Prognostic Value of C-reactive Protein in Acute Ischemic Stroke Patients: A Review

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Acute ischemic stroke is increasingly recognized as a condition deeply influenced by inflammatory processes that modulate neuronal injury and recovery. C-reactive protein (CRP), a liver-derived acute-phase protein, has attracted interest as a biomarker for predicting neurological deficits and long-term disability in these patients. This review critically examines the empirical evidence connecting elevated CRP levels with stroke severity, subsequent neurological impairment, and functional outcomes, noting both supportive findings and inconsistencies across studies. Mechanistic perspectives are addressed, including the possibility that CRP reflects or contributes to underlying inflammatory cascades exacerbating cerebral damage. Clinical implications of integrating CRP into risk stratification and management protocols are discussed, alongside a careful consideration of unresolved challenges such as methodological heterogeneity, confounding influences, and uncertainties regarding optimal cut-off values and timing of assessment, highlighting directions for future research.

1. INTRODUCTION

Acute ischemic stroke represents a leading cause of mortality and long-term disability worldwide, placing substantial demands on healthcare resources and dramatically affecting patient quality of life. Accurate prognostic assessment in the early phases of stroke is essential to guide clinical decision-making, optimize resource allocation, and facilitate individualized management strategies. Biomarkers capable of reflecting underlying disease processes and predicting future neurological deficits are therefore of keen clinical interest, as they may enable timely intervention and improved outcomes. Within this framework, the inflammatory response has emerged as a critical factor influencing neuronal injury, with C-reactive protein serving as a widely accessible indicator of systemic inflammation. This review aims to examine the potential utility of CRP as a prognostic biomarker in acute ischemic stroke, evaluating its pathophysiological relevance, empirical associations with stroke severity and disability, and the practical considerations for clinical integration.

A. Pathophysiological Rationale

Inflammation constitutes a central mechanism in the development and evolution of acute ischemic stroke, contributing both to immediate neuronal damage and subsequent neurological deficits. Following cerebral ischemia, a cascade of inflammatory mediators, including cytokines and acute-phase proteins, is rapidly triggered, amplifying tissue injury and affecting clinical outcomes [1]. C-reactive protein, which is synthesized by the liver in response to pro-inflammatory signals, serves as a marker detectable in peripheral blood, reflecting the intensity of systemic inflammation present after stroke onset [2]. Elevated CRP levels may indicate ongoing endothelial dysfunction, disruption of the blood-brain barrier, or secondary complications, making it a plausible candidate for prognostic assessment. Given its rapid elevation, standardization of measurement, and association with indices of stroke severity, CRP holds promise as a biomarker, potentially aiding clinicians in risk stratification and early identification of patients at greater risk for adverse outcomes [3].

B. Review of Empirical Evidence

Recent empirical investigations provide a multifaceted perspective on the association between CRP levels and outcomes following acute ischemic stroke. Multiple studies have demonstrated that elevated CRP measured within the initial 24 hours after stroke onset is associated with increased stroke severity as reflected by baseline NIHSS scores and predicts poorer long-term functional status on the modified Rankin Scale (mRS) [2]. For example, **(author?)** [2] established an optimal CRP cut-off of 6.34 mg/L, yielding a sensitivity of 68.2% and specificity of 85.7% for predicting unfavorable outcomes at three months, with CRP remaining an independent risk factor after multivariate adjustment [2]. Meta-analytic syntheses corroborate the predictive value of high-sensitivity CRP (hs-CRP) for mortality and recurrent stroke, yet also emphasize substantial heterogeneity across studies and varied prognostic accuracy depending on the timing of measurement [4]. Furthermore, while some research supports a robust relationship between CRP changes and disability pro-

gression, other investigations have reported weak correlations or failed to demonstrate independent predictive utility beyond established clinical factors [5].

C. Mechanistic Considerations

Another facet of the prognostic capacity of CRP in acute ischemic stroke lies in its proposed mechanistic links to both the perpetuation and reflection of pathological processes underlying neurological injury. CRP may contribute to post-stroke outcomes through the amplification of systemic and local inflammation, exacerbating neuronal dysfunction and potentially fostering secondary complications such as infections or hemorrhagic transformation [6]. Elevated CRP is also associated with atherosclerotic burden and microvascular dysfunction, mechanisms that could promote recurrent vascular events and impede tissue recovery [7]. In this context, there remains active debate regarding whether CRP serves primarily as an indicator of heightened inflammatory states or actively participates as a mediator that directly influences prognosis and recovery trajectories. The coexistence of high CRP with other inflammatory markers and adverse outcomes suggests that both the reflective and interventional roles of CRP merit attention in the ongoing study of stroke pathophysiology and risk assessment [8].

D. Clinical Implications and Limitations

However, the clinical application of CRP as a prognostic biomarker in acute ischemic stroke is complicated by several critical challenges that temper its promise for risk stratification and targeted interventions. While elevated high-sensitivity CRP measured within the first 72 hours offers adjunct predictive value for adverse outcomes and recurrence, variability in optimal cut-off points, timing of assessment, and the impact of comorbidities undermines universal utility [9]. Methodological heterogeneity across studies—including differences in assay techniques, timing of measurement, and population characteristics—creates inconsistent thresholds for clinical decision-making and limits its generalizability [5]. Moreover, confounding factors such as age, infection, and concurrent therapies complicate causal interpretation, raising questions regarding whether CRP acts as an independent driver of pathology or simply as a downstream marker [10]. Consequently, although integration of CRP into prognostic models may contribute additional risk information, its incorporation into practice requires established protocols, improved specificity, and validation in diverse real-world settings.

2. CONCLUSION

Collectively, the evidence indicates that C-reactive protein possesses the potential to function as an accessible biomarker for prognostication in acute ischemic stroke, particularly when measured within defined temporal windows. Nevertheless, unresolved issues related to methodological variability, population diversity, and confounding variables diminish the consistency of CRP's prognostic accuracy and constrain its widespread implementation. Current studies do not fully establish whether CRP independently drives adverse outcomes or serves only as a marker of underlying inflammation, and the absence of universally accepted cut-off values further complicates its integration into standardized clinical protocols. Consequently, future research should prioritize the development of robust, multicenter trials that clarify causal relationships, delineate appropriate thresholds, and address the influence of comorbid conditions and therapies on CRP interpretation. Advancing these research efforts will ultimately determine whether CRP can be routinely incorporated into individualized risk stratification and guide management strategies in acute ischemic stroke care.

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