

PhD THESIS: THE IMPACT OF LIPIDIC PROFILE AS A PREDICTIVE BIOMARKER ON ACUTE STROKE PROGNOSIS

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Stroke represents a clinical syndrome defined as a focal neurological deficit due to a vascular injury of the central nervous system. It represents one of the primary causes of death and disability worldwide, ischemic stroke representing 80% of the total number of cases. Stroke is not an unique pathology, due to associated risk factors and physiopathological mechanisms with a direct role in its incidence.

The impact of the lipidic profile over stroke prognosis represented a well justified choice because lipidic profile has always played an important role in ischemic stroke physiopathology, even though it was always associated with a bad prognosis. The current tendencies in research started to prove the opposite, and showed a paradoxical relationship which this has over the prognosis of stroke, even though dyslipidemia remains one of the risk factors in ischemic stroke.

In the general part, we presented the current state of knowledge which included data referring to stroke (definition, epidemiology, classification, physiopathology, methods of diagnosis and methods of treatment), data regarding biomarkers and their predictive role in stroke, this being presented in a separate study attached to the PhD thesis. We also presented the lipidic profile, both the classical one and regarding fatty acids, with the description of the lipidic paradox. The general part was based on 40 references.

The personal contribution included three studies which led finally to the accomplishment of the proposed objectives.

In the first study, we identified and presented 23 biomarkers, and we described their role as risk factors, detection markers, prognostic predictors, and their use as therapeutic targets. These biomarkers offered significant data regarding the improvement of clinical practice. We considered that from these biomarkers, we can use in the future especially those biomarkers which are used for risk stratification, especially in patients who never presented stroke or transient ischemic stroke, and we underlined the significance of PAPP-A or VEGF. We also analyzed the diagnostic power in atherothrombotic stroke of haptoglobin or serum amyloid A.

In the second study, we followed-up prospectively 298 patients with the diagnosis of ischemic stroke in a 6-month period (January - June 2022) who were admitted in the 1st Neurology Clinic of Emergency Clinical County Hospital. The purpose of the study was the analysis of the classical and extended lipidic profile including fatty acids as potential neuroprotective biomarkers on the prognosis of ischemic stroke patients. We collected clinical, paraclinical data and prognostic data. We used a method which consisted of high-performance liquid chromatography coupled with mass spectrometry for the quantification of the serum level of fatty acids. We observed a negative correlation between NIHSS score at admission and the serum value of total cholesterol, and triglyceride level. The ratio between eicosapentaenoic (EPA) and arachidonic acid presented a negative correlation, whereas the ration

between docosahexaenoic (DHA) and eicosapentaenoic acid was positively correlated with all prognostic parameters, and therefore showed a potentially neuroprotective role for eicosapentaenoic acid in the prevention of severe ischemic stroke. We therefore concluded that the impact of lipidic profile paradox and the dependency relationship between fatty acids is a significant predictive factor for functional prognosis and disability prognosis of patients admitted with ischemic stroke.

In the third study, we followed-up prospectively 274 patients admitted with the diagnosis of ischemic stroke in the 1st Neurology Clinic of the Emergency County Clinical Hospital of Targu Mures in a 6-month period (January-June 2022), and we excluded all patients with transient ischemic attack or stroke mimic pathologies, which were confirmed after the admission of patients. The purpose of the study was to establish the relationship between ischemic stroke and fatty acids. We collected clinical data regarding risk factors and paraclinical data represented by the serum values of fatty acids, and we used the same method which we mentioned before of high-performance liquid chromatography coupled with mass spectrometry. We observed that smoking is the risk factor with the highest influence on fatty acids, being inversely proportional with the serum values of DHA and EPA, especially in female patients and in patients with recurrent stroke, regardless of sex. We concluded therefore that a more effective control over risk factors, especially in removing modifiable lifestyle risk factors, can influence the fatty acids' profile and the ratio between Omega-3 and Omega-6 in patients with ischemic stroke.

Knowing the potentially predictive biomarkers with establishing sensitivity and specificity of these biomarkers in the clinical practice of the neurology physicians is an interest point for future research, considering the progressive development of the precision medicine.

Early detection of high-risk patient in ischemic stroke shows the need for serum biomarkers as supplementary tools for determining future complications and for accurately predicting short term prognosis, this fact having a major influence over the acute phase of treatment (for example for administering intravenous thrombolysis with rt-PA).

From our knowledge, this is the only complex study in Romania which presents in a complete manner both the peripheral biomarkers with an impact on ischemic stroke patients' prognosis, together with the study of the lipidic profile impact and the extended lipidic profile (fatty acids) on the functional and disability prognosis of these patients.