Supplemental data 1

Calculation of Cutoff Values for CVD Mortality

The cutoff values for cardiovascular disease mortality based on total and free serum indoxyl sulfate IS and PCS concentrations, cardiac function markers, and laboratory data were calculated using ROC analysis (Table S1).

Table S1. ROC-Derived Cutoff Values for Predicting CVD Mortality

Variables	Cutoff value
Age (year)	65
DW (kg)	46
BW (kg)	49.6
HR (bpm)	139
SBP (mm Hg)	89
DBP (mm Hg)	66
Cardio-Thoracic Ratio (%)	53.7
Ferritin (ng/mL)	302
Fe (μg/dL)	89
PTH (pg/mL)	847
CK-MB (ng/mL)	3.2
NT-proBNP (pg/mL)	6120
IS total (μM)	139
IS free (μM)	5.1
PCS total (μM)	455
PCS free (μM)	8.1
IS + PCS score	495.8

DW, dry weight; BW, body weight; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; Fe, serum iron; PTH, parathyroid hormone; CK-MB, creatine kinase–myocardial band; NT-proBNP, N-terminal pro-B-type natriuretic peptide; hsTnT, high-sensitivity troponin T; IS, indoxyl sulfate; PCS, p-cresyl sulfate; ROC, receiver operating characteristic

Supplemental data 2

Survival Rate Comparison Using the Kaplan–Meier Method

Patients were divided into high- and low-value groups using the cutoff values shown in Table S1, and survival curves were analyzed. The analysis revealed significant differences in survival rates according to IS, NT-proBNP, and age (Figure S1).

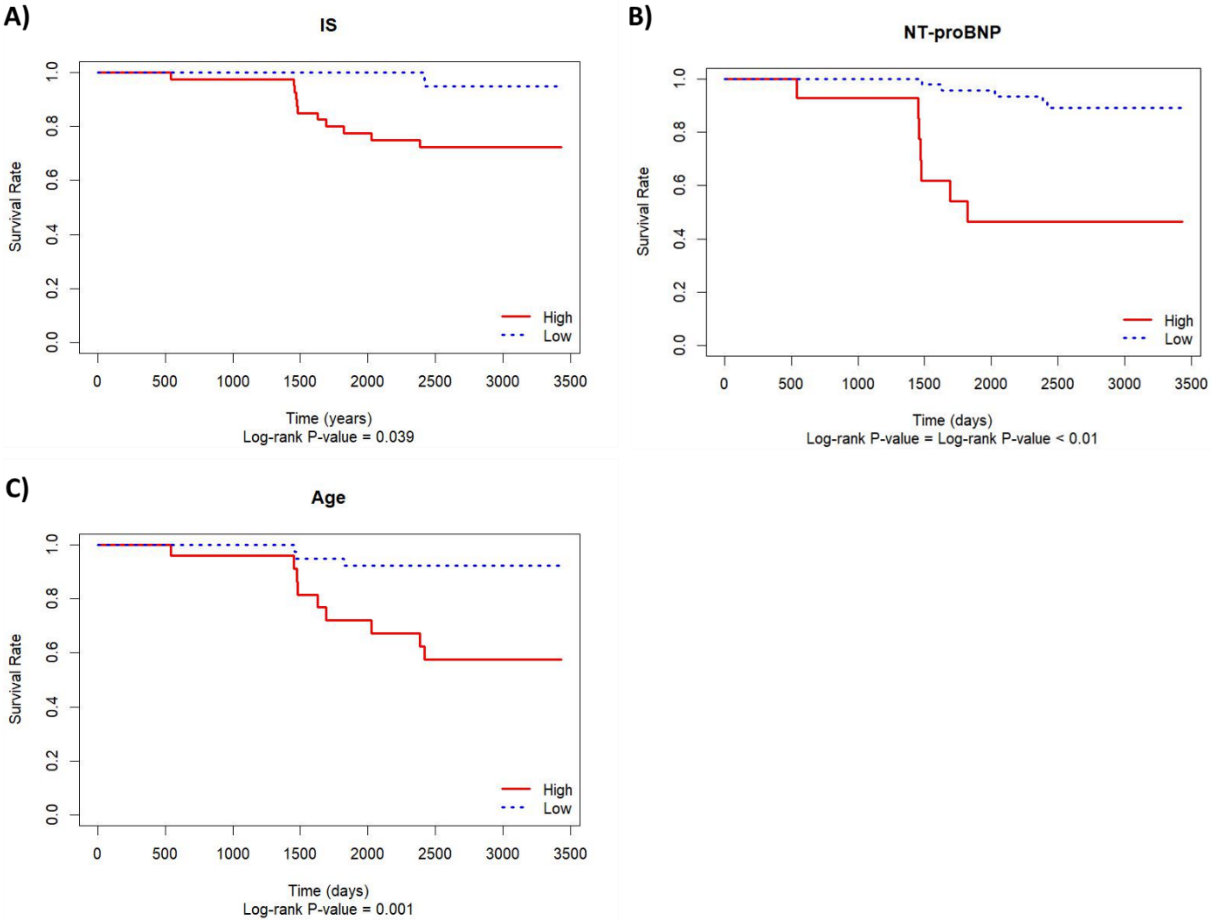

Figure S1. Kaplan–Meier Survival Curves for Key Variables

Survival curves comparing the high-value (red solid line) and low-value (blue dotted line) groups for (A) indoxyl sulfate (IS), (B) N-terminal pro-B-type natriuretic peptide (NT-proBNP), and (C) age

Supplemental data 3

Univariate Analysis Based on Cox Proportional Hazards Model

Univariate analysis was conducted using the Cox proportional hazards model to identify the candidate risk factors for CVD mortality (Table S2). Factors with P-values below 0.2 were selected as potential risk factors for CVD mortality. While systolic blood pressure (SBP) and cardiothoracic ratio (CTR) were significant in the univariate analysis, SBP was excluded because its hazard ratio was below 1, suggesting a protective rather than harmful effect. CTR was also excluded because of 21 missing values, which could compromise the reliability of the analysis.

Table S2. Univariate Cox Proportional Hazards Analysis for CVD Mortality Risk Factors

	Hazard Ratio	95% CI	P value
Age (year)	6.46	1.75–23.9	< 0.01
Sex (Female)	0.83	0.26–2.61	0.75
DW (kg)	1.04	0.27–3.92	0.95
BW (kg)	1.30	0.35–4.81	0.69
HR (bpm)	1.46	0.19–11.5	0.72
SBP (mmHg)	0.44	0.13–1.45	0.18
DBP (mmHg)	1.91	0.24–15.1	0.54
Hypertension (+)	1.46	0.39–5.52	0.58
Diabetes (+)	0.94	0.20–4.36	0.94
Cardio-Thoracic Ratio (%)	3.15	0.84–11.8	0.09
Ferritin (ng/mL)	1.77	0.56–5.57	0.33
Fe (μg/dL)	2.06	0.67–6.40	0.21
PTH (pg/mL)	2.83	0.36–22.2	0.32
CK-MB (ng/mL)	1.52	0.46–5.50	0.49
NT-proBNP (pg/mL)	7.62	2.40–24.2	<0.01
IS total (μM)	6.50	0.84–50.4	0.07
IS free (μM)	3.31	0.90–12.2	0.07
PCS total (μM)	2.46	0.67–9.01	0.18
PCS free (μM)	2.30	0.69–7.64	0.17

DW, dry weight; BW, body weight; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; Fe, serum iron; PTH, parathyroid hormone; CK-MB, creatine kinase–myocardial band; NT-proBNP, N-terminal pro-B-type natriuretic peptide; hsTnT, high-sensitivity troponin T; IS, indoxyl sulfate; PCS, p-cresyl sulfate; CI, confidence interval; HR, hazard ratio

Supplemental data 4

Multivariate Analysis Based on Cox proportional Hazards Model

The multivariate Cox proportional hazards analysis results and corresponding forest plots are presented (Figure S2). Multivariate analysis revealed that all incorporated covariates (total IS level, total PCS level, NT-proBNP level, and age) were significant risk factors for CVD mortality. Notably, the total IS and PCS levels emerged as independent risk factors for CVD mortality beyond the established CVD risk factors of age and NT-proBNP.

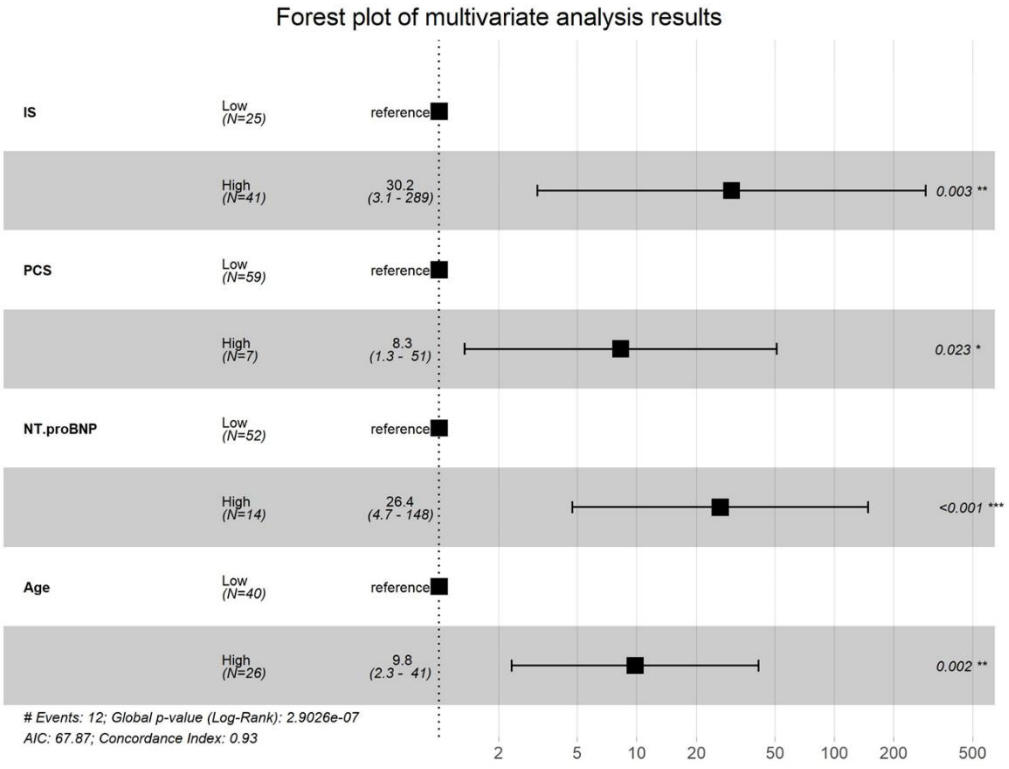

Figure S2. Forest Plot of Multivariate Cox Proportional Hazards Analysis for Cardiovascular Disease (CVD) Mortality