

# Greater Serum Concentrations of N-terminal Pro-B-type Natriuretic Peptide, High Sensitivity C-reactive Protein and Inteleukin-6 Predict Poor Outcomes After Stroke

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### Introduction

Studies delineating clinical utility of stroke biomarkers are encouraged. Greater serum concentrations of N-terminal pro-B-type natriuretic peptide (NT-proBNP), high sensitivity C-reactive protein (hsCRP) and inteleukin-6 (IL -6) concentrations were implicated in poor outcomes of stroke patients.

In acute ischemic and hemorrhagic stroke patients we investigated the association of NT-proBNP, hsCRP and IL-6 serum concentrations with stroke severity, and with functional and cognitive outcomes at discharge.

### Methods

Patient recruitment for this single-center observational cohort study took place in the Department of Neurology of Klaipeda University Hospital, Klaipeda, Lithuania between July 2007 and December 2010.

Patients were eligible for the study if they were diagnosed with ischemic or hemorrhagic stroke and were admitted for treatment within 48 hours of symptom onset. Exclusion criteria covered inability to comprehend the study assignments due to severe neurological impairment, inability to communicate in Lithuanian and severe concomitant somatic or psychiatric disease.

Seventy eight patients (53 men; median age 72 years) met the study criteria and were evaluated for:

- Clinical stroke severity (Scandinavian Stroke Scale or SSS);
- Functional status before stroke (modified Rankin scale or mRS)
- Cerebrovascular disease risk factors.

Within 24-hours of admission blood samples were drawn for assesment of NT-proBNP, hsCRP and IL-6 serum concentration.

At hospital discharge patients were evaluated for:

- Cognitive outcomes (Mini Mental State Examination);
- Functional outcomes (mRS).

## Results

Seventy (90%) patients were diagnosed with ischemic stroke and 8 (10%) patients – with hemorrhagic stroke. The most prevalent cerebrovascular disease risk factors were arterial hypertension (63%) and atrial fibrillation (28%), followed by smoking (20%) and diabetes mellitus (14%). Median SSS score on admission was 39.5 (26–50). Median serum concentrations of NT-proBNP, hsCRP and IL-6 were 578.65 (108.43–2277.75) ng/L, 0.81 (0.29–2.87) mg/dl and 12.83 (6.50–29.80) pg/ml, respectively.

Greater NT-proBNP and hsCRP serum concentrations were associated with greater clinical stroke severity, adjusting for patients' gender, age, stroke type, admission mRS score, and presence of heart failure ( $\beta$ =-0.292; p=0.012 and  $\beta$ =-0.303, p=0.009)

At discharge, mdian mRS and MMSE discharge scores were 4 (2-5) and 22 (14-26), respectively.

In multivariable adjusted regression models with IL-6, hsCRP and NT-proBNP considered together, IL-6 and hsCRP remained associated with worse functional ( $\beta$ =0.210; p=0.022) and cognitive ( $\beta$ =-0.269; p=0.014) outcomes at discharge, respectively.

$Association \ of \ functional \ outcomes \ and \ cognitive \ outcomes \ at \ discharge \ with \ serum \ concentrations \ of \ IL-6, \ hs CRP$	
and NT-proBNP in univariable and multivariable regression analyses; beta (p).	

	Univariable		Adjusted <sup>a</sup>		Multivariable <sup>b</sup>	
Variable	ß-value	p-value	ß-value	p-value	ß-value	p-value
Functional outcome:	modified Rankin Scal	e score				

Ln NT-proBNP	0.414	< 0.001	0.064	0.24		
Ln hsCRP	0.485	<0.001	0.108	0.272		
Ln IL-6	0.535	<0.001	0.202	0.036	0.210	0.022
R <sup>2</sup> (p)				-		0.62 (<0.001)

Ln NT-proBNP	-0.361	0.004	-0.036	0.788		
Ln hsCRP	-0.498	<0.001	-0.233	0.032	-0.269	0.014
Ln IL-6	-0.392	0.002	-0.052	0.660		1
R <sup>2</sup> (p)						0.47 (<0.001)

In receiver operating characteristic analyses, the investigated blood biomarkers provided with minimal increase of predictive values for discharge outcome above SSS score, age and gender.

Prognostic models	Area under the ROC curve (95%				
	Confidence interval); p-value				
Model 1: Age, gender and clinical stroke severity <sup>a</sup>	0.794 (0.675-0.912); p<0.001				
Model 1 + hsCRP	0.852 (0.758-0.946); p<0.001				
Model 1+ NT-proBNP	0.816 (0.708-0.925); p<0.001				
Model 1 + IL-6	0.873 (0.790-0.956); p<0.001				

<sup>a</sup> – score on the Scandinavian Stroke Scale

### Conclusions

In acute stroke patients, greater NT-proBNP and hsCRP serum concentration are independently associated with greater clinical stroke severity. Elevated concentrations of IL-6 and hsCRP are associated with worse functional and cognitive discharge outcomes, respectively.

### **Learning Objectives**

To learn that greater inflammatory marker and NTproBNP concentrations are associated with poor discharge outcomes in acute cerebrovascular disease patients.

#### References

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