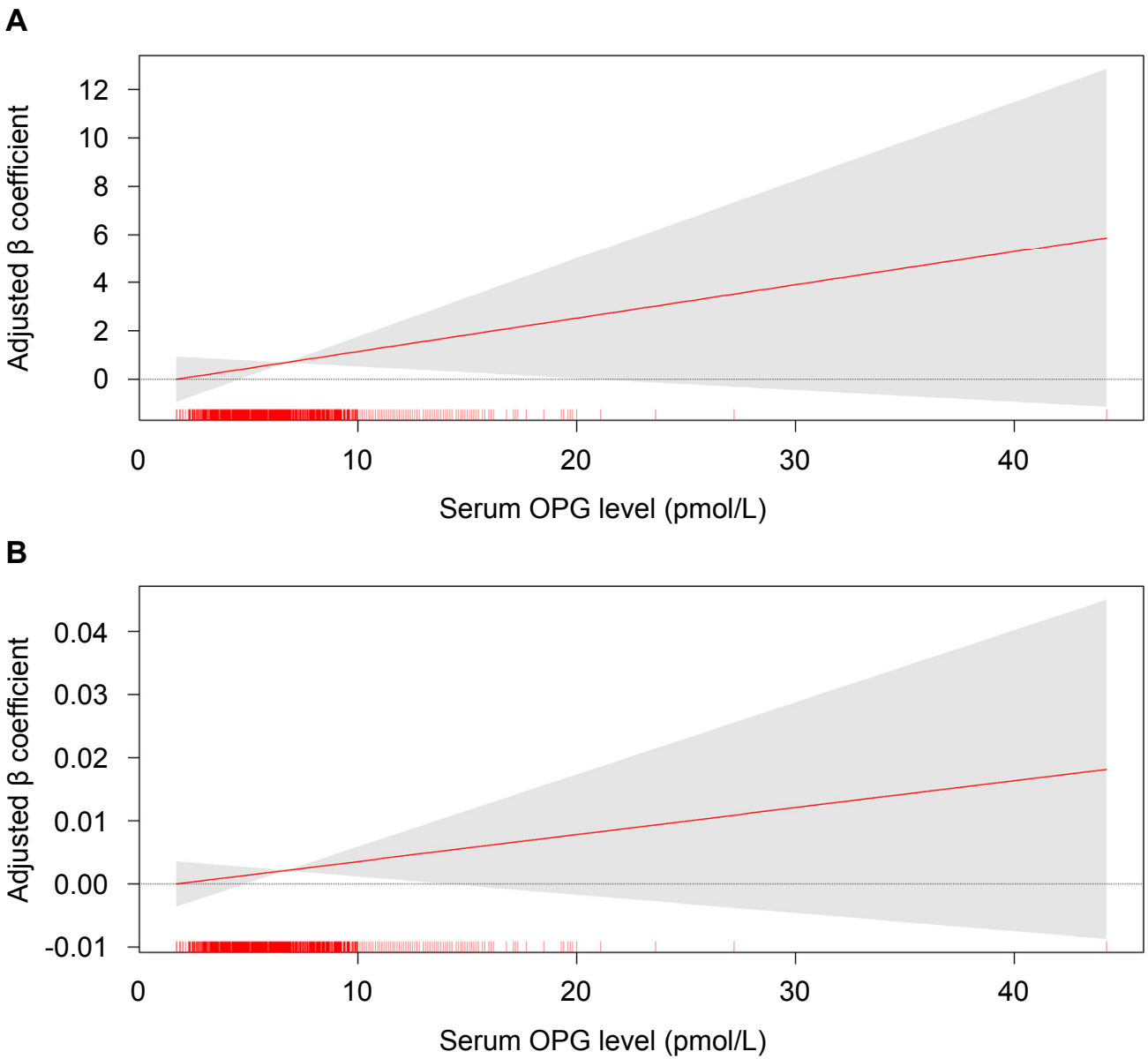

Figure S2. Restricted cubic spline of serum OPG on SD and CoV of SBP

Note: Adjusted β coefficient of serum OPG as a continuous variable for SD (A) and CoV (B) of SBP is depicted. The models were adjusted for age, gender, Charlson comorbidity index, smoking history, BMI, SBP, DBP, medication (ACEi/ARBs, diuretics, number of antihypertensive drugs, statins), hemoglobin, albumin, HDL-C, fasting serum glucose, hs-CRP, 25(OH) vitamin D levels, eGFR, and 24-hour urine protein. Abbreviations: OPG, osteoprotegerin.

Table S1. Multivariate linear regression analyses of serum OPG level (*per* pmol/L) for diastolic BPV

	Unadjusted		Adjusted	
	β coefficient (95%CIs)	*P* value	β coefficient (95%CIs)	*P* value
ARV of DBP	0.070 (0.006, 0.134)	0.033	0.017 (-0.068, 0.102)	0.696
SD of DBP	0.010 (-0.038, 0.057)	0.685	0.020 (-0.044, 0.083)	0.547
CoV of DBP	0.001 (0.000, 0.001)	0.019	0.000 (0.000, 0.001)	0.438

Note: Models were adjusted for age, gender, Charlson comorbidity index, smoking history, BMI, SBP, DBP, medication (ACEi/ARBs, diuretics, number of antihypertensive drugs, statins), hemoglobin, albumin, HDL-C, fasting serum glucose, hs-CRP, 25(OH) vitamin D levels, eGFR, and 24-hour urine protein.

Abbreviations: ARV, average real variability; CI, confidence interval; CoV, coefficient of variation; DBP, diastolic blood pressure; OPG, osteoprotegerin; SD; standard deviation.

Table S2. Multivariate linear regression analyses of serum OPG level (*per* pmol/L) for systolic BPV in subjects with BP measurements no less than 5 times during follow-up periods

	Unadjusted		Adjusted	
	β coefficient (95%CIs)	*P* value	β coefficient (95%CIs)	*P* value
ARV of SBP	0.367 (0.258, 0.475)	< 0.001	0.121 (-0.022, 0.264)	0.096
SD of SBP	0.317 (0.231, 0.404)	< 0.001	0.149 (0.034, 0.264)	0.011
CoV of SBP	0.002 (0.001, 0.003)	< 0.001	0.001 (0.000, 0.002)	0.025

Note: Models were adjusted for age, gender, Charlson comorbidity index, smoking history, BMI, SBP, DBP, medication (ACEi/ARBs, diuretics, number of antihypertensive drugs, statins), hemoglobin, albumin, HDL-C, fasting serum glucose, hs-CRP, 25(OH) vitamin D levels, eGFR, and 24-hour urine protein.
Abbreviations: ARV, average real variability; CI, confidene interval; CoV, coefficient of variation; SBP, systolic blood pressure; SD; standard deviation.

Table S3. Multivariate linear regression analyses of serum OPG level (*per* pmol/L) for diastolic BPV in subjects with BP measurements no less than 5 times during follow-up periods

	Unadjusted		Adjusted	
	β coefficient (95%CIs)	*P* value	β coefficient (95%CIs)	*P* value
ARV of DBP	0.106 (0.026, 0.186)	0.009	0.071 (-0.036, 0.178)	0.193
SD of DBP	0.060 (-0.001, 0.122)	0.054	0.072 (-0.010, 0.155)	0.086
CoV of DBP	0.002 (0.001, 0.002)	< 0.001	0.001 (0.000, 0.002)	0.055

Note: Models were adjusted for age, gender, Charlson comorbidity index, smoking history, BMI, SBP, DBP, medications (ACEi/ARBs, diuretics, number of antihypertensive drugs, statins), hemoglobin, albumin, HDL-C, fasting serum glucose, hs-CRP, 25(OH) vitamin D levels, eGFR, and 24-hour urine protein. Abbreviations: ARV, average real variability; CI, confidence interval; CoV, coefficient of variation; DBP, diastolic blood pressure; SD; standard deviation.

Table S4. Multivariate linear regression analyses of serum OPG level (*per* pmol/L) for CoV of SBP in various subgroups

	Unadjusted		Adjusted	
	β coefficient (95%CIs)	*P* for interaction	β coefficient (95%CIs)	*P* for interaction
Age < 60 years	0.002 (0.001, 0.003)	0.035	0.000 (-0.001, 0.001)	0.492
Age ≥ 60 years	0.001 (0.000, 0.002)		0.001 (0.000, 0.002)	
Male	0.002 (0.001, 0.002)	0.687	0.001 (0.000, 0.002)	0.485
Female	0.001 (0.000, 0.002)		0.000 (-0.001, 0.001)	
CCI ≤ 3	0.002 (0.001, 0.003)	< 0.001	0.001 (0.000, 0.002)	0.002
CCI ≥ 4	0.000 (-0.001, 0.001)		0.000 (-0.001, 0.002)	
History of DM (-)	0.002 (0.001, 0.003)	0.006	0.001 (0.000, 0.002)	0.04
History of DM (+)	0.000 (-0.001, 0.001)		0.000 (-0.001, 0.001)	
BMI < 23 kg/m^2	0.001 (0.000, 0.002)	0.605	0.000 (-0.002, 0.001)	0.633
BMI ≥ 23 kg/m^2	0.002 (0.001, 0.002)		0.001 (0.000, 0.002)	
Number of anti-HTN drugs ≤2	0.002 (0.001, 0.002)	0.327	0.000 (0.000, 0.001)	0.765
Number of anti-HTN drugs ≥ 3	0.001 (0.000, 0.002)		0.001 (-0.001, 0.002)	
eGFR ≥ 45 mL/min./1.73m^2	0.002 (0.002, 0.003)	0.019	0.001 (0.000, 0.002)	0.234
eGFR < 45 mL/min./1.73m^2	0.001 (0.000, 0.002)		0.000 (-0.001, 0.001)	
24-hour urine protein < 200 mg	0.003 (0.002, 0.004)	0.028	0.001 (0.000, 0.003)	0.066
24-hour urine protein ≥ 200 mg	0.001 (0.000, 0.002)		0.000 (0.000, 0.001)	

Note: Models were adjusted for age, gender, Charlson comorbidity index, smoking history, BMI, SBP, DBP, medication (ACEi/ARBs, diuretics, number of antihypertensive drugs, statins), hemoglobin, albumin, HDL-C, fasting serum glucose, hs-CRP, 25(OH) vitamin D levels, eGFR, and 24-hour urine protein. Abbreviations: CI, confidence interval; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; HTN, hypertension.

Table S5. Multivariate linear regression analyses of serum OPG level (*per* pmol/L) for ARV of DBP in various subgroups

	Unadjusted		Adjusted	
	β coefficient (95%CIs)	*P* for interaction	β coefficient (95%CIs)	*P* for interaction
Age < 60 years	0.168 (0.051, 0.284)	0.120	-0.012 (-0.159, 0.134)	0.933
Age ≥ 60 years	0.071 (-0.024, 0.165)		0.051 (-0.064, 0.165)	
Male	0.086 (0.002, 0.171)	0.887	0.077 (-0.041, 0.196)	0.616
Female	0.048 (-0.050, 0.145)		-0.051 (-0.177, 0.076)	
CCI ≤ 3	0.051 (-0.038, 0.140)	0.690	0.040 (-0.072, 0.152)	0.468
CCI ≥ 4	-0.002 (-0.122, 0.117)		-0.021 (-0.172, 0.130)	
History of DM (-)	0.021 (-0.077, 0.120)	0.918	0.049 (-0.081, 0.180)	0.743
History of DM (+)	0.030 (-0.071, 0.132)		-0.022 (-0.148, 0.104)	
BMI < 23 kg/m^2	0.034 (-0.081, 0.149)	0.931	-0.070 (-0.241, 0.101)	0.408
BMI ≥ 23 kg/m^2	0.086 (0.009, 0.163)		0.056 (-0.043, 0.156)	
Number of anti-HTN drugs ≤2	0.060 (-0.013, 0.134)	0.616	-0.006 (-0.104, 0.901)	0.934
Number of anti-HTN drugs ≥ 3	0.046 (-0.086, 0.178)		0.080 (-0.093, 0.253)	
eGFR ≥ 45 mL/min./1.73m^2	0.060 (-0.061, 0.182)	0.874	0.054 (-0.101, 0.210)	0.803
eGFR < 45 mL/min./1.73m^2	0.041 (-0.049, 0.131)		0.028 (-0.089, 0.145)	
24-hour urine protein < 200 mg	0.045 (-0.099, 0.188)	0.619	0.085 (-0.108, 0.278)	0.843
24-hour urine protein ≥ 200 mg	0.060 (-0.014, 0.133)		0.003 (-0.094, 0.100)	

Note: Models were adjusted for age, gender, Charlson comorbidity index, smoking history, BMI, SBP, DBP, medication (ACEi/ARBs, diuretics, number of antihypertensive drugs, statins), hemoglobin, albumin, HDL-C, fasting serum glucose, hs-CRP, 25(OH) vitamin D levels, eGFR, and 24-hour urine protein. Abbreviations: CI, confidence interval; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; HTN, hypertension.

Table S6. Multivariate linear regression analyses of serum OPG level (*per* pmol/L) for SD of DBP in various subgroups

	Unadjusted		Adjusted	
	β coefficient (95%CIs)	*P* for interaction	β coefficient (95%CIs)	*P* for interaction
Age < 60 years	0.070 (-0.008, 0.148)	0.274	0.011 (-0.099, 0.120)	0.762
Age ≥ 60 years	0.015 (-0.048, 0.077)		0.033 (-0.054, 0.119)	
Male	0.019 (-0.008, 0.075)	0.0717	0.096 (0.007, 0.186)	0.278
Female	0.003 (-0.063, 0.068)		-0.080 (-0.174, 0.014)	
CCI ≤ 3	0.001 (-0.064, 0.065)	0.860	0.027 (-0.059, 0.113)	0.610
CCI ≥ 4	-0.008 (-0.080, 0.064)		0.027 (-0.079, 0.133)	
History of DM (-)	-0.011 (-0.081, 0.060)	0.996	0.046 (-0.055, 0.146)	0.913
History of DM (+)	-0.011 (-0.074, 0.053)		-0.012 (-0.102, 0.078)	
BMI < 23 kg/m^2	0.024 (-0.055, 0.103)	0.734	-0.057 (-0.187, 0.072)	0.637
BMI ≥ 23 kg/m^2	0.008 (-0.043, 0.059)		0.047 (-0.028, 0.121)	
Number of anti-HTN drugs ≤2	0.015 (-0.033, 0.064)	0.445	-0.014 (-0.086, 0.058)	0.728
Number of anti-HTN drugs ≥ 3	-0.021 (-0.113, 0.070)		0.098 (-0.037, 0.233)	
eGFR ≥ 45 mL/min./1.73m^2	0.056 (-0.033, 0.146)	0.039	0.089 (-0.033, 0.211)	0.496
eGFR < 45 mL/min./1.73m^2	0.003 (-0.053, 0.059)		0.035 (-0.049, 0.119)	
24-hour urine protein < 200 mg	-0.005 (-0.106, 0.096)	0.852	0.039 (-0.101, 0.178)	0.735
24-hour urine protein ≥ 200 mg	0.006 (-0.046, 0.058)		0.017 (-0.056, 0.091)	

Note: Models were adjusted for age, gender, Charlson comorbidity index, smoking history, BMI, SBP, DBP, medication (ACEi/ARBs, diuretics, number of antihypertensive drugs, statins), hemoglobin, albumin, HDL-C, fasting serum glucose, hs-CRP, 25(OH) vitamin D levels, eGFR, and 24-hour urine protein. Abbreviations: CI, confidence interval; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; HTN, hypertension.

Table S7. Multivariate linear regression analyses of serum OPG level (*per* pmol/L) for CoV of DBP in various subgroups

	Unadjusted		Adjusted	
	β coefficient (95%CIs)	*P* for interaction	β coefficient (95%CIs)	*P* for interaction
Age < 60 years	0.001 (0.000, 0.002)	0.221	0.000 (-0.001, 0.002)	0.825
Age ≥ 60 years	0.000 (0.000, 0.001)		0.000 (-0.001, 0.002)	
Male	0.000 (0.000, 0.001)	0.226	-0.001 (-0.002, 0.000)	0.167
Female	0.001 (0.000, 0.002)		0.001 (0.000, 0.003)	
CCI ≤ 3	0.000 (0.000, 0.001)	0.699	0.000 (-0.001, 0.002)	0.572
CCI ≥ 4	0.000 (-0.001, 0.001)		0.000 (-0.001, 0.002)	
History of DM (-)	0.000 (-0.001, 0.001)	0.964	0.001 (-0.001, 0.002)	0.849
History of DM (+)	0.000 (-0.001, 0.001)		0.000 (-0.001, 0.001)	
BMI < 23 kg/m^2	0.001 (0.000, 0.002)	0.919	-0.001 (-0.002, 0.001)	0.457
BMI ≥ 23 kg/m^2	0.001 (0.000, 0.001)		0.001 (0.000, 0.002)	
Number of anti-HTN drugs ≤2	0.001 (0.000, 0.001)	0.683	0.000 (-0.001, 0.001)	0.675
Number of anti-HTN drugs ≥ 3	0.001 (-0.001, 0.002)		0.001 (0.000, 0.003)	
eGFR ≥ 45 mL/min./1.73m^2	0.001 (0.000, 0.003)	0.194	0.001 (0.000, 0.003)	0.363
eGFR < 45 mL/min./1.73m^2	0.001 (0.000, 0.001)		0.000 (-0.001, 0.002)	
24-hour urine protein < 200 mg	0.001 (-0.001, 0.002)	0.885	0.000 (-0.001, 0.002)	0.698
24-hour urine protein ≥ 200 mg	0.001 (0.000, 0.001)		0.000 (-0.001, 0.001)	

Note: Models were adjusted for age, gender, Charlson comorbidity index, smoking history, BMI, SBP, DBP, medication (ACEi/ARBs, diuretics, number of antihypertensive drugs, statins), hemoglobin, albumin, HDL-C, fasting serum glucose, hs-CRP, 25(OH) vitamin D levels, eGFR, and 24-hour urine protein. Abbreviations: CI, confidence interval; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; HTN, hypertension.