

## Short Communication:

# Diagnostic utility of biomarker panels in ischemic stroke

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## Abstract:

Biomarker panels may have several applications in stroke. They may be useful to differentiate ischemic stroke and transient ischemic attacks from hemorrhagic stroke and other stroke mimics. In such studies it will be important to determine whether the biomarker panel can add to neuroimaging diagnosis of stroke, and potentially aid in the early diagnosis of brain ischemia.

It should also be determined if biomarker panels may be a significant diagnostic tool in settings where neuroimaging is not readily available or in patients where mild brain ischemic injury is not well visualized by MRI.

Biomarker panels may also be useful to determine cause of stroke, particularly in patients where cause cannot be ascertained using current technology. Biomarker panels may also find applications to stratify risk of future stroke, provide prognostic information, or potentially identify patients most likely to benefit from stroke treatments such as reperfusion or hypothermia.

**Keywords:** Biomarkers , stroke

## Introduction:

Given the heterogeneity in ischemic stroke, a single biomarker may not be able to sufficiently reflect the underlying complexity. This has kindled interest in the use of biomarker panels. A biomarker panel is a group of markers that reflect different pathophysiological processes of a disease. In stroke such markers might provide information about atherosclerosis, thrombus formation, inflammation, oxidative stress, endothelial injury, blood brain barrier disruption and cerebral ischemia. A common approach to improve classification is the use of multiple markers.

## Application of biomarkers panel in stroke:

Biomarker panels may have several applications in stroke. They may be useful to differentiate ischemic stroke and transient ischemic attacks from hemorrhagic stroke and other stroke mimics. In such studies it will be important to determine whether the biomarker panel can add to neuroimaging diagnosis of stroke, and potentially aid in the early diagnosis of brain ischemia.

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Biomarker panels may also be useful to determine cause of stroke, particularly in patients where cause cannot be ascertained using current technology. Biomarker panels may also find applications to stratify risk of future stroke,

provide prognostic information, or potentially identify patients most likely to benefit from stroke treatments such as reperfusion or hypothermia.<sup>73</sup>

Biomarker panels have also been evaluated for the diagnosis of ischemic stroke.

These include a panel of 5 proteins (MMP9, BNGF, vWF, MCP-1, S100B)<sup>74</sup>, a panel of 4 proteins (MMP9, brain natriuretic factor, D-dimer, and S100B)<sup>75</sup>, and a panel of 5 proteins (eotaxin, epidermal growth factor receptor, S100A12, metalloproteinase inhibitor-4 and prolactin).<sup>76</sup> The combination of multiple markers in a panel has consistently demonstrated improved sensitivity and specificity to identify acute ischemic stroke compared to individual markers. Though none have provided sufficient evidence to demonstrate clinical utility, the results support the concept of combining multiple markers into a panel.

A panel of 5 protein markers (S100B, B-type neurotrophic growth factor (BNGF), von Willebrand factor (vWF), MMP-9, monocyte chemoattractant protein-1) was initially evaluated in 223 patients with acute stroke (82 ischemic, 103 hemorrhagic) compared to 214 healthy controls. It was able to distinguish stroke from controls with 92% sensitivity and 93% specificity. Samples were acquired from plasma within 6 hours of stroke onset and evaluated by ELISA. Over 50 proteins were initially evaluated and reduced to the 5 markers.

The final model of the 5 markers was developed using logistic regression and evaluated in the derivation cohort.<sup>74</sup>

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Date of Submission: 2 May 2020

Date of Peer Review: 21 May 2020

Date of Acceptance: 18 June 2020

Date of Publishing: 30 June 2020

Author Declaration: Source of support: Nil , Conflict of interest: Nil

Ethics Committee Approval obtained for this study? NA

Was informed consent obtained from the subjects involved in the study? NA

For any images presented appropriate consent has been obtained from the subjects: NA

Plagiarism Checked: YES

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DOI: 10.36848/APAD/2020/13511.51662