

## ONLINE SUPPLEMENTAL MATERIALS

### **Associations of Blood Biomarkers with Glomerular Filtration Rate in Patients with TIA and Stroke: Population-Based Study**

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**Supplementary Table I:** Biomarker Measurement Methods and Intra- and inter-assay coefficients of variation

<b>Biomarker</b>	<b>N</b>	<b>Measurement System</b>	<b>Intra-assay CV%</b>	<b>Inter-assay CV%</b>
<i>Inflammatory markers</i>				
IL-6, pg/ml	1158	Randox microchip	21	13.4
CRP, mg/l	914	Randox microchip	5.7	11.1
NGAL, ng/ml	977	Randox microchip	4.7	9.0
sTNFR-1, ng/ml	1210	Randox microchip	7.8	14.1
<i>Thrombotic or anti-atherogenic Markers</i>				
TM, ng/ml	1213	Randox microchip	10.1	14.1
Fibrinogen, g/L	1036	Stago analyzer	2.3	5.7
vWF, iu/ml	1047	Stago analyzer	4.6	4.6
P-selectin, ng/ml	1059	ELISA	4.9	9.0
PZ, ng/ml	1021	ELISA	4.9	14.8
D-dimer, ng/ml	1189	Stago analyzer	4.3	4.3
Anti-PC, U/ml	901	ELISA	6.7	8.2
ADAMTS-13, U/ml	865	ELISA	8.9	8.2
<i>Markers of cardiac or neuronal function/injury</i>				
Nt-proBNP, pmol/l	1049	ELISA	8.6	10.1
hFABP, ng/ml	1213	Randox microchip	14.6	10.8
NSE, ng/ml	1211	Randox microchip	7.5	20.0
BDNF, pg/ml	1208	Randox microchip	9.6	11.1

Total samples analysed differ because of constraints on sample size, where warfarin may have affected protein synthesis, and according to the materials available. CV indicates coefficient of variation, IL-6, interleukin-6; CRP, C-reactive protein; NGAL, neutrophil gelatinase-associated lipocalin; sTNFR-1, soluble tumor necrosis factor receptor type 1; TM, thrombomodulin; vWF, von Willebrand Factor; PZ, protein Z; anti-PC, anti-phosphorylcholine antibodies; PT, prothrombin time; APTT, activated partial thromboplastin time; Nt-proBNP, N-terminal pro-B-type natriuretic peptide; hFABP, heart type fatty acid binding protein; NSE, neurone specific enolase; BDNF, brain-derived neurotrophic factor.

**Supplementary Table II: Correlations of biomarkers (Spearman rank correlation, p-value)**

	CRP	NGAL	sTNFR-1	TM	Fibrinogen	vWF	P-selectin	PZ	D-dimer	Anti-PC	ADAMTS-13	NT-proBNP	hFABP	NSE	BDNF
<b>IL-6</b>	0.46	0.35	0.47	0.13	0.45	0.46	0.18	-0.18	0.50	-0.08	-0.30	0.29	0.39	0.24	0.23
	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.06	<0.001	<0.001	<0.001	<0.001	<0.001
<b>CRP</b>		0.25	0.33	0.08	0.47	0.29	0.11	-0.02	0.33	0.001	-0.09	0.13	0.21	0.11	0.12
		<0.001	<0.004	0.01	<0.001	<0.001	0.01	0.74	<0.001	0.98	0.06	<0.001	<0.001	0.001	<0.001
<b>NGAL</b>			0.45	0.25	0.21	0.23	0.19	-0.14	0.36	0.01	-0.14	0.18	0.31	0.30	0.38
			<0.001	<0.001	<0.001	<0.001	<0.001	0.001	<0.001	0.90	0.003	<0.001	<0.001	<0.001	<0.001
<b>sTNFR-1</b>				0.42	0.32	0.42	0.19	-0.14	0.54	-0.10	-0.20	0.32	0.53	0.21	0.17
				<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.01	<0.001	<0.001	<0.001	<0.001	<0.001
<b>TM</b>					0.01	0.15	0.06	-0.02	0.24	-0.08	-0.02	0.10	0.33	0.09	0.02
					0.89	<0.001	0.13	0.61	<0.001	0.05	0.64	0.001	<0.001	0.002	0.56
<b>Fibrinogen</b>						0.42	0.09	-0.06	0.41	-0.03	0.002	0.17	0.24	0.11	0.15
						<0.001	0.004	0.07	<0.001	0.33	0.95	<0.001	<0.001	0.003	<0.001
<b>vWF</b>							0.12	-0.09	0.47	-0.06	-0.19	0.30	0.43	0.15	0.12
							<0.001	0.01	<0.001	0.07	<0.001	<0.001	<0.001	<0.001	0.001
<b>P-selectin</b>								-0.01	0.22	-0.01	-0.01	0.09	0.13	0.14	0.14
								0.73	<0.001	0.73	0.84	0.01	<0.001	<0.001	<0.001
<b>Protein Z</b>									-0.11	0.03	0.07	-0.07	-0.09	-0.03	-0.06
									0.004	0.40	0.03	0.40	0.02	0.41	0.14
<b>D-dimer</b>										-0.10	-0.30	0.35	0.44	0.20	0.16
										0.02	<0.001	<0.001	<0.001	<0.001	<0.001
<b>Anti-PC</b>											0.16	0.03	-0.09	0.07	-0.003
											<0.001	0.36	0.32	0.11	0.94
<b>ADAMTS-13</b>													-0.04	-0.23	-0.09
													0.24	<0.001	0.03
<b>NT-proBNP</b>														0.31	0.08
														<0.001	0.007
<b>hFABP</b>															0.17
															<0.001
<b>NSE</b>															0.47
															<0.001

**Supplementary Table III:** Correlations of biomarker levels with eGFR in TIA, minor and major stroke subgroups (Spearman rank correlation, p-value)

Biomarker	TIA		Minor Stroke (NIHSS≤3)		Major Stroke (NIHSS>3)		P value for difference
	eGFR R	eGFR p-value	eGFR R	eGFR p-value	eGFR R	eGFR p-value	
<i>Inflammatory markers</i>							
IL-6	-0.18	0.001	-0.25	<0.001	-0.13	0.395	0.23
CRP	-0.09	0.086	-0.12	0.016	0.13	0.129	0.04
NGAL	-0.28	<0.001	-0.31	<0.001	-0.20	0.005	0.41
sTNFR-1	-0.36	<0.001	-0.46	<0.001	-0.46	<0.001	0.15
<i>Thrombotic or anti-atherogenic markers</i>							
TM	-0.29	<0.001	-0.34	<0.001	-0.43	<0.001	0.11
Fibrinogen	-0.20	<0.001	-0.22	<0.001	-0.03	0.666	0.03
vWF	-0.35	<0.001	-0.26	<0.001	-0.25	<0.001	0.29
P-selectin	-0.10	0.078	-0.08	0.128	-0.09	0.103	0.96
Protein Z	0.11	0.056	-0.04	0.409	0.05	0.352	0.13
D-dimer	-0.43	<0.001	-0.42	<0.001	-0.18	0.003	<0.001
Anti-PC	0.08	0.173	0.09	0.087	-0.06	0.412	0.20
ADAMTS-13	0.17	0.002	0.06	0.301	0.01	0.856	0.16
<i>Markers of cardiac or neuronal function/injury</i>							
NT-proBNP	-0.32	<0.001	-0.42	<0.001	-0.39	<0.001	0.29
hFABP	-0.56	<0.001	-0.60	<0.001	-0.61	<0.001	0.55
NSE	0.01	0.845	-0.14	0.001	-0.05	0.391	0.08
BDNF	0.04	0.459	-0.02	0.726	0.09	0.141	0.54

IL-6, interleukin-6; CRP, C-reactive protein; NGAL, neutrophil gelatinase-associated lipocalin; sTNFR-1, soluble tumor necrosis factor receptor type 1; TM, thrombomodulin; vWF, von Willebrand Factor; PZ, protein Z; anti-PC, anti-phosphorylcholine antibodies; PT, prothrombin time; APTT, activated partial thromboplastin time; Nt-proBNP, N-terminal pro-B-type natriuretic peptide; hFABP, heart type fatty acid binding protein; NSE, neurone specific enolase; BDNF, brain-derived neurotrophic factor; NIHSS, National Institutes of Health Stroke Scale.

**Supplementary Table IV:** Correlations of biomarker levels with eGFR-FAS (eGFR estimated using the Full Age Spectrum) on both linear and log-log scales using Spearman rank and Pearson correlations

Biomarker	eGFR		Log eGFR		Log eGFR	
	R (unadjusted)	p-value	R <sup>2</sup> (unadjusted)	p-value	R <sup>2</sup> (age-adjusted)	p-value
<i>Inflammatory markers</i>						
IL-6	-0.23	<0.001	0.05	<0.001	0.001	0.23
CRP	-0.08	0.02	0.008	0.009	0.001	0.29
NGAL	-0.27	<0.001	0.07	<0.001	0.03	<0.001
sTNFR-1	-0.45	<0.001	0.23	<0.001	0.11	<0.001
<i>Thrombotic or anti-atherogenic markers</i>						
TM	-0.35	<0.001	0.11	<0.001	0.09	<0.001
Fibrinogen	-0.18	<0.001	0.02	<0.001	0.01	0.02
vWF	-0.32	<0.001	0.10	<0.001	0.02	<0.001
P-selectin	-0.09	0.005	0.004	0.04	0.001	0.46
Protein Z	0.05	0.08	0.002	0.16	0.001	0.35
D-dimer	-0.43	<0.001	0.17	<0.001	0.006	0.01
Anti-PC	0.09	0.009	0.006	0.02	0.003	0.10
ADAMTS-13	0.14	<0.001	0.01	0.001	0.002	0.25
<i>Markers of cardiac or neuronal function/injury</i>						
NT-proBNP	-0.43	<0.001	0.16	<0.001	0.03	<0.001
hFABP	-0.60	<0.001	0.37	<0.001	0.19	<0.001
NSE	-0.07	0.01	0.007	0.004	0.004	0.03
BDNF	-0.006	0.84	0.00005	0.80	0.0002	0.66

Anti-PC indicates antiphosphorylcholin; BDNF, brain-derived neurotrophic factor; CRP, C-reactive protein; hFABP, heart-type fatty-acid-binding protein; IL6, interleukin-6; NGAL, neutrophil-gelatinase-associated lipocalin; NSE, neuron-specific enolase; NT-proBNP, N-terminal pro-B-type natriuretic peptide; sTNFR-1, soluble tumor necrosis factor  $\alpha$  receptor-1; TM, thrombomodulin; and vWF, von Willebrand factor.