

Supplemental Material

Supplemental Table 1. Coefficient of variation (CV) for assays of biomarkers.

Biomarkers	Intra-assay CV	Inter-assay CV
Albumin (g/dL)	3% - 4%	NA
Ferritin (ng/ml)	6%	NA
hsCRP (mg/L)	5% (4% - 6%)	6% (4% - 10%)
IGF-1 ($\mu\text{g}/\text{ml}$)	4.3% (3% - 4.5%)	6.9% (6% - 8%)
IL-6 (pg/ml)	4% (3% - 6%)	5% (5% - 8%)
Orosomuroid (g/L)	5% - 7%	NA
sICAM-1 (ng/ml)	4% (3% - 5%)	5% (4% - 7%)
sVCAM-1 (ng/ml)	3.5% (2% - 4%)	6% (5% - 8%)
TNF (pg/ml)	8% - 10%	5% (4% - 7%)
TnT ($\mu\text{g}/\text{L}$)	8%	NA
PLT ($10^3/\mu\text{l}$)	5% - 7%	NA
WBC ($10^3/\mu\text{l}$)	6%	NA

Abbreviations: hsCRP, high-sensitivity C-reactive protein; IGF-1, insulin-like growth factor 1; IL-6, interleukin 6; sICAM-1, soluble intracellular adhesion molecule 1; sVCAM-1, soluble vascular cellular adhesion molecule 1; TNF, tumor necrosis factor α ; PLT, platelet count ; TnT, troponin T; WBC, white blood cell count.

NA, not assessed: Inter-assay CVs were in general not available for those biomarkers that were analyzed in the clinical chemistry laboratory at Karolinska University Hospital.

Supplemental Table 2. Causes of 149 deaths during 60 months' follow-up in 543 chronic kidney disease stage 5 patients starting on dialysis.

Causes of death	N (% of total)
Cardiovascular related deaths^a	81 (54%)
Non-cardiovascular related deaths^a	68 (46%)
Infectious complications	25 (17%)
Malignancies	10 (7%)
Withdrawal from treatment/dementia/ cachexia	15 (10%)
Cause of death uncertain	18 (12%)
Total deaths	149 (100%)

^a Values are presented as number of patients who died and in bracket the corresponding percentage.

Supplemental Table 3: Correlation matrix (Spearman's rank correlation) coefficient showing associations between investigated biomarkers (except serum albumin) in 543 chronic kidney disease stage 5 patients starting on dialysis.

Biomarker	Ferritin (ng/ml; n=531)	IGF-1 (µg/ml)	IL-6 (pg/ml)	hsCRP (mg/L)	sICAM-1 (ng/ml)	sVCAM-1 (ng/ml)	PLT (10 ³ /µl)	TNF (pg/ml)	TnT (µg/L)	WBC (10 ³ /µl)
IGF-1 (µg/ml; n=375)	-0.07									
IL-6 (pg/ml; n=502)	0.11^a	-0.20^c								
hsCRP (mg/L)	0.16^c	-0.15^b	0.54^c							
sICAM-1 (ng/ml; n=329)	0.03	-0.14^a	0.28^c	0.37^c						
sVCAM-1 (ng/ml; n=329)	0.16^b	-0.17^b	0.26^c	0.26^c	0.33^c					
PLT (10 ³ /µl; n=497)	0.03	-0.10	0.09^a	0.210^c	0.05	-0.21^c				
TNF (pg/ml; n=461)	0.11^a	-0.07	0.17^c	0.16^c	0.35^c	0.42^c	-0.17^c			
TnT (µg/L; n=394)	0.10^a	-0.20^b	0.29^c	0.23^c	0.23^c	0.27^c	0.15^b	0.09		
WBC (10 ³ /µl; n=521)	0.03	-0.053	0.30^c	0.41^c	0.15^a	-0.01	0.48^c	-0.05	0.12^a	

Orosomuroid (g/L; n=393)	0.10	0.06	0.42^c	0.65^c	0.40^c	0.07	0.17^c	0.19^c	0.11^a	0.35^c
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a: p<0.05, b: p<0.01, c: p<0.001.

Abbreviations: high-sensitivity C-reactive protein (hsCRP); insulin-like growth factor 1 (IGF-1); interleukin 6 (IL-6); soluble intracellular adhesion molecule (sIVAM-1); soluble vascular cellular adhesion molecule 1 (sVCAM-1); tumor necrosis factor (TNF); platelet count (PLT); troponin T (TnT); WBC (white blood cell).

Supplemental Table 4. Comparison of circulating biomarkers by etiology of renal disease in chronic kidney disease stage 5 patients (n=543).

Biomarkers	CGN (n=126)	DM (n=159)	HT/RVD (n=113)	Others (n=145)	P value
Albumin (g/dL; n=543)	3.4 (2.8 – 4.1)	3.1 (2.2 – 3.8)	3.1 (2.7 – 4.0)	3.5 (2.7 – 4.1)	<0.001
Ferritin (ng/ml; n=531)	117 (29 - 263)	116 (38 - 270)	140 (32 - 336)	134 (44 – 368)	0.11
hsCRP (mg/L; n=543)	3.5 (0.6 – 18.9)	6.3 (0.6 – 31.0)	6.7 (1.1 – 56.0)	3.7 (0.6 – 26.3)	0.005
IGF-1 (µg /ml; n=375)	200 (82 - 361)	136 (61 - 264)	187 (90 - 340)	181 (90 - 365)	<0.001
IL-6 (pg/ml; n=502)	4.5 (1.7 – 11.9)	7.3 (2.6 – 22.0)	6.7 (2.4 – 18.4)	5.8 (1.9 – 16.4)	<0.001
Orosomuroid (g/L; n=393)	1.1 (0.7 – 1.7)	1.0 (0.6 – 1.6)	1.2 (0.8 – 2.1)	1.1 (0.8 – 1.6)	<0.001
sICAM-1 (ng/ml; n=329)	244 (168 - 313)	247 (187 - 473)	248 (167 - 385)	240 (162 - 362)	0.20
sVCAM-1 (ng/ml; n=329)	1144 (801 - 1707)	1420 (899 - 2229)	1322 (863 - 2041)	1275 (752 - 1900)	0.005
PLT (10 ³ /µl; n=497)	237 (147 - 345)	280 (171 - 403)	271 (163 - 391)	234 (134 - 349)	<0.001
TNF (pg/ml; n=461)	10.8 (6.9 – 20.0)	12.5 (6.7 – 21.3)	12.8 (8.0 – 22.0)	12.3 (7.3 – 22.8)	0.02
TnT (µg/L; n=394)	0.03 (0.01 – 0.13)	0.11 (0.02 – 0.39)	0.04 (0.01 – 0.14)	0.02 (0.01 – 0.10)	<0.001
WBC (10 ³ /µl; n=521)	7.6 (5.5 – 11.2)	8.0 (5.2 – 12.3)	8.3 (5.2 – 12.4)	6.4 (4.5 – 9.9)	<0.001

Data presented as median (range of 10th - 90th percentile) concentration of biomarkers.

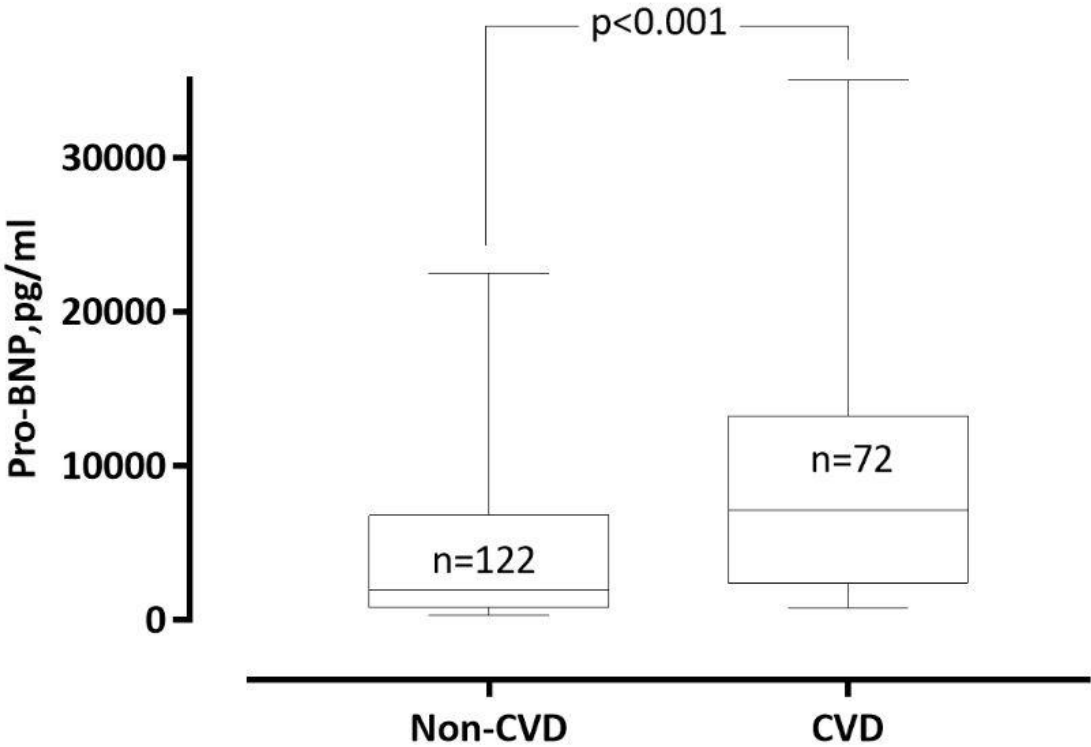
Abbreviations: CGN, chronic glomerulonephritis; DM, diabetes mellitus; HT/RVD, hypertension/renal vascular disease; hsCRP; high-sensitivity C-reactive protein; IGF-1, insulin-like growth factor 1; IL-6, interleukin 6; sICAM-1, soluble intracellular adhesion molecule (sIVAM-1); sVCAM-1, soluble vascular cellular adhesion molecule 1; PLT; platelet count count; TNF, tumor necrosis factor; TnT, troponin T; WBC, white blood cell count.

Supplemental Table 5. All-cause mortality with baseline cardiovascular disease (CVD) included as variable. Hazard ratios (95% confidence interval, CI) for all-cause mortality over 60 months' follow-up for demographic and clinical parameters, and for each evaluated biomarker, adjusted for all other variables included in the table.

Variables	Hazard Ratio (95% CI)	P value
Age (<i>above vs below 59 years</i>)	1.43 (1.00 - 2.07)	0.06
Gender (<i>male vs female</i>)	0.97 (0.67- 1.41)	0.87
CVD (<i>present vs absent</i>)	1.55 (1.06 – 2.29)	0.03
Diabetes mellitus (<i>present vs absent</i>)	1.51 (1.03 – 2.22)	0.03
Smoking (<i>yes vs no</i>)	1.26 (0.83 - 1.89)	0.28
SGA (<i>malnourished vs well nourished</i>)	2.33 (1.59 – 3.41)	<0.001
eGFR (<i>below vs above 6.9 ml/min/1.73m²</i>)	1.45 (1.01 – 2.07)	0.05
Calendar year period (<i>2010 – 2014 vs 2006 - 2009</i>)	1.18 (0.59 – 2.33)	0.64
Calendar year period (<i>2010 – 2014 vs 2000 - 2005</i>)	0.90 (0.45 – 1.79)	0.75
Calendar year period (<i>2010 – 2014 vs 1994 - 1999</i>)	0.81 (0.38 – 1.72)	0.58
WBC (<i>above vs below 8.0×10³/μl</i>)	1.78 (1.23 – 2.57)	0.002
IL-6 (<i>above vs below 6.7 pg/ml</i>)	1.74 (1.16 - 2.61)	0.008
TnT (<i>above vs below 0.06 μg/L</i>)	1.31 (0.89 – 1.91)	0.17
hsCRP (<i>above vs below 6.4 mg/L</i>)	1.25 (0.80 – 1.95)	0.42
Albumin (<i>below vs above 3.3 g/dL</i>)	1.21 (0.85 – 1.73)	0.59
PLT (<i>above vs below 261×10³/μl l</i>)	1.17 (0.81 – 1.70)	0.40
sVCAM-1 (<i>above vs below 1356 ng/ml</i>)	1.13 (0.75 – 1.71)	0.55
Ferritin (<i>above vs below 122 ng/ml</i>)	1.08 (0.77 – 1.52)	0.66
sICAM-1 (<i>above vs below 249 ng/ml</i>)	1.06 (0.76 – 1.48)	0.72
IGF-1 (<i>above vs below 155 μg/ml</i>)	0.93 (0.64 - 1.37)	0.72
TNF (<i>above vs below 12.1 pg/ml</i>)	0.63 (0.42 – 0.94)	0.02
Orosomuroid (<i>above vs below 1.1 g/L</i>)	0.58 (0.39 – 0.86)	0.006

Abbreviations: estimated glomerular filter rate (eGFR); high-sensitivity C-reactive protein (hsCRP); insulin-like growth factor 1 (IGF-1); interleukin 6 (IL-6); SGA (Subjective global assessment of nutritional status); soluble intracellular adhesion molecule (sIVAM-1); soluble vascular cellular adhesion molecule 1 (sVCAM-1); tumor necrosis factor (TNF); platelet count (PLT); troponin T (TnT); WBC (white blood cell).

Supplemental Figure 1.



N-terminal pro-brain natriuretic peptide (NTpro-BNP) in 194 patients with or without cardiovascular disease (CVD).