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CANDIDATE PLASMA PROTEIN BIOMARKERS FOR PREOPERATIVE STROKE RECURRENCE AND SYMPTOMATIC STATUS IN CASES WITH CAROTID STENOSIS – AN EXPLORATORY ANALYSIS

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Background and aims: Symptomatic carotid stenosis (CS) (≥50%, NASCET) causes a high risk of stroke recurrence, which asymptomatic CS does not. We aimed to identify potential plasma protein biomarkers associated with preoperative ipsilateral ischemic stroke recurrence (PIISR) after presenting event and symptomatic status (SS), using broad proteomic profiling.

Methods: Prospective cohort study including 168 consecutive participants with CS: 139 symptomatic, of which 18 had a PIISR, and 29 asymptomatic. Relative levels of 5420 plasma proteins were analyzed using Olink Explore HT. Firth logistic regressions were used to estimate OR and 95% CI for proteins and outcomes. Since most PIISR preceded blood sampling (n=15), we adjusted for NfL (neuroaxonal injury biomarker) in multivariable regressions. For SS, multivariate analysis adjusted for CS degree and stroke >6 months before presenting event. Multiple-testing correction used the estimate of the effective multiplicity

(M*eff*), with *P* 0.05/260=0.0002 considered significant and $P<0.001$ suggestive.

Results: Four proteins were suggestively associated with PIISR. For FAM167A and ING2 elevated levels increased the odds of recurrence (OR (95% CI): 5.1 (2.0-14.9) and 3.6 (1.6-9.1), respectively). For NPIPB6 and CA4 elevated levels decreased the odds of recurrence (0.2 (0.1 to 0.6) and 0.3 (0.2 to 0.7), respectively). Five proteins were suggestively associated with SS, one directly, namely ALPK2 (3.1 (1.6-6.8)), and four inversely: CD276 (0.1 (0.03-0.4), ADAMTS8 (0.2 (0.09-0.6)), ENPP1 (0.2 (0.05-0.5)) and GOLGA8F_G (0.4 (0.3-0.7)).

Conclusions: We identified novel candidate plasma protein biomarkers of CS PIISR and SS. Replication in other stroke cohorts and further investigations into the putative role of these proteins for CS are warranted.

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