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## Inflammatory Biomarker and Stroke Rehabilitation a New Point of View about the Role in Prognostic Factor

Patrizio Sale<sup>1\*</sup>, Niki Ragazzo<sup>2</sup> and Anna Maria Cortese<sup>2</sup>

<sup>1</sup>Department of Neurorehabilitation, I.R.C.C.S. San Camillo Hospital, via Alberoni 70, Venice, Italy

<sup>2</sup>Department of Neuroscience, Rehabilitation Unit, Irccs San Camillo, Padua, Italy

\*Corresponding author: Patrizio Sale, Department of Neurorehabilitation, I.R.C.C.S. San Camillo Hospital, via Alberoni 70, 30126, Venice, Italy, Tel: + 39 3357104681; E-mail: [patrizio.sale@gmail.com](mailto:patrizio.sale@gmail.com)

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### Introduction

According to the World Health Organization (WHO), stroke and other cerebrovascular diseases are the second leading cause of death worldwide [1]. Sequelae include partial paralysis, difficulties with memory, thinking, language, and movements. The most common cause of stroke is the sudden occlusion of a blood vessel by a thrombus or embolus, resulting in an almost immediate loss of oxygen and glucose to the cerebral tissue. It is well known that the inflammatory process has an impact on post-ischemic tissue damage in the brain [2,3-7]. Inflammation is an extremely important and complex biological process of the immune system activated in response to harmful stimuli such as pathogens and cell damage. In the last years many efforts have been made to find useful diagnostic markers to be used as disease monitor in patients after stroke. The ideal marker should be involved in the the post-stroke events which include the removal of pathogens and damaged cells and/or the healing process. In particular, neutrophil/granulocyte [8,9] and macrophage/microglia [10,11] have been identified as the principal actors in post-ischemic processes.

Recent studies have shown that T-cells also have an impact on tissue damage [12-20]. Several studies have seen that an attenuation of the inflammatory process could be a possible way to widen the therapeutic window after the acute event [8,11,12]. However, other studies pointed out that the inflammatory response is necessary in order, for example, to remove dead neurons and other brain cells in the ischaemic core, and promote astrogliosis. Consequently, it is not possible to strictly categorize the inflammatory process as being either beneficial or deleterious in relation to stroke [13]. A few recent clinical studies looked at the post-stroke inflammatory responses within the brain [14,15].

High fibrinogen plasma levels are considered as an independent predictor of myocardial infarction and ischemic stroke [16-18], furthermore Potpara and colleagues identified the association of plasma high fibrinogen levels with poor functional 30-day outcome in ischemic stroke [19].

Our recent experience in inflammatory biomarker and stroke rehabilitation demonstrated a fundamental role of fibrinogen plasmatic levels on patient admission to the stroke rehabilitative care and its correlation with gain in activities of daily living (ADL) at on discharge from rehabilitative care.

In particular, we analysed the correlation with effectiveness of the Functional Independence Measure (eFIM) scale and the plasmatic levels of fibrinogen. The FIM is a basic indicator of severity of disability for evaluating ADL in subjects with stroke. Total scores range from 18

to 126 and indicate to what extent an individual is capable to reach independence in ADL. In our study we used the FIM effectiveness, calculated as  $(\text{FIM at discharge} - \text{FIM on admission}) / (126 - \text{FIM on admission})$  according to Koh and colleagues [20]. FIM effectiveness, which is independent from FIM on admission, has been used to compare patients with various degrees of disability severity. Another indicator used to predict and to measure the cost of the rehabilitative treatment is the rehabilitative Length of Stay (rLOS). The rLOS value represents the total number of rehabilitation days from admission to discharge.

From September 2015 to May 2016 we enrolled and analysed data from 33 patients at their first ischemic stroke on admission to our Rehabilitation Hospital. Their diagnoses of ischemic stroke were confirmed with CT scan and/or MRI brain scans. All subjects enrolled in the study underwent a multi-disciplinary rehabilitative approach and high intensity therapy. In particular, all underwent routine inpatient rehabilitation, consisting of a daily 3-hours physiotherapy session, including both dexterity and gait training, according to individually tailored exercise schedule.

Using the Pearson test we found a statistical correlation between eFIM and fibrinogen level with  $r=0.4147$  and a  $p=0.0096$  and between LOS and fibrinogen levels with  $r=0.5282$  and a  $p=0.005$ . So far our results showed that post-stroke fibrinogen level is significantly associated with ADL functions and hospital costs in post-acute ischemic stroke.

The extent of this analysis to other inflammatory markers in stroke patients on admission to the rehabilitation unit could be an important low cost and reproducible study looking at factors influencing rLOS as well as useful tool to improve rehabilitation resources planning for stroke patients from early days. Fibrinogen could be candidate as a significant predictor of the rLOS in patients with ischemic stroke as it is simple to measure, inexpensive, available biomarker and may be used as a practical tool to guide the economic burden of stroke. On that basis in the future, however, additional studies are required to confirm our results.

### References

1. World Health Organization (2011) The Top 10 Causes of Death. Fact sheet number 310 Geneva.
2. Lakhan SE, Kirchgessner A, Hofer M (2009) Inflammatory mechanisms in ischemic stroke: therapeutic approaches. *J Transl Med* 7: 97.
3. Brea D, Sobrino T, Ramos-Cabrer P, Castillo J (2009) Inflammatory and neuroimmunomodulatory changes in acute cerebral ischemia. *Cerebrovasc Dis* 27 Suppl 1: 48-64.

4. Iadecola C, Alexander M (2001) Cerebral ischemia and inflammation. *Curr Opin Neurol* 14: 89-94.
5. Muir KW, Tyrrell P, Sattar N, Warburton E (2007) Inflammation and ischaemic stroke. *Curr Opin Neurol* 20: 334-342.
6. Veldhuis WB, Derksen JW, Floris S, Van Der Meide PH, De Vries HE, et al. (2003) Interferon-beta blocks infiltration of inflammatory cells and reduces infarct volume after ischemic stroke in the rat. *J Cereb Blood Flow Metab* 23: 1029-1039.
7. Barone FC, Hillegass LM, Price WJ, White RF, Lee EV, et al. (1991) Polymorphonuclear leukocyte infiltration into cerebral focal ischemic tissue: myeloperoxidase activity assay and histologic verification. *J Neurosci Res* 29: 336-345.
8. Matsuo Y, Kihara T, Ikeda M, Ninomiya M, Onodera H, et al. (1995) Role of neutrophils in radical production during ischemia and reperfusion of the rat brain: effect of neutrophil depletion on extracellular ascorbyl radical formation. *J Cereb Blood Flow Metab* 15: 941-947.
9. Satoh S, Kobayashi T, Hitomi A, Ikegaki I, Suzuki Y, et al. (1999) Inhibition of neutrophil migration by a protein kinase inhibitor for the treatment of ischemic brain infarction. *Jpn J Pharmacol* 80: 41-48.
10. Shichita T, Sugiyama Y, Ooboshi H, Sugimori H, Nakagawa R, et al. (2009) Pivotal role of cerebral interleukin-17-producing gammadelta T cells in the delayed phase of ischemic brain injury. *Nat Med* 15: 946-950.
11. Campanella M, Sciorati C, Tarozzo G, Beltramo M (2002) Flow cytometric analysis of inflammatory cells in ischemic rat brain. *Stroke* 33: 586-592.
12. Brait VH, Arumugam TV, Drummond GR, Sobey CG (2012) Importance of T lymphocytes in brain injury, immunodeficiency, and recovery after cerebral ischemia. *J Cereb Blood Flow and Metab* 32: 598-611.
13. Grønberg NV, Johansen FF, Kristiansen U, Hasseldam H (2013) Leukocyte infiltration in experimental stroke. *J Neuroinflammation* 10: 115.
14. Rosell A, Cuadrado E, Ortega-Aznar A, Hernández-Guillamon M, Lo EH, et al. (2008) MMP-9-positive neutrophil infiltration is associated to blood-brain barrier breakdown and basal lamina type IV collagen degradation during hemorrhagic transformation after human ischemic stroke. *Stroke* 39: 1121-1126.
15. Pappata S, Levasseur M, Gunn RN, Myers R, Crouzel C, et al. (2000) Thalamic microglial activation in ischemic stroke detected in vivo by PET and [<sup>11</sup>C]PK1195. *Neurology* 55: 1052-1054.
16. Eidelman RS, Hennekens CH (2003) Fibrinogen: a predictor of stroke and marker of atherosclerosis. *Eur Heart J* 24: 499-500.
17. Siegerink B, Rosendaal FR, Algra A (2009) Genetic variation in fibrinogen; its relationship to fibrinogen levels and the risk of myocardial infarction and ischemic stroke. *J Thromb Haemost* 7: 385-390.
18. Potpara TS, Polovina MM, Djikic D, Marinkovic JM, Kocic N, et al. (2014) The association of CHA2DS2-VASc score and blood biomarkers with ischemic stroke outcomes: the Belgrade stroke study. *PLoS One* 9: e106439.
19. Pikijsa S, Trkulja V, Mutzenbach JS, McCoy MR, Ganger P, et al. (2016) Fibrinogen consumption is related to intracranial clot burden in acute ischemic stroke: a retrospective hyperdense artery study. *J Transl Med* 14: 250.
20. Koh GC, Chen CH, Petrella R, Thind A (2013) Rehabilitation impact indices and their independent predictors: a systematic review. *BMJ Open* 3: e003483.