Inflammatory Burden and Early Outcomes after Primary PCI: Pathophysiological Insights and Prognostic Implication

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Received: 28 October 2024, **Accepted:** 17 November 2024, **Published:** 20 November 2024

Abstract

Background: Acute ST-segment elevation myocardial infarction (STEMI) remains a leading cause of morbidity and mortality worldwide despite significant advances in reperfusion strategies, particularly primary percutaneous coronary intervention (PCI). Beyond epicardial coronary artery occlusion, the inflammatory response triggered by plaque rupture and myocardial ischemia plays a central role in determining the extent of myocardial injury and subsequent clinical outcomes. In this context, the concept of inflammatory burden has emerged as a critical determinant of short-term prognosis following primary PCI. Inflammatory burden reflects the complex interplay between innate and adaptive immune activation, endothelial dysfunction, and thrombotic pathways. Circulating inflammatory biomarkers and composite indices—such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), and high-sensitivity C-reactive protein (hs-CRP)—have gained increasing attention as accessible and cost-effective tools for risk stratification. These indices integrate multiple components of the inflammatory cascade and may better capture the global inflammatory milieu compared to single biomarkers.

Accumulating evidence suggests that elevated inflammatory burden is strongly associated with adverse early outcomes after primary PCI, including impaired myocardial reperfusion, no-reflow phenomenon, larger infarct size, reduced left ventricular function, and increased risk of in-hospital mortality and major adverse cardiovascular events. Moreover, inflammation contributes to microvascular obstruction and reperfusion injury, further limiting the benefits of timely revascularization.

The aim of this review is to provide a comprehensive overview of the pathophysiological mechanisms linking inflammation to myocardial injury in the setting of primary PCI, evaluate the prognostic value of various inflammatory burden indices, and explore their potential role in early risk stratification and clinical decision-making. Additionally, emerging therapeutic strategies targeting inflammation in acute coronary syndromes will be discussed. Understanding and integrating inflammatory burden into routine clinical assessment may enhance prognostic precision and open new avenues for personalized management in patients undergoing primary PCI.

Keywords: *Inflammatory Burden, Primary PCI*

Introduction

Primary percutaneous coronary intervention (PCI) represents the gold standard for reperfusion in patients presenting with ST-segment elevation myocardial infarction (STEMI), significantly reducing mortality and improving clinical outcomes when performed in a timely manner. However, despite successful restoration of epicardial coronary blood flow, a substantial proportion of patients continue to experience adverse short-term outcomes, including microvascular obstruction, no-reflow phenomenon, impaired left ventricular recovery, and early mortality. This paradox highlights that myocardial reperfusion is not solely dependent on mechanical restoration of coronary patency but is also profoundly

influenced by underlying biological processes, particularly inflammation [1].

Inflammation plays a pivotal role in all stages of atherosclerosis, from plaque initiation and progression to destabilization and rupture. In the acute phase of myocardial infarction, the inflammatory response is rapidly amplified, involving activation of circulating leukocytes, release of pro-inflammatory cytokines, endothelial dysfunction, and interaction with platelets and the coagulation cascade. This complex inflammatory milieu contributes not only to coronary thrombosis but also to reperfusion injury and microvascular damage following PCI, thereby limiting myocardial salvage despite successful revascularization [2].

In recent years, there has been growing interest in quantifying the systemic inflammatory response through readily available hematological and biochemical markers. Composite inflammatory indices—such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII)—have emerged as practical tools that integrate multiple components of the immune response. These indices provide a more comprehensive reflection of inflammatory burden compared to isolated biomarkers and have demonstrated promising associations with adverse cardiovascular outcomes in patients with acute coronary syndromes [3].

Despite these advances, current risk stratification models in STEMI primarily focus on clinical presentation, hemodynamic parameters, and angiographic findings, with limited incorporation of inflammatory markers. As a result, an important dimension of patient risk—namely, the magnitude of the inflammatory response—remains under-recognized in routine clinical practice. Furthermore, while numerous studies have evaluated individual inflammatory biomarkers, there is still a lack of unified understanding regarding the comparative prognostic value, mechanistic relevance, and clinical applicability of different inflammatory burden indices in the setting of primary PCI [4].

Therefore, a critical need exists to synthesize current evidence on the role of inflammatory burden in determining early outcomes after primary PCI. This includes elucidating the underlying pathophysiological mechanisms, evaluating the prognostic performance of various inflammatory indices, and exploring their integration into clinical risk assessment frameworks. Addressing this gap may not only improve early risk stratification but also support the development of targeted anti-inflammatory strategies aimed at enhancing myocardial recovery and reducing adverse events.

The aim of this review is to provide a comprehensive and clinically relevant analysis of inflammatory burden in STEMI patients undergoing primary PCI, with a particular focus on its pathophysiological basis, prognostic significance, and potential implications for personalized cardiovascular care.

athophysiological Basis of Inflammation in STEMI and Primary PCI

Acute ST-segment elevation myocardial infarction (STEMI) is fundamentally driven by the rupture or erosion of an atherosclerotic plaque, which exposes thrombogenic material to circulating blood and initiates a cascade of platelet activation, coagulation, and inflammatory responses. The inflammatory component is not merely a bystander but a central mediator in plaque destabilization, as activated macrophages, T-lymphocytes, and cytokines weaken the fibrous cap through matrix degradation and apoptosis of vascular smooth muscle cells. This pro-inflammatory microenvironment predisposes plaques to rupture, thereby triggering acute coronary occlusion and myocardial ischemia [5].

Following coronary occlusion, ischemic myocardial tissue rapidly activates the innate immune system. Damaged cardiomyocytes release danger-associated molecular patterns (DAMPs), which stimulate pattern recognition receptors such as Toll-like receptors on immune cells. This leads to the activation of downstream signaling pathways, including nuclear factor-kappa B (NF-κB), resulting in the release of pro-inflammatory cytokines such as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α). These mediators amplify leukocyte recruitment and promote systemic inflammatory activation, which can be detected through circulating biomarkers shortly after symptom onset [6].

Neutrophils are among the earliest responders in the infarcted myocardium and play a dual role in host defense and tissue injury. They infiltrate the ischemic area within hours, releasing reactive oxygen species (ROS), proteolytic enzymes, and neutrophil extracellular traps (NETs), all of which contribute

to endothelial damage and microvascular obstruction. While these processes are essential for clearing necrotic tissue, excessive neutrophil activation exacerbates myocardial injury and impairs microcirculatory perfusion, thereby limiting the benefits of reperfusion therapy [7].

Platelets also serve as key mediators linking thrombosis and inflammation. Beyond their role in clot formation, activated platelets interact with leukocytes through surface adhesion molecules such as P-selectin and CD40 ligand, promoting leukocyte activation and cytokine release. Platelet-leukocyte aggregates further enhance thrombo-inflammatory responses and contribute to microvascular plugging. This interplay explains why composite indices incorporating platelet counts and leukocyte subtypes may better reflect the overall inflammatory burden in STEMI patients [8].

The process of reperfusion, although essential for myocardial salvage, paradoxically introduces additional injury known as ischemia–reperfusion injury. Restoration of blood flow leads to a sudden influx of oxygen and inflammatory mediators, resulting in oxidative stress, calcium overload, endothelial dysfunction, and mitochondrial damage. These mechanisms promote microvascular obstruction and the no-reflow phenomenon, which are strongly associated with worse short-term outcomes despite successful epicardial recanalization during primary PCI [9].

Endothelial dysfunction represents another critical component of the inflammatory cascade in STEMI. Activated endothelial cells express adhesion molecules such as ICAM-1 and VCAM-1, facilitating leukocyte adhesion and transmigration into myocardial tissue. Simultaneously, impaired nitric oxide bioavailability and increased oxidative stress further compromise vasodilation and microvascular integrity. This endothelial activation contributes to impaired tissue-level perfusion even after angiographically successful PCI [10].

The adaptive immune system also participates in the later phases of myocardial injury and repair. T-lymphocytes and monocyte-derived macrophages regulate the balance between pro-inflammatory and reparative processes. While initial inflammation is necessary for debris clearance, prolonged or dysregulated immune activation can lead to adverse ventricular remodeling, fibrosis, and progression to heart failure. Therefore, the magnitude and duration of inflammatory activation are key determinants of clinical outcomes [11].

Importantly, systemic inflammatory response is not confined to the myocardium but reflects a whole-body reaction involving the bone marrow, spleen, and circulating immune cells. This systemic nature explains why peripheral blood-derived indices such as neutrophil-to-lymphocyte ratio (NLR) and systemic immune-inflammation index (SII) can serve as surrogates of myocardial inflammatory activity. These indices capture the balance between pro-inflammatory (neutrophils, platelets) and regulatory (lymphocytes) components, providing insight into the patient's immuno-inflammatory status [12].

In summary, inflammation in STEMI is a multifaceted process that begins with plaque destabilization and extends through myocardial injury, reperfusion, and healing. It involves complex interactions between immune cells, platelets, endothelial function, and oxidative stress. Understanding these mechanisms provides a strong biological rationale for the use of inflammatory burden indices as prognostic tools in patients undergoing primary PCI.

Inflammatory Biomarkers and Composite Indices: Definitions and Clinical Relevance

The assessment of inflammatory burden in patients with ST-segment elevation myocardial infarction (STEMI) has evolved significantly with the increasing recognition of inflammation as a central determinant of outcomes. Traditional inflammatory biomarkers such as C-reactive protein (CRP), interleukins, and leukocyte counts have long been associated with cardiovascular risk; however, their isolated use may not fully capture the complexity of the inflammatory response. This has led to the development of composite inflammatory indices that integrate multiple hematological parameters to better reflect the balance between pro-inflammatory and regulatory immune pathways [13].

Among the most extensively studied biomarkers is high-sensitivity C-reactive protein (hs-CRP), an acute-phase reactant synthesized by the liver in response to interleukin-6 stimulation. Elevated hs-CRP levels have been consistently associated with increased infarct size, impaired myocardial reperfusion, and higher rates of early adverse cardiovascular events following primary PCI. Importantly, hs-CRP

reflects systemic inflammation rather than localized coronary pathology alone, making it a robust but non-specific marker of inflammatory burden in acute coronary syndromes [14].

Interleukin-6 (IL-6) represents another key cytokine in the inflammatory cascade and has emerged as a strong predictor of cardiovascular outcomes. Elevated IL-6 levels are linked to enhanced coagulation activity, endothelial dysfunction, and myocardial injury. Clinical trials targeting the IL-1β/IL-6 pathway have further highlighted its causal role in atherosclerosis and post-infarction inflammation, suggesting that upstream inflammatory signaling pathways may serve both as biomarkers and therapeutic targets [15].

Hematological indices derived from routine complete blood counts have gained substantial attention due to their simplicity, cost-effectiveness, and reproducibility. The neutrophil-to-lymphocyte ratio (NLR) is one of the most widely investigated indices, reflecting the balance between innate immune activation (neutrophilia) and adaptive immune regulation (lymphopenia). Elevated NLR has been strongly associated with impaired coronary flow, increased risk of no-reflow, and higher in-hospital mortality in STEMI patients undergoing primary PCI, making it a valuable prognostic marker in acute settings [16].

Similarly, the platelet-to-lymphocyte ratio (PLR) incorporates both thrombotic and inflammatory components, as platelets play a central role in atherothrombosis and inflammatory signaling. Higher PLR values have been associated with worse angiographic outcomes, increased thrombus burden, and adverse clinical events. However, compared to NLR, PLR may be more influenced by platelet reactivity and comorbid conditions, which can affect its specificity in certain patient populations [17].

The systemic immune-inflammation index (SII), calculated as platelet count × neutrophil count / lymphocyte count, represents a more comprehensive marker that integrates three key cellular components of inflammation and thrombosis. SII has demonstrated superior prognostic performance compared to NLR and PLR in several cardiovascular settings, including STEMI. Elevated SII levels have been linked to increased risk of microvascular obstruction, larger infarct size, and early major adverse cardiovascular events following primary PCI [18].

Other emerging indices, such as the monocyte-to-lymphocyte ratio (MLR) and derived neutrophil indices, have also been explored as markers of inflammatory activation. Monocytes play a critical role in plaque destabilization and post-infarction remodeling, and their relative elevation may indicate a heightened pro-inflammatory state. Although promising, these markers require further validation before widespread clinical adoption [19].

One of the key advantages of composite inflammatory indices lies in their ability to reflect the dynamic interplay between different immune cell populations rather than relying on a single parameter. This multidimensional approach provides a more accurate representation of the patient's inflammatory status and may improve risk stratification beyond traditional clinical and angiographic variables. Additionally, these indices are readily available at hospital admission, allowing for early identification of high-risk patients [20].

Despite their potential, several limitations must be considered. Inflammatory indices can be influenced by various factors, including infections, chronic inflammatory diseases, medications, and hematological disorders. Furthermore, there is currently no standardized cut-off value for many of these indices, which may limit their generalizability across different populations. Therefore, their interpretation should always be integrated within the broader clinical context [21].

In summary, inflammatory biomarkers and composite indices provide valuable insights into the systemic inflammatory response in STEMI patients undergoing primary PCI. Among these, NLR, PLR, and SII have emerged as practical and prognostically significant tools. Their integration into clinical practice holds promise for improving early risk stratification, although further standardization and validation are required.

Impact of Inflammatory Burden on Early Clinical Outcomes after Primary PCI

The clinical relevance of inflammatory burden after primary PCI lies in its close association with early adverse events that determine short-term prognosis in STEMI. Even when epicardial patency is successfully restored, patients with heightened inflammatory activation remain more susceptible to

inadequate tissue-level reperfusion, larger infarct size, early heart failure, and mortality. The acute inflammatory surge following reperfusion amplifies oxidative stress, endothelial dysfunction, neutrophil activation, and microvascular injury, all of which may attenuate the expected benefit of timely PCI and contribute to early clinical deterioration [22].

One of the most well-established associations is between inflammatory burden and the **no-reflow phenomenon**. No-reflow represents impaired myocardial perfusion despite successful reopening of the infarct-related artery and is strongly influenced by distal embolization, endothelial swelling, neutrophil plugging, and platelet-leukocyte interactions. Elevated inflammatory indices, particularly the systemic immune-inflammation index (SII), have been shown to independently predict the occurrence of no-reflow in STEMI patients undergoing primary PCI. These findings support the concept that systemic inflammatory activation reflects microvascular dysfunction and plays a direct role in limiting myocardial reperfusion [23].

Inflammatory burden is also closely linked to **impaired coronary flow and in-hospital mortality**. Elevated neutrophil-to-lymphocyte ratio (NLR) has been associated with reduced coronary perfusion as measured by corrected TIMI frame count and with increased short-term mortality. Mechanistically, neutrophilia reflects heightened innate immune activation and oxidative stress, while lymphopenia may indicate physiological stress and impaired immune regulation. Together, these changes create a pro-inflammatory and pro-thrombotic environment that adversely affects both procedural success and early survival [24].

Another major clinical consequence of increased inflammatory activity is **early left ventricular dysfunction and heart failure**. Biomarkers such as high-sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6) rise rapidly after myocardial infarction and correlate with infarct size and ventricular remodeling. Elevated levels of these markers have been associated with reduced left ventricular ejection fraction, increased incidence of acute heart failure, and worse in-hospital outcomes. Persistent inflammatory activation after reperfusion further contributes to adverse myocardial remodeling and impaired functional recovery [25].

This association is further supported by studies evaluating hematological indices. Higher NLR levels on admission have been linked to significantly increased rates of in-hospital heart failure in STEMI patients undergoing primary PCI. The graded relationship between NLR and heart failure incidence suggests that inflammatory burden is not only a marker of disease severity but also a contributor to myocardial dysfunction and clinical instability during the acute phase [26].

Beyond individual outcomes, inflammatory burden integrates multiple early complications into a unified prognostic framework. Patients with elevated inflammatory indices are more likely to experience a combination of no-reflow, larger infarction, early heart failure, and increased mortality. This highlights the role of inflammation as a central mediator linking ischemic injury, reperfusion damage, and systemic response. Importantly, inflammatory indices provide early and readily available information that may enhance traditional risk stratification models [27].

In summary, increased inflammatory burden is strongly associated with adverse short-term outcomes following primary PCI, including no-reflow phenomenon, impaired coronary perfusion, left ventricular dysfunction, heart failure, and mortality. These findings underscore the importance of incorporating inflammatory assessment into early clinical evaluation, as it may improve risk prediction and guide more tailored management strategies in STEMI patients.

Specific Inflammatory Indices and Their Prognostic Performance after Primary PCI

Among the available inflammatory markers, the **neutrophil-to-lymphocyte ratio (NLR)** is the most extensively studied in STEMI patients undergoing primary PCI. Its clinical value lies in capturing two critical biological processes: neutrophilia as a marker of acute innate inflammatory activation and lymphopenia as an indicator of physiological stress and impaired immune regulation. Numerous studies have demonstrated that elevated admission NLR is associated with impaired myocardial reperfusion, increased incidence of no-reflow, in-hospital heart failure, and mortality, supporting its role as a simple yet powerful prognostic marker in acute coronary settings [28].

The robustness of NLR as a prognostic tool is supported by both observational studies and meta-analyses. Higher NLR levels have been consistently linked with adverse angiographic outcomes, including reduced TIMI flow and impaired myocardial blush grade after PCI. Furthermore, patients in higher NLR categories show a stepwise increase in adverse clinical events, including heart failure and early mortality. This graded relationship highlights the ability of NLR to reflect the severity of systemic inflammatory activation and its direct clinical consequences [29].

The **platelet-to-lymphocyte ratio (PLR)** offers an alternative perspective by incorporating both thrombotic and inflammatory pathways. Platelets contribute not only to thrombus formation but also to inflammatory signaling through interactions with leukocytes and endothelial cells. Elevated PLR has been associated with higher thrombus burden, increased likelihood of distal embolization, and worse short-term outcomes, including major adverse cardiovascular events. However, PLR may be influenced by platelet reactivity and comorbid conditions, which can affect its specificity compared to NLR [30].

The **systemic immune-inflammation index (SII)** has emerged as a more comprehensive marker that integrates neutrophils, lymphocytes, and platelets into a single parameter. This index reflects the combined effects of inflammation, immune regulation, and thrombosis. In STEMI patients undergoing primary PCI, elevated SII has been independently associated with no-reflow phenomenon, larger infarct size, and increased short-term mortality. Comparative analyses suggest that SII may outperform NLR and PLR in certain contexts due to its broader representation of the inflammatory response, although further validation is required [31].

When comparing these indices, it becomes evident that each provides unique but overlapping information. NLR has the strongest evidence base and is widely applicable in clinical practice, while SII offers a more integrative assessment of thrombo-inflammatory activity. PLR may be particularly useful in patients with high platelet reactivity or thrombotic burden. However, variability in study design, patient populations, and cut-off values limits direct comparison, and no single index has yet been universally established as superior [32].

Beyond hematological indices, **high-sensitivity C-reactive protein (hs-CRP)** and **interleukin-6 (IL-6)** remain important biomarkers due to their direct involvement in inflammatory signaling pathways. Elevated levels of hs-CRP and IL-6 have been associated with increased infarct size, microvascular obstruction, and adverse ventricular remodeling. These markers provide mechanistic insight into the inflammatory cascade and have been linked to outcomes in both observational studies and interventional trials targeting inflammatory pathways [33].

From a practical standpoint, the ideal inflammatory marker should be rapidly available, cost-effective, and clinically meaningful. NLR fulfills many of these criteria and is currently the most feasible tool for routine use. SII shows promise as a more comprehensive index but requires further standardization, while hs-CRP and IL-6 offer deeper biological relevance but are less readily available in acute settings. Therefore, a combined approach that integrates simple hematological indices with selected biochemical markers may provide the most accurate assessment of inflammatory burden [34].

In summary, inflammatory indices such as NLR, PLR, and SII have demonstrated significant prognostic value in patients undergoing primary PCI. While each has its strengths and limitations, their collective use enhances early risk stratification and provides insight into the underlying inflammatory state driving clinical outcomes.

Inflammatory Burden and No-Reflow/Microvascular Obstruction after Primary PCI

No-reflow and microvascular obstruction represent two of the most important mechanisms through which inflammatory burden worsens early outcomes after primary PCI. Although the infarct-related epicardial artery may be successfully reopened, effective myocardial reperfusion can still fail at the microcirculatory level. This discordance reflects a complex interplay between distal embolization, endothelial swelling, capillary destruction, reperfusion injury, and thrombo-inflammatory activation. In this setting, inflammation is not merely associated with no-reflow but appears to be one of its central biological drivers, linking systemic immune activation with impaired tissue-level perfusion and larger effective infarct size [35].

The pathogenesis of no-reflow begins before PCI and intensifies during reperfusion. Plaque rupture and thrombus formation trigger intense activation of neutrophils, platelets, and inflammatory mediators. During intervention, distal embolization of thrombotic and atherosclerotic debris into the microcirculation may further obstruct capillary perfusion. At the same time, activated neutrophils adhere to the endothelium, release reactive oxygen species and proteolytic enzymes, and promote local endothelial injury. This inflammatory-endothelial interaction leads to vasomotor dysfunction, tissue edema, and capillary plugging, all of which contribute to persistent microvascular hypoperfusion despite restoration of TIMI flow in the epicardial vessel [36].

Neutrophils play a particularly prominent role in this process. Their early recruitment to the ischemic myocardium is accompanied by degranulation, oxidative burst, and formation of neutrophil extracellular traps, which amplify thrombosis and microvascular obstruction. These mechanisms help explain why elevated neutrophil count and higher neutrophil-based indices are consistently associated with no-reflow after primary PCI. Inflammatory activation therefore acts not only as a marker of injury severity but also as an active mediator of microvascular damage, reinforcing the close biological link between systemic inflammation and failed myocardial reperfusion [37].

Among the available indices, the neutrophil-to-lymphocyte ratio and systemic immune-inflammation index have shown particularly strong associations with no-reflow. Higher admission values of these markers identify patients with a more intense thrombo-inflammatory state, characterized by excessive innate immune activation, relative suppression of adaptive immune regulation, and heightened platelet involvement. Clinical studies have demonstrated that elevated SII independently predicts no-reflow after primary PCI, while NLR has also shown strong discriminatory value in identifying patients at risk of impaired post-procedural myocardial perfusion. These findings support the use of admission inflammatory indices as practical surrogates of microvascular vulnerability [38].

Platelet-mediated inflammation further contributes to no-reflow and microvascular obstruction. Activated platelets promote leukocyte recruitment, interact with neutrophils through P-selectin and other adhesion pathways, and facilitate the formation of microthrombi within the distal coronary circulation. This provides a mechanistic basis for the prognostic relevance of platelet-containing indices such as PLR and SII. Patients with higher platelet-associated inflammatory burden may therefore be especially prone to distal embolization, persistent microvascular obstruction, and suboptimal myocardial blush despite technically successful PCI [39].

Microvascular obstruction is closely related to infarct size, adverse ventricular remodeling, and subsequent heart failure. Imaging studies, particularly those using cardiac magnetic resonance, have shown that microvascular obstruction is not simply an angiographic curiosity but a marker of more severe myocardial damage with important prognostic implications. Since inflammatory burden contributes to endothelial injury, capillary leakage, and reperfusion-related tissue destruction, elevated inflammatory indices may indirectly identify patients at risk of larger infarcts and poorer ventricular recovery. Thus, the prognostic significance of inflammation in STEMI extends beyond procedural complications to structural and functional myocardial consequences [40].

From a clinical perspective, the relationship between inflammatory burden and no-reflow has important implications for risk stratification and targeted therapy. Early identification of patients with elevated inflammatory indices may help recognize those at higher risk of failed tissue reperfusion, prompting closer monitoring and consideration of adjunctive strategies aimed at reducing thrombo-inflammatory injury. Although current evidence supports the prognostic role of these indices, their integration into standardized treatment pathways remains incomplete. Future studies should determine whether inflammation-guided approaches can improve procedural success and short-term outcomes in STEMI patients undergoing primary PCI [41]

Clinical Implications and Risk Stratification Value of Inflammatory Burden after Primary PCI

The growing evidence linking inflammatory burden with no-reflow, heart failure, and early mortality after primary PCI has important implications for bedside risk stratification. Current prognostic models in STEMI, including TIMI and GRACE-based assessments, primarily rely on age, hemodynamic status,

electrocardiographic changes, renal function, and conventional biochemical markers. While these variables remain clinically essential, they do not fully capture the thrombo-inflammatory response that substantially influences myocardial reperfusion, infarct expansion, and early recovery. Inflammatory indices therefore represent a valuable complementary dimension that may refine short-term prognostic assessment beyond traditional tools [42].

One of the main strengths of inflammatory burden indices is their immediate availability at hospital admission. Parameters such as neutrophil count, lymphocyte count, platelet count, and derived indices including NLR, PLR, and SII are obtained from routine complete blood count testing without additional cost or delay. This makes them particularly attractive in acute STEMI care, where rapid decision-making is essential. In contrast to more specialized biomarkers, these indices can be incorporated into the earliest phase of assessment, before or immediately after primary PCI, allowing clinicians to identify patients at higher risk of adverse in-hospital evolution [43].

From a practical standpoint, elevated inflammatory indices may help identify patients who require more intensive surveillance during the acute phase. Patients with marked inflammatory activation are more likely to develop no-reflow, left ventricular dysfunction, malignant arrhythmias, hemodynamic instability, and early heart failure. Recognition of this risk profile may support closer hemodynamic monitoring, earlier echocardiographic reassessment, more cautious discharge planning, and lower threshold for escalation of supportive therapy. Thus, inflammatory burden may function as a bridge between laboratory data and individualized clinical vigilance [44].

Inflammatory assessment may also complement angiographic and procedural findings. For example, a patient with apparently successful epicardial reperfusion but markedly elevated NLR or SII may still carry substantial risk of microvascular dysfunction and adverse remodeling. In such cases, inflammation-based risk recognition could add prognostic nuance beyond final TIMI flow alone. This is particularly relevant because angiographic success does not always translate into adequate tissue reperfusion, and inflammatory indices may help explain part of this discrepancy by reflecting ongoing endothelial and immune-mediated microvascular injury [45].

Another important consideration is the potential integration of inflammatory burden into multimarker or composite risk models. Rather than replacing established predictors, inflammatory indices are most likely to be clinically useful when combined with clinical presentation, infarct location, Killip class, troponin elevation, and imaging parameters. Such an integrated approach may improve risk discrimination and facilitate a more personalized estimation of short-term prognosis. However, before routine incorporation into formal scoring systems, further validation is needed to define optimal cut-off values, timing of measurement, and incremental predictive gain across diverse populations [46].

Despite their promise, inflammatory indices should not be interpreted in isolation. Their levels may be influenced by non-cardiac conditions such as infection, chronic inflammatory disease, malignancy, hematologic abnormalities, or recent medication exposure. This lack of absolute specificity means that clinical context remains essential when applying these markers in STEMI. A high NLR or SII may indicate severe infarction-related inflammation, but it may also reflect concurrent systemic illness. Therefore, inflammatory burden indices should be viewed as biologically informative adjuncts rather than stand-alone determinants of prognosis [47].

Standardization remains a major challenge for clinical implementation. Different studies have used varying sampling times, different threshold values, and heterogeneous definitions of short-term outcomes. As a result, the generalizability of proposed cut-offs remains limited. In addition, inflammatory responses are dynamic, and a single admission value may not fully reflect the temporal evolution of immune activation after STEMI. Serial assessment may provide additional prognostic information, although this approach requires further study before routine use can be recommended [48].

Conclusion

Inflammatory burden has emerged as a central determinant of early outcomes in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. Beyond the restoration of epicardial coronary flow, the extent of systemic and local inflammatory

activation plays a critical role in shaping myocardial reperfusion, microvascular integrity, infarct size, and early clinical recovery. This paradigm underscores the limitation of relying solely on angiographic success as a marker of effective treatment, highlighting the need to consider underlying biological processes that influence patient prognosis.

Composite inflammatory indices such as neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and systemic immune-inflammation index provide practical and accessible tools for quantifying this inflammatory response. Their consistent association with adverse short-term outcomes—including no-reflow phenomenon, left ventricular dysfunction, heart failure, and in-hospital mortality—supports their role as valuable adjuncts in early risk stratification. Importantly, these indices offer real-time insight into the balance between pro-inflammatory and regulatory immune pathways, bridging the gap between laboratory findings and clinical outcomes.

Despite their potential, several challenges remain before widespread clinical implementation can be achieved. Variability in cut-off values, timing of measurement, and influence of comorbid conditions limit their current standardization. Moreover, while these markers demonstrate strong prognostic associations, their integration into established risk models and their impact on guiding therapeutic decisions require further validation through prospective studies.

Looking forward, the incorporation of inflammatory burden into clinical practice may represent a step toward more personalized management of STEMI patients. Combining inflammatory indices with clinical, angiographic, and imaging parameters could enhance risk prediction and identify patients who may benefit from closer monitoring or targeted therapeutic strategies. In addition, ongoing research into anti-inflammatory therapies offers the potential to directly modulate the biological processes underlying adverse outcomes.

In conclusion, inflammatory burden represents a key link between myocardial injury and clinical prognosis after primary PCI. Its assessment provides valuable insight into the mechanisms driving early complications and offers a promising avenue for improving risk stratification and patient-centered care in acute myocardial infarction.

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