

Supplementary Table 1. Univariate Analysis of Clinical Factors Influencing PIGF

	Coefficient	95% CI	P
Demographics and Risk Factors			
Age (≥ 65 y)	2.37	1.51 to 3.24	< 0.0001
Sex (male)	0.30	-0.59 to 1.20	0.51
Diabetes	1.76	0.81 to 2.70	0.0003
Hypertension	2.49	1.60 to 3.38	< 0.0001
Dyslipidemia	-0.08	-0.97 to 0.81	0.86
Smoking	0.89	0.02 to 1.77	0.045
Obesity	-0.20	-1.15 to 0.75	0.68
CKD (stage difference)	1.38	1.16 to 1.61	< 0.0001
Previous CAD	1.27	0.17 to 2.38	0.024
Previous stroke	3.25	1.50 to 4.99	0.0003
Current Medications			
RAS blocker	0.85	0.06 to 1.73	0.06
CCB	1.41	0.50 to 2.32	0.0024
β blocker	1.53	0.30 to 2.76	0.015
MR antagonist	0.77	-1.03 to 2.56	0.40
Lipid-lowering agent	0.24	-0.80 to 1.29	0.65
Diuretic	1.79	0.76 to 2.82	0.0007
Antiplatelet agent	2.49	1.55 to 3.42	< 0.0001
Laboratory Results			

Hemoglobin (<10.0 g/dL)	4.03	2.84 to 5.23	< 0.0001
Albumin (<3.0 mg/dL)	3.29	2.12 to 4.45	< 0.0001
Calcium (>10.0 mg/dL)	0.97	-0.62 to 2.56	0.23
Phosphorus (>4.5 mg/dL)	2.56	1.37 to 3.75	< 0.0001
CRP (>0.2 mg/dL)	3.12	2.26 to 3.98	< 0.0001
HbA1c (≥6.5 %)	0.26	-0.79 to 1.31	0.63
LDL cholesterol (≥140 mg/dL)	-0.15	-1.12 to 0.83	0.77
HDL cholesterol (<40 mg/dL)	3.44	2.34 to 4.55	< 0.0001
Triglycerides (≥150 mg/dL)	0.35	-0.58 to 1.29	0.46

Supplementary Table 2. Multivariate Analysis of Clinical Factors Influencing PIGF

	Coefficient	95% CI	P
Demographics and Risk Factors			
Age (≥ 65 y)	0.43	-0.38 to 1.25	0.30
Diabetes	0.31	-0.54 to 1.17	0.47
Hypertension	0.63	-0.34 to 1.61	0.20
Smoking	-0.14	-0.91 to 0.64	0.73
CKD (stage difference)	0.81	0.55 to 1.08	< 0.0001
Previous CAD	-0.33	-1.50 to 0.84	0.58
Previous stroke	0.62	-0.85 to 2.09	0.41
Current Medications			
RAS blocker	-0.54	-1.38 to 0.30	0.21
CCB	-0.33	-1.22 to 0.55	0.46
β blocker	0.21	-0.89 to 1.32	0.71
Diuretic	-0.07	-0.99 to 0.85	0.88
Antiplatelet agent	1.48	0.48 to 2.49	0.004
Laboratory Results			
Hemoglobin (<10.0 g/dL)	0.73	-0.36 to 1.81	0.19
Albumin (<3.0 g/dL)	2.99	1.97 to 4.00	< 0.0001
Phosphorus (>4.5 mg/dL)	-0.35	-1.44 to 0.74	0.53
CRP (>2.0 mg/dL)	1.47	0.68 to 2.26	0.005
HDL cholesterol (<40 mg/dL)	1.78	0.81 to 2.74	< 0.0001

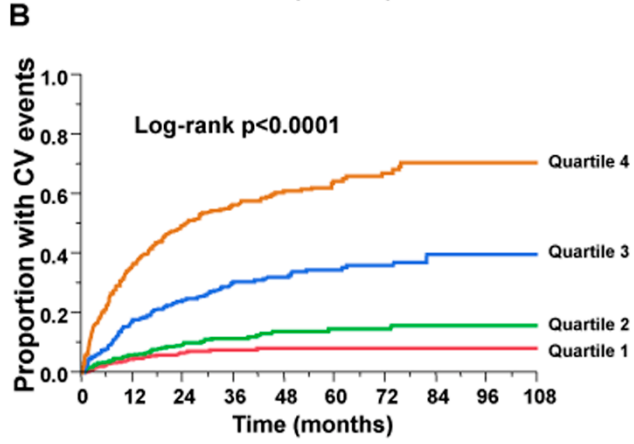
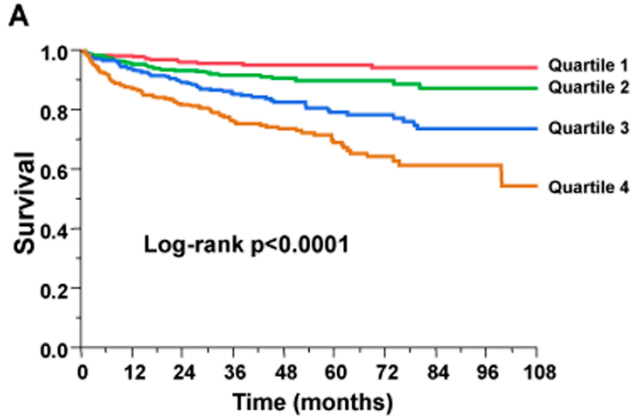
Supplementary Table 3. Risk of Atherosclerotic Disease and Heart Failure by baseline PIGF level

	Unadjusted	Model 1	Model 2	Model 3	Model 4	Model 5
Atherosclerotic Disease						
Quartile 1	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
Quartile 2	1.57 (0.91–2.76)	1.26 (0.78–2.22)	1.24 (0.71–2.20)	1.17 (0.66–2.10)	1.33 (0.73–2.45)	1.57 (0.91–2.76)
Quartile 3	3.45 (2.15–5.78)	2.56 (1.59–4.30)	2.45 (1.51–4.14)	2.39 (1.48–4.04)	2.29 (1.39–3.92)	3.45 (2.15–5.78)
Quartile 4	8.23 (5.31–13.4)	6.51 (4.18–10.7)	4.97 (3.12–8.28)	5.18 (3.25–8.65)	6.69 (4.09–11.4)	8.23 (5.31–13.4)
for each 10 pg/mL increase	1.95 (1.75–2.16)	1.91 (1.70–2.14)	1.84 (1.61–2.09)	1.79 (1.57–2.04)	1.90 (1.65–2.18)	1.95 (1.75–2.16)
Heart Failure						
Quartile 1	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
Quartile 2	2.64 (1.15–6.79)	2.05 (0.89–5.29)	1.94 (0.83–5.05)	2.46 (1.00–6.74)	3.12 (1.21–9.02)	2.64 (1.15–6.79)
Quartile 3	8.16 (3.97–19.7)	5.94 (2.87–14.4)	5.42 (2.60–13.2)	6.09 (2.89–15.0)	6.15 (2.79–15.7)	8.16 (3.97–19.7)
Quartile 4	16.7 (8.34–39.6)	13.2 (6.54–31.4)	11.9 (5.81–28.6)	12.4 (6.09–30.0)	10.6 (5.17–25.7)	16.7 (8.34–39.6)
for each 10 pg/mL increase	1.98 (1.76–2.20)	1.96 (1.73–2.20)	1.80 (1.57–2.05)	1.85 (1.60–2.13)	1.70 (1.44–1.96)	1.98 (1.76–2.20)

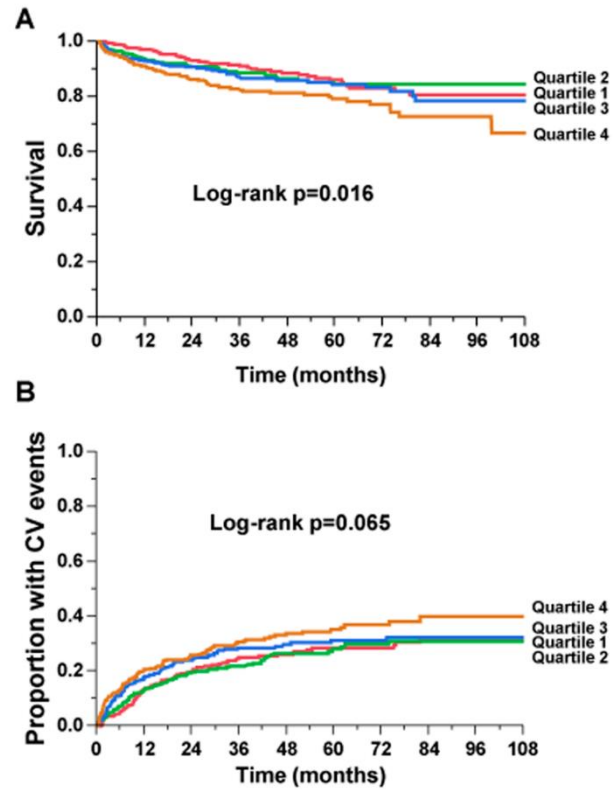
Model 1 adjusted for age and sex. Model 2 adjusted for covariates in Model 1 plus risk factors including diabetes, hypertension, dyslipidemia, obesity, smoking, previous coronary artery disease, previous stroke, and CKD stage. Model 3 adjusted for covariates in Model 2 plus current medications including renin angiotensin system blockers, calcium channel blockers, β blockers, mineralocorticoid receptor antagonists, lipid-lowering agents, diuretics, and antiplatelet agents. Model 4 adjusted for covariates in Model 3 plus laboratory data including hemoglobin, serum albumin, serum calcium, phosphorus, serum C-reactive protein, HbA1c, LDL cholesterol, HDL cholesterol, and triglycerides. Model 5 adjusted

for covariates in Model 4 plus BNP.

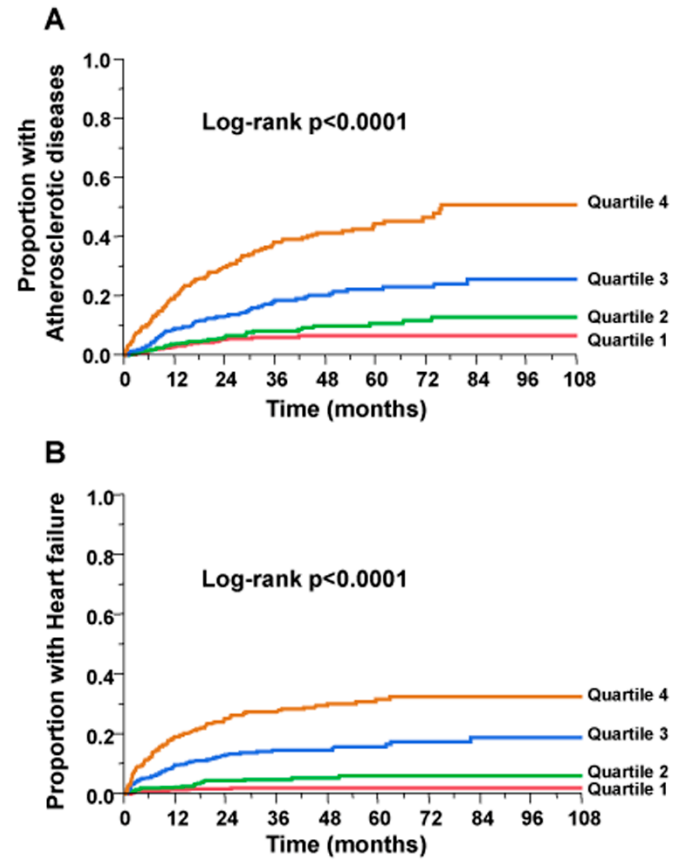
Supplementary Figure 1. Kaplan-Meier curves for All-cause mortality and Cardiovascular events by Baseline PIGF Quartile



Supplementary Figure 2. Kaplan-Meier curves for All-cause mortality and Cardiovascular events by Baseline VEGF Quartile



Supplementary Figure 3. Kaplan-Meier curves for Atherosclerotic Disease and Heart Failure by Baseline PIGF Quartile



Supplementary Figure 4. Prognostic value of PIGF, BNP versus combination use of PIGF and BNP on All-cause mortality and Cardiovascular events.

