EARLY DIAGNOSTIC BIOMARKERS IN ACUTE ISCHEMIC STROKE: CLINICAL SIGNIFICANCE AND FUTURE PERSPECTIVES

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Abstract
Acute ischemic stroke (AIS) is a leading cause of mortality and long-term disability worldwide. Rapid and accurate diagnosis is critical for effective treatment and improved patient outcomes. Neuroimaging remains the gold standard for diagnosis; however, it may be limited by availability, cost, and time constraints. Consequently, there is growing interest in identifying reliable early diagnostic biomarkers that can facilitate prompt diagnosis, guide therapeutic decisions, and predict prognosis. This article reviews current knowledge regarding early diagnostic biomarkers in acute ischemic stroke, including inflammatory markers, neuronal injury biomarkers, glial markers, endothelial dysfunction indicators, and microRNAs. The clinical significance, diagnostic accuracy, and future perspectives of these biomarkers are discussed, highlighting their potential role in precision medicine and stroke management.
Keywords: acute ischemic stroke, biomarkers, early diagnosis, neuroinflammation, neuronal injury, precision medicine

INTRODUCTION

Acute ischemic stroke (AIS) occurs as a result of sudden interruption of cerebral blood flow, leading to irreversible neuronal damage if not promptly treated. It accounts for approximately 85% of all stroke cases and represents a major public health burden globally. Early diagnosis and timely reperfusion therapy, such as thrombolysis and mechanical thrombectomy, significantly reduce morbidity and mortality.

Currently, neuroimaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI) are essential for diagnosing AIS and excluding hemorrhagic stroke. However, these modalities may be inaccessible in prehospital settings or resource-limited regions. Moreover, early ischemic changes may not always be evident on initial imaging.

In this context, blood-based biomarkers have emerged as promising tools for early detection of AIS. Ideal biomarkers should be highly sensitive, specific, rapidly measurable, and capable of differentiating ischemic stroke from stroke mimics. Advances in molecular biology and proteomics have led to the identification of numerous candidate biomarkers reflecting different pathophysiological processes of ischemic brain injury.

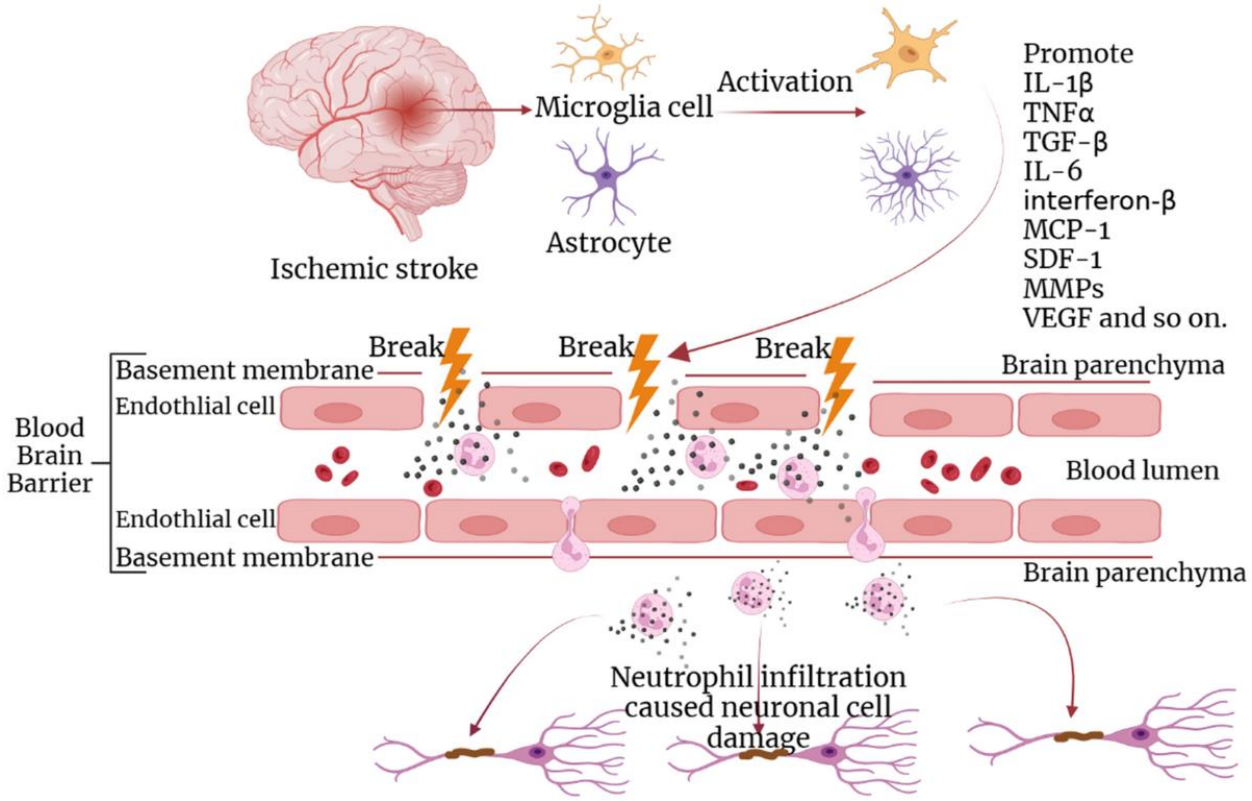
This article aims to provide a comprehensive overview of early diagnostic biomarkers in acute ischemic stroke, their clinical relevance, and future directions in stroke diagnostics.

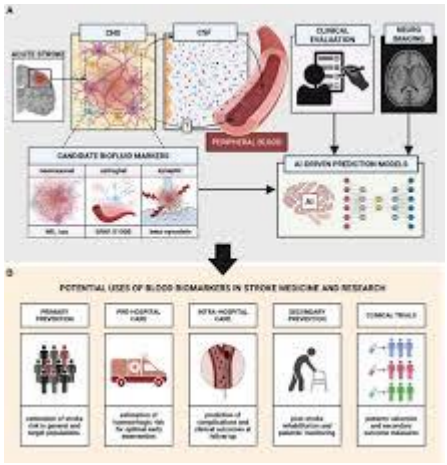
Materials and Methods

This narrative review is based on an extensive search of peer-reviewed literature published between 2000 and 2025. Databases including PubMed, Scopus, Web of Science, and Google Scholar were systematically searched using keywords such as *acute ischemic stroke*, *early biomarkers*, *neuroinflammation*, *neuronal injury markers*, *glial biomarkers*, and *microRNAs*.

Original research articles, clinical trials, systematic reviews, and meta-analyses focusing on early diagnostic biomarkers in AIS were included. Studies involving animal models and translational research were also reviewed to assess emerging biomarkers. Articles lacking methodological rigor or clinical relevance were excluded.

Pathophysiological Basis of Biomarker Release





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The pathophysiology of AIS involves a cascade of events triggered by cerebral hypoxia and energy failure. Neuronal depolarization, excitotoxicity, oxidative stress, inflammation, and blood–brain barrier (BBB) disruption result in the release of various molecules into the systemic circulation. These molecules serve as potential biomarkers reflecting the extent and timing of ischemic injury.

Results

Inflammatory Biomarkers

Inflammation plays a central role in ischemic brain injury. Elevated levels of C-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interleukin-1β (IL-1β) have been consistently observed in the early phase of AIS. High CRP and IL-6 levels correlate with infarct size and poor clinical outcomes, although their specificity is limited.

Neuronal Injury Biomarkers

Neuron-specific enolase (NSE), ubiquitin carboxy-terminal hydrolase L1 (UCH-L1), and tau protein are released following neuronal damage. NSE levels increase within hours of stroke onset and are associated with stroke severity. Tau protein reflects axonal injury and has shown potential in distinguishing ischemic stroke from transient ischemic attack (TIA).

Glial Biomarkers

Glial fibrillary acidic protein (GFAP) is a marker of astrocytic injury and BBB disruption. While GFAP is more specific for hemorrhagic stroke, moderate elevations may also be detected in ischemic stroke, particularly in large infarctions. S100B protein is another glial marker associated with cerebral edema and prognosis.

Endothelial Dysfunction and Coagulation Markers

Endothelial activation and thrombosis are key components of AIS. Elevated levels of matrix metalloproteinase-9 (MMP-9), von Willebrand factor (vWF), and D-dimer have been reported in the hyperacute phase. MMP-9 is associated with BBB breakdown and hemorrhagic transformation.

MicroRNAs and Novel Molecular Biomarkers

MicroRNAs (miRNAs) are small non-coding RNAs involved in gene regulation. Several circulating miRNAs, such as miR-124, miR-21, and miR-210, have demonstrated diagnostic potential in AIS. These biomarkers offer high stability and specificity, making them promising candidates for future clinical application.

Discussion

The identification of early diagnostic biomarkers in AIS represents a significant advancement in stroke medicine. While no single biomarker currently meets all criteria for ideal diagnostic performance, combinations of biomarkers reflecting different pathophysiological pathways may enhance accuracy.

Inflammatory and neuronal injury markers provide valuable information regarding stroke severity and prognosis, whereas endothelial and coagulation markers assist in understanding thrombotic mechanisms. Emerging molecular biomarkers, particularly miRNAs, hold promise for rapid, point-of-care testing and personalized treatment strategies.

Challenges remain regarding standardization, assay availability, and validation in large, multicenter clinical trials. Integration of biomarker data with clinical assessment and neuroimaging may represent the optimal diagnostic approach.

Future Perspectives

Future research should focus on:

- Development of rapid bedside biomarker assays
- Validation of multimarker panels
- Integration of biomarkers with artificial intelligence and clinical decision support systems
- Personalized risk stratification and treatment optimization

The application of precision medicine in stroke care is expected to significantly improve early diagnosis and therapeutic outcomes.

Conclusion

Early diagnostic biomarkers offer significant potential for improving the rapid detection and management of acute ischemic stroke. Although neuroimaging remains indispensable, blood-based biomarkers may serve as valuable adjuncts, particularly in prehospital and emergency settings. Continued research and technological innovation are essential to translate these biomarkers into routine clinical practice.

References

1. Whiteley W, et al. **Blood biomarkers for the diagnosis of acute stroke**. Stroke.
2. Jickling GC, Sharp FR. **Biomarker panels in ischemic stroke**. Nat Rev Neurol.
3. Foerch C, et al. **Glial biomarkers in acute stroke**. Neurology.
4. Liu DZ, et al. **MicroRNAs in ischemic stroke diagnosis**. Stroke.