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Editorial

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Inflammation in Cardiac Surgery: Pathophysiology, Clinical Phenotypes, and Emerging Therapeutic Implications

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Editorial

The systemic inflammatory response triggered by cardiac surgery represents one of the most complex and clinically relevant biological processes in contemporary perioperative medicine. Traditionally regarded as an unavoidable epiphenomenon of Cardiopulmonary Bypass (CPB) and surgical trauma, inflammation is now increasingly recognized as a central determinant of postoperative organ dysfunction, recovery kinetics, and longer-term outcomes. At a mechanistic level, cardiac surgery activates converging inflammatory pathways driven by blood–biomaterial interaction, ischemia–reperfusion injury, tissue trauma, and neurohumoral stress. These stimuli induce complement activation, cytokine release, leukocyte recruitment, endothelial dysfunction, and immune–metabolic reprogramming, processes that frequently extend well beyond the operative period [1–3]. Importantly, the inflammatory response is neither transient nor homogeneous, but displays marked interindividual variability. Accumulating evidence supports the existence of distinct inflammatory phenotypes following cardiac surgery, characterized by differences in magnitude, duration, and balance between pro-inflammatory activation and compensatory anti-inflammatory responses [4]. Patient-specific factors—including age, obesity, diabetes, frailty, chronic kidney disease, and pre-existing inflammatory burden—critically modulate these trajectories, offering a biological explanation for the wide variability in postoperative outcomes observed among patients undergoing similar procedures [5]. Clinically, dysregulated inflammation has been consistently associated with major postoperative complications, including acute kidney injury, atrial fibrillation, vasoplegic syndrome, acute lung injury, delirium, and prolonged intensive care unit stay [6–8]. Conversely, excessive counter-regulatory immune suppression may predispose to secondary infections and delayed recovery, underscoring that postoperative morbidity often reflects maladaptive immune dynamics rather than isolated organ-specific insults [9]. Despite this complexity, perioperative management strategies in cardiac surgery have historically relied on largely uniform approaches, with limited integration of inflammatory biology into risk stratification or therapeutic decision-making. Large randomized trials, while methodologically robust, often lack

the granularity required to capture inflammatory heterogeneity and tend to exclude biologically fragile patients. As a result, clinically relevant inflammatory phenotypes may remain underrepresented in population-based evidence [10].

Emerging Therapeutic Strategies and Immunomodulatory Stewardship

Over the past decade, therapeutic efforts aimed at mitigating perioperative inflammation have evolved toward a paradigm of immunomodulatory stewardship, integrating technological, pharmacological, and physiology-driven interventions. At the circuit level, advances in CPB technology—including biocompatible surface coatings and circuit optimization—aim to attenuate complement activation, leukocyte adhesion, and endothelial injury. While clinical outcomes remain heterogeneous, recent studies suggest that selected technologies may reduce inflammatory burden and organ dysfunction in specific procedural contexts, supporting a tailored rather than universal adoption [11]. Hemoadsorption has emerged as a potential adjunct in complex or high-risk cardiac surgery characterized by severe systemic inflammation or vasoplegia. Recent randomized trials and meta-analyses indicate potential benefits on inflammatory mediators and hemodynamic stability in selected populations, although consistent improvements in hard clinical endpoints have not been uniformly demonstrated [12–14]. These findings reinforce the concept that hemoadsorption should be considered a phenotype-directed intervention rather than a routine strategy. Pharmacological modulation of inflammation remains an area of active investigation. Perioperative corticosteroids exemplify the challenges of broad anti-inflammatory approaches: while capable of attenuating inflammatory signaling, their net clinical effect is highly dependent on timing, dosage, patient comorbidities, and infection risk. Contemporary consensus statements emphasize evidence-based standardization combined with selective personalization rather than routine administration [15]. Among inflammation-linked syndromes, post-CPB vasoplegia has gained increasing attention as a biologically distinct entity. Beyond conventional vasopressors, angiotensin II has been explored as a targeted therapeutic option in refractory cases, supported by emerging physiological and clinical evidence [16,17]. This evolution reflects a broader shift toward phenotype-guided therapy.

Endotheliopathy, Glycocalyx Disruption, and Precision Perioperative Medicine

An expanding body of literature implicates endothelial dysfunction and glycocalyx degradation as central mechanisms linking inflammation to organ injury in cardiac surgery. Experimental and clinical studies demonstrate that glycocalyx shedding during CPB contributes to capillary leak, microcirculatory impairment, and postoperative organ dysfunction [18,19]. These insights have renewed interest in perioperative strategies aimed at preserving endothelial integrity, including optimized fluid management, avoidance of excessive hemodilution, and refined hemodynamic targets. Collectively, these advances align with the emerging paradigm of precision perioperative medicine, in which inflammatory and endothelial phenotyping may ultimately inform individualized perioperative pathways [20]. While validated tools for routine clinical implementation remain limited, this framework underscores the limitations of “one-size-fits-all” strategies in a biologically heterogeneous population. In this context, rigorously documented clinical observations retain substantial scientific value. High-quality case reports can illuminate extreme inflammatory phenotypes, unexpected therapeutic responses, or failure of standard strategies, often serving as early signals that guide hypothesis generation and subsequent trial design.

Conclusion

Inflammation in cardiac surgery should be conceptualized not as an unavoidable consequence of intervention, but as a dynamic and potentially modifiable biological process with direct clinical relevance. Progress in perioperative outcomes will depend on recognizing inflammatory heterogeneity, integrating surgical and anesthesiological expertise, and

translating high-quality clinical observation into mechanistic insight. Inflammation is not merely a byproduct of cardiac surgery; it is one of its most informative biological determinants and a key target for future therapeutic refinement.

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