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SYSTEMIC INFLAMMATORY REACTIONS ASSOCIATED WITH EXTRACORPOREAL CIRCULATION: AN INTEGRATIVE REVIEW

REAÇÕES INFLAMATÓRIAS SISTÊMICAS ASSOCIADAS À CIRCULAÇÃO EXTRACORPÓREA: UMA REVISÃO INTEGRATIVA

REACCIONES INFLAMATORIAS SISTÉMICAS ASOCIADAS CON LA CIRCULACIÓN EXTRACORPÓREA: UNA REVISIÓN INTEGRADORA

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ABSTRACT

Extracorporeal circulation (ECC) represents an indispensable life support technology for modern cardiac surgery, enabling the correction of complex defects. However, the interaction of blood with the artificial circuit paradoxically triggers Systemic Inflammatory Response Syndrome (SIRS), the main vector of postoperative morbidity. This study aims to document, through a literature review, the fundamentals of ECC and its relationship with SIRS. It analyzes the pathophysiology of this inflammatory response, its clinical and laboratory implications, and the role of the biomedical perfusionist, responsible for circuit management, intraoperative laboratory monitoring, and the application of mitigation strategies, such as the use of coated circuits, ultrafiltration, and hypothermia control. It concludes that SIRS is an intrinsic pathophysiological consequence of ECC, mediated by a complex biochemical cascade. A detailed understanding of these mechanisms and active management by the biomedical perfusionist are fundamental to minimizing the inflammatory response and improving the patient's postoperative prognosis.

Keywords: Extracorporeal Circulation. Systemic Inflammatory Response. Cardiac Surgery. Perfusion.

RESUMO

A Circulação Extracorpórea (CEC) representa uma tecnologia de suporte vital indispensável para a cirurgia cardíaca moderna, possibilitando a correção de defeitos complexos. Contudo,

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a interação do sangue com o circuito artificial desencadeia, paradoxalmente, a Síndrome da Resposta Inflamatória Sistêmica (SIRS), principal vetor de morbidade pós-operatória. Este estudo objetiva documentar, por meio de uma revisão de literatura, os fundamentos da CEC e sua relação com a SIRS. Analisa-se a fisiopatologia desta resposta inflamatória, suas implicações clínicas e laboratoriais, e a atuação do biomédico perfusionista, responsável pelo manejo do circuito, monitoramento laboratorial intraoperatório e aplicação de estratégias de mitigação, como o uso de circuitos revestidos, ultrafiltração e controle da hipotermia. Conclui-se que a SIRS é uma consequência fisiopatológica intrínseca à CEC, mediada por uma complexa cascata bioquímica. A compreensão detalhada desses mecanismos e o manejo ativo pelo biomédico perfusionista são fundamentais para minimizar a resposta inflamatória e melhorar o prognóstico do paciente no pós-operatório.

Palavras-chave: Circulação Extracorpórea. Resposta Inflamatória Sistêmica. Cirurgia Cardíaca. Perfusão.

RESUMEN

La circulación extracorpórea (CEC) representa una tecnología de soporte vital indispensable para la cirugía cardíaca moderna, permitiendo la corrección de defectos complejos. Sin embargo, la interacción de la sangre con el circuito artificial desencadena, paradójicamente, el Síndrome de Respuesta Inflamatoria Sistémica (SRIS), principal vector de morbilidad postoperatoria. Este estudio busca documentar, mediante una revisión bibliográfica, los fundamentos de la CEC y su relación con el SRIS. Analiza la fisiopatología de esta respuesta inflamatoria, sus implicaciones clínicas y de laboratorio, y el papel del perfusionista biomédico, responsable del manejo del circuito, la monitorización intraoperatoria de laboratorio y la aplicación de estrategias de mitigación, como el uso de circuitos recubiertos, la ultrafiltración y el control de la hipotermia. Concluye que el SRIS es una consecuencia fisiopatológica intrínseca de la CEC, mediada por una compleja cascada bioquímica. Una comprensión detallada de estos mecanismos y el manejo activo por parte del perfusionista biomédico son fundamentales para minimizar la respuesta inflamatoria y mejorar el pronóstico postoperatorio del paciente.

Palabras clave: Circulación Extracorpórea. Respuesta Inflamatoria Sistémica. Cirugía Cardíaca. Perfusión.

1 INTRODUCTION

The advent of modern cardiac surgery represents one of the most significant achievements of medicine in the twentieth century, comparable to the mastery of atomic energy or the conquest of outer space (Braile, 2010). This evolution was inseparable from the development of a revolutionary life support technology: Cardiopulmonary Bypass (CPB). Prior to its implementation, the correction of complex heart defects, which required manipulation of the heart's internal structures, was considered a practically impossible task (Braile, 2010; Nascimento *et al.*, 2017). CPB emerged as the solution to this challenge, allowing the surgeon to operate in an immobile, bloodless operative field without the heartbeat (Machado *et al.*, 2011).

Cardiopulmonary Bypass (CPB) is a life support technique that diverts the patient's blood flow to an external circuit, allowing the temporary replacement of the heart's pumping and lungs' gas exchange functions (Rodrigues, 2018). During the procedure, venous blood is drained from the body, usually from the right atrium, and conducted to the circuit of the heart-lung machine, which takes on the role of these vital organs (Machado *et al.*, 2011). This temporary bypass, known as cardiopulmonary bypass, allows surgeons to work on the heart without the interference of its movement and the presence of blood, ensuring the arrival of oxygenated blood to all tissues and organs of the body (Machado *et al.*, 2011).

However, the history of CEC is marked by an inherent paradox. While it functions as indispensable life support, taking over the vital functions of the heart and lungs, the procedure also imposes considerable physiological challenges on the patient. The use of the external circuit can trigger a series of systemic changes, the most notable being the Systemic Inflammatory Response Syndrome (SIRS). This duality – being a means of cure and, at the same time, a vector of potential complications – makes the in-depth understanding of CPB a topic of continuous study and of extreme clinical relevance (Zarbock *et al.*, 2015).

Thus, this article proposes to document, based on the available scientific literature, the foundations and clinical impacts of CPB, with particular emphasis on its relationship with the systemic inflammatory response, as well as its clinical and laboratory implications, seeking to elucidate the main mediators and the consequences of this process in different systems of the human organism, contextualizing this theme with the performance of the biomedical professional, whose role is central in the management and mitigation of the risks associated with this complex procedure (Souza; Elias, 2006).

2 METHODOLOGY

To produce this content, an exploratory bibliographic research was carried out with a

qualitative approach in narrative format, thus, therefore, without using explicit and systematic criteria for the collection and analysis of bibliographic material, according to Mendes, Silveira and Galvão (2008). This methodology, according to these authors, is adequate for the foundation of academic productions, but both the selection and the interpretation of the content may be subject to the subjectivity of the authors.

The repositories used to survey the scientific content were Google Scholar, PubMed, and Scielo, using search descriptors for both Portuguese and English, such as: cardiopulmonary bypass, cardiopulmonary perfusion, CPB, systemic inflammatory reactions, extracorporeal circulation, blood circulation, surgical procedures, perfusion; in addition to books related to the theme.

To be included in this review, we selected both articles that strictly discuss the proposed theme, i.e., that relate CPB to the various systemic inflammatory reactions triggered in the human body, and others that explain CPB in a didactically detailed way, from its conceptualization and contextualization of its evolutionary history, to the advantages and disadvantages of the procedure for human health.

All other articles were excluded that, although carrying any of the descriptors used in the search, had content that diverged from the proposal of this study.

3 RESULTS

30 scientific productions were selected, including 20 articles and 10 academic papers, published between 1990 and 2025, in addition to 2 books, from which we extracted the pertinent theoretical framework and organized it as follows:

3.1 CONCEPTUALIZATION AND DEFINITION OF THE CEC

In essence, CPB consists of a set of machines, devices and techniques that aim to temporarily replace the vital functions of the heart and lungs (Mota *et al.*, 2024). This replacement is necessary to create a bloodless and immobile surgical drape, allowing the surgeon to correct cardiac lesions under direct vision (Souza; Elias, 2006).

The process involves diverting blood from the patient's circulatory system to an artificial circuit, where oxygenation, removal of carbon dioxide, and control of body temperature occur, before the blood is reinfused into the patient (Mota *et al.*, 2024).

Therefore, CPB is defined as the method that maintains blood circulation and breathing artificially, providing the surgeon with the necessary time to perform complex procedures, while the myocardium is protected from ischemia (Souza; Elias 2006). During this period of artificial support, organic physiology, including acid-base balance,

hemodynamics, and coagulation, must be rigorously monitored and adjusted by the perfusionist (Mota *et al.*, 2024).

The advent of this technology not only made interventions that were previously unthinkable possible, but also boosted the development of a highly technical and scientific specialty, perfusion, which requires deep theoretical knowledge in cardiovascular physiology, pharmacology, and blood biochemistry on the part of the biomedical specialist (Souza; Elias 2006).

3.2 COMPONENTS AND CIRCUIT WORKING PRINCIPLE

The operating principle is based on the drainage of the patient's venous blood, its processing (oxygenation, carbon dioxide removal and temperature control) and subsequent reinfusion into the arterial circulation (Mota; Rodrigues; Évora, 2008). The circuit consists of disposable elements and a perfusion machine that provides the propulsion.

The CPB circuit is composed of the following essential elements, following the flow of the patient's drained blood:

Venous and Arterial Cannulas: these are the devices responsible for connecting the patient to the circuit. The venous blood, which returns from the body, is drained through cannulas inserted into the venae cavae, directing the flow to the reservoir. The processed blood is reintroduced into the systemic circulation through an arterial cannula, usually positioned in the aorta (Guimarães; Babylon; Reis, 2018).

Venous Reservoir: This is the first component of the circuit to receive the patient's blood. The reservoir acts primarily as a collector and volume controller, accommodating blood from the venous line and surgical aspirators. Its structure has mesh filters to remove microaggregates and devices that minimize foaming and air entering the system (Souza; Elias, 2006).

Propulsion Pumps (Arterial Pump): constitute the driving unit of the circuit, replacing the ventricular function of the heart. There are two predominant models (Silva, 2017):

Roller Pump (Peristaltic): It is the most common type in arterial perfusion. It generates blood flow by compressing the tube against a bed, creating a peristaltic effect. Its flow is accurate and directly proportional to the rotational speed, but it requires rigorous calibration to avoid damage to the blood (occlusive perfusion).

Centrifugal Pump: Uses a rotor that propels the blood by centrifugal force, being a non-occlusive system. It tends to be less traumatic to the figurative elements of the blood and is widely used in prolonged circulatory assists (Medeiros Júnior, 2011).

Membrane Oxygenator and Heat Exchanger: This set fully replaces the body's lung

function and thermoregulatory capacity.

Membrane oxygenator, is the modern artificial lung. Gas exchange occurs through a semipermeable membrane (usually hollow fibers of microporous polypropylene), which separates the blood from the oxygenating gas. This technology avoids direct contact between blood and gas, significantly reducing the incidence of gas embolism and cellular trauma compared to older bubble models (Souza; Elias, 2006).

Heat Exchanger: Component integrated into the oxygenator. It allows blood temperature to be adjusted through the circulation of cold or hot water, and is essential to induce hypothermia (reducing the metabolism and oxygen demand of the tissues) and, subsequently, to rewarm the patient (Mota; Rodrigues; Évora, 2008).

Arterial Filter: Positioned in the arterial line after the oxygenator, it is the last safety barrier before the blood returns to the patient. Its main function is to remove any microbubbles of air and particles, reducing the risk of systemic embolism (Souza; Elias, 2006).

Cardioplegia System: An accessory system, with a dedicated roller pump, is used for the administration of the cardioplegic solution. This solution, rich in potassium and usually cooled, is essential to induce and maintain cardiac arrest (asystole), protecting the myocardium from ischemic damage during the surgical period (Silva, 2017).

3.3 ADVANTAGES AND DISADVANTAGES INHERENT TO THE PROCEDURE

The main benefit of CPB lies in offering the surgeon ideal conditions for the procedure to be performed. Among the advantages we can list:

Bloodless and Immobile Surgical Field: Allows controlled cardiac arrest (through cardioplegia) and complete diversion of blood flow, creating a clear, dry and motionless operative field. This condition is indispensable for delicate procedures, such as valve replacement or the correction of complex congenital heart diseases.

Metabolic and Hemodynamic Control: The perfusion machine takes control of total cardiac output and oxygenation. The perfusionist can closely monitor and adjust blood flow, oxygenation, and carbon dioxide concentration. (Souza; Elias, 2006; Guimarães; Babylon; Reis, 2018):

Myocardial and Brain Protection: The possibility of inducing controlled hypothermia (cooling of the patient) reduces tissue metabolism. This decrease in oxygen consumption is crucial to protect ischemia-sensitive organs, such as the brain and the heart itself, during the aortic clamping period.

Correction of Complex Anomalies: CPB allows the execution of surgeries that require time and precision, such as repairs of complex aneurysms and the surgery of multiple valve

replacement.

Despite the surgical benefits, the interaction of blood with the non-endothelial surfaces of the CPB circuit and the mechanical trauma inherent to pumping cause a series of adverse effects in the body, known as the "CPB syndrome" (Silva, 2017). The main disadvantages are:

Activation of the Systemic Inflammatory Response (SIRS): The contact of blood with the artificial material of the circuit (plastic, membranes) is interpreted by the body as an aggressor. This triggers a massive inflammatory cascade, releasing cytokines, activating complement, and promoting neutrophil migration. SIRS can lead to multi-organ dysfunction in the postoperative period (Mota; Rodrigues; Évora, 2008).

Hematologic Disorders: Infusion requires full anticoagulation with heparin, increasing the risk of postoperative hemorrhage. In addition, mechanical trauma from pumps can lead to hemolysis (destruction of red blood cells) and the consumption of platelets and coagulation factors, predisposing the patient to bleeding and transfusion complications (Alves, 2022).

Organ Dysfunction: Pulmonary: CPB is associated with pulmonary edema and acute respiratory distress syndrome, in part due to lung endothelial injury resulting from SIRS.

Renal: Hypoperfusion and inflammatory mediators can lead to acute kidney injury, which is a predictor of mortality (Pontes *et al.*, 2007).

Neurological: There is a risk of cerebrovascular accidents (CVA) or transient cognitive dysfunction, caused by embolism (microbubbles of air, particles, or clots) that passes through the arterial circuit (Alves, 2022).

Vasoactive and Homeostasis: Hemodilution (necessary to "fill" the circuit) and changes in temperature affect hydroelectrolyte balance and blood pressure regulation, requiring constant monitoring and intervention (Silva, 2017).

3.4 CPB AS A VECTOR OF SYSTEMIC INFLAMMATORY RESPONSE (SIRS)

Despite being a saving technology, the use of Cardiopulmonary Bypass (CPB) is recognized as the main inducer of Systemic Inflammatory Response Syndrome (SIRS) in patients undergoing cardiac surgery (Moura; Pomerantzeff; Gomes, 2001). This inflammatory response is the pathophysiological basis for much postoperative morbidity, including renal, pulmonary, and hematological dysfunctions (Rodrigues, 2018).

3.4.1 Definition and pathophysiology of SIRS

SIRS is not a specific disease, but rather a clinical manifestation of a dysregulated immune activation of the body in the face of a serious insult (such as infection, trauma,

ischemia-reperfusion or, in this context, the use of CPB) (Baddam; Burns, 2025).

CPB induces SIRS because the body recognizes the artificial circuit as a foreign agent, triggering a defense cascade that becomes harmful when left unchecked. Clinically, SIRS is characterized by the presence of two or more of the following criteria (Moura; Pomerantzeff; Gomes, 2001):

Table 1

Aspects manifested in clinical lesions in SIRS

Characteristics of SIRS	
Demonstrations	Body temperature > 38°C (fever) or < 36°C (hypothermia).
	Heart rate > 90 beats per minute (tachycardia).
	Respiratory rate > 20 breaths per minute or partial pressure of carbon dioxide PaCO2 < 32 mmHg.
	Leukocyte Count > 12,000/mm³ < 4,000/mm³ or more than 10% of immature forms.

Source: Journois, 1999.

SIRS activation in the context of CPB is a complex event, resulting from the combination of multiple factors that act synergistically, as detailed by Rodrigues (2018) and Souza and Elias (2006).

The inflammatory response induced by CPB occurs in two main phases:

Table 2

Phases of the inflammatory response induced by CPB

Phase	**Main Engine**	**Mediators and Consequences**
Initial Phase (Contact)	Immediate contact of the blood with the synthetic (non-endothelial) surface of the CPB circuit.	**Contact System/Kallikrein-Kinin Activation:** • **Bradykinin release**. **Activation of the Complement System (Alternative Way):** • Generation of **Anaphylatoxins (C3a and C5a)** (Souza; Elias, 2006). **Macrophage/Monocyte Activation:** • Release of **Pro-inflammatory Cytokines** (TNF, IL-1, IL-6) (Brazil *et al.*, 1999).
Late Phase (Ischemia-Reperfusion)	Aortic clamping (ischemia) followed by forceps release (reperfusion) (Moura; Pomerantzeff; Gomes, 2001).	**Oxidative Stress:** • Production of **Oxygen Free Radicals (ROS)** (Moura; Pomerantzeff; Gomes, 2001). **Endothelial and Neutrophil Activation:** • Adherence of neutrophils to the endothelium. • Release of **Cytotoxic Enzymes and Elastases** (Souza; Elias, 2006).

Source: Based on Brasil *et al.*, 1999. Moura; Pomerantzeff; Gomes, 2001. Souza; Elias, 2006.

In summary, CPB functions as a multifactorial trigger that disrupts blood and vascular

homeostasis, transforming a localized protective response into a deleterious systemic reaction that threatens the integrity of multiple organs (Rodrigues, 2018).

3.4.2 Mechanisms of activation of the inflammatory response by CPB

The Systemic Inflammatory Response (SIRS) associated with Cardiopulmonary Bypass (CPB) is not triggered by a single factor, but rather by the convergence of multiple mechanisms that transform surgical trauma and exposure of blood to synthetic surfaces into a generalized biochemical aggression (Brasil *et al.*, 1999). The central pathophysiological mechanisms that activate SIRS in CPB are divided and interconnected, as follows:

Table 3

Pathophysiological mechanisms that activate SIRS in CPB

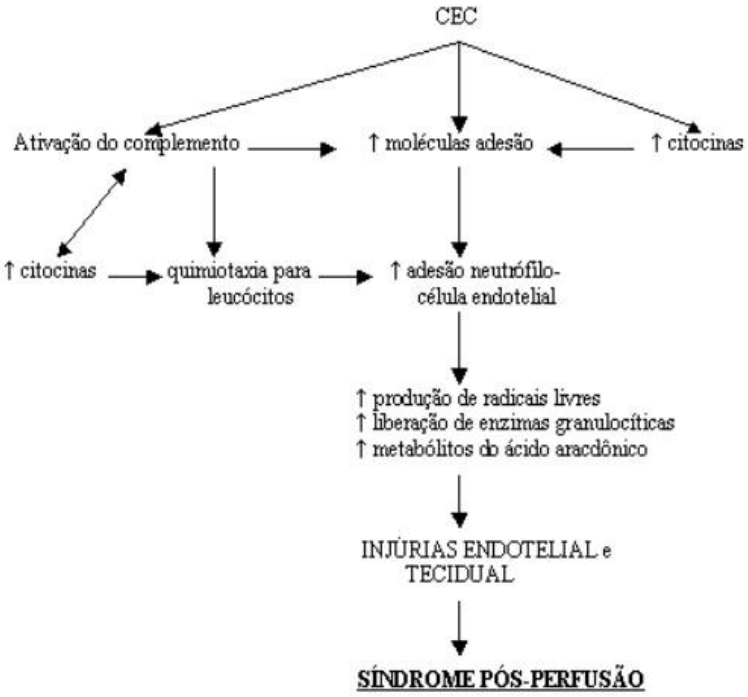
Activating Mechanism	Process Breakdown	Consequences and Mediators
1. Blood Contact with Non-Endothelial Surfaces **(Main and immediate activation vector) (Moura; Pomerantzeff; Gomes, 2001)**	The blood meets the plastic surfaces of the circuit (oxygenator, tubes, reservoirs).	**Activation of the Complement System (Alternative Way):** • Production of **C3a** and **C5a**. • C5a recruits and activates leukocytes, increases vascular permeability (Souza; Elias, 2006). **Contact System/Kallikrein-Kinin Activation:** • Activation of **Factor XII (Hageman).** • Production of **Bradykinin** (vasodilator, increases capillary permeability) (Moura; Pomerantzeff; Gomes, 2001). **Coagulation Activation and Fibrinolysis:** • Activation of the intrinsic (Factor XII) and extrinsic (Tissue Factor) pathways (Rodrigues, 2018). • **Thrombin** and **Fibrin generation**; platelet and factor consumption.
2. Ischemia and Reperfusion Injury (I/R) **(Second most powerful engine) (Moura; Pomerantzeff; Gomes, 2001)**	**Ischemia (Aortic Clamping):** • Interruption of blood flow, hypoxia, and depletion of ATP. **Reperfusion (Impingement Removal):** • Resumption of flow floods the fabric with O_2.	**Oxidative Stress:** • Massive production of **Reactive Oxygen Species (ROS)/Free Radicals**. • Oxidative damage to membranes, endothelial dysfunction and inflammatory amplification (neutrophil activation).

Source: Based on Moura; Pomerantzeff; Gomes, 2001. Rodrigues, 2018. Souza; Elias, 2006.

In addition, the operation of the CPB machine also contributes to injury and inflammation, as the shear and mechanical trauma imposed by the non-pulsatile flow of roller or centrifugal pumps damage the figurative elements of the blood, such as red blood cells and platelets. Lysis of red blood cells (hemolysis) and platelet activation and consumption contribute to coagulopathy and the release of inflammatory mediators (Rodrigues, 2018).

Figure 1

Main immunological mechanisms involved post-CPB



Source: Henriques; Forte, 2000.

Understanding these mechanisms is essential for the development of perfusion mitigation strategies, which aim to minimize exposure, ischemia, and mechanical trauma (Brasil *et al.*, 1999).

3.4.3 Main inflammatory mediators involved

Systemic Inflammatory Response Syndrome (SIRS) associated with CPB is a "storm of cytokines" and other chemical mediators that, when released in excess and in an uncontrolled manner, cause widespread cell damage and organ dysfunction (Brasil *et al.*, 1999). The activation of the contact and ischemia-reperfusion mechanisms results in the production of several bioactive molecules, which can be classified into main systems, as shown in the table below:

Table 4

Inflammatory mediators involved in CPB-associated SIRS

Mediator	System	Main Effects
Cytokines (General)	Cytokines (Pro-Inflammatory)	They coordinate the inflammatory response. Produced by monocytes, macrophages and activated neutrophils. Responsible for a large part of the clinical manifestations of SIRS.
TNF-alpha	Cytokines (Pro-Inflammatory)	Main mediator of acute phase response. It causes fever, peripheral vasodilation, and hypotension (shock). It activates the endothelium and induces other cytokines.
Interleukin 1 (IL-1)	Cytokines (Pro-Inflammatory)	It acts synergistically with TNF. Potent fever inducer (action on the hypothalamus). It promotes lymphocyte activation and induces acute phase protein synthesis by the liver.
Interleukin 6 (IL-6)	Cytokines (Pro-Inflammatory)	Cytokine measured post-CPB as it reflects the intensity of SIRS. Main responsible for the synthesis of C Reactive Protein. Related to myocardial dysfunction and vasoplegic syndrome.
Interleukin 8 (IL-8)	Cytokines (Pro-Inflammatory)	The main function is the recruitment and activation of neutrophils to the endothelium, contributing to lung and vascular injury.
Interleukin 10 (IL-10)	Cytokines (Anti-inflammatory)	Main anti-inflammatory cytokine involved. It inhibits the synthesis of TNF, IL-1 and IL-6. An imbalance between IL-6 (pro) and IL-10 (anti) is a marker of SIRS severity.
C3a and C5a	Complement System	Anaphylatoxins responsible for the degranulation of mast cells and basophils (releasing histamine). C5a is a potent neutrophil chemoattractant, essential for the development of Acute Lung Injury
Bradykinin	Kallikrein-Kinin System	Result of Factor XII activation. It causes intense vasodilation and dramatic increase in capillary permeability (generalized edema). Contribution to hypotension (Vasoplegia Syndrome).
Thrombin and Fibrin	Coagulation System	They form fibrin microaggregates and activate platelets (due to trauma and coagulopathic activation).
Thromboxane A2	(Released by Platelets/Syst. Coagulation)	Released by activated platelets. It is a potent vasoconstrictor and platelet aggregator.

Source: Moura *et al.*, 2001.

The understanding of these mediators justifies the need for interventions, such as the use of corticosteroids (to inhibit the release of cytokines) or ultrafiltration (to remove some mediators from plasma) in CPB (Brasil *et al.*, 1999).

3.5 CLINICAL AND LABORATORY IMPLICATIONS OF POST-CPB SIRS

The clinical unfolding of this exacerbated inflammatory response is diverse, affecting multiple organs and systems:

Pulmonary: One of the most serious manifestations is pulmonary dysfunction, which can progress to Acute Respiratory Distress Syndrome (ARDS). The increase in capillary vascular permeability induced by inflammatory mediators (such as cytokines and neutrophil elastase) results in noncardiogenic pulmonary edema, prolonging the time of mechanical ventilation (Light; Junior, 2002).

Cardiovascular: Vasodilation and imbalance between pro- and anti-inflammatory mediators can lead to hemodynamic instability and the need for inotropic support, increasing

postoperative morbidity and mortality.

Renal: Acute kidney injury (AKI) is a common complication, correlated with CPB time and tissue hypoperfusion during surgery. Studies have shown that longer CPB time is a significant risk factor for the development of AKI (Paulitsch, 2009).

From the laboratory point of view, Post-CPB SIRS is characterized by the activation of several signaling cascades, including the complement system, coagulation, and the massive release of chemical mediators, whose measurements are crucial for the biomedical professional.

The release of pro-inflammatory cytokines, such as IL-6 Interleukins and Tumor Necrosis Factor (TNF), is the central hallmark of SIRS. TNF and IL-6 are released in response to blood contact with the CPB circuit and by ischemia-reperfusion injury, acting as predictors of organ dysfunction (Moura; Pomerantzeff; Gomes, 2001). High and prolonged levels of IL-6 are associated with longer hospital stays (Cardoso *et al.*, 2021).

The clinical analysis laboratory plays a key role in the early identification of SIRS and the exclusion of infection, the main complication of SIRS progression.

C-reactive protein (CRP) is an acute phase reagent for hepatic synthesis, widely used, but with limitations in post-CPB SIRS due to its low specificity. CRP levels increase significantly in the first 6 to 12 hours after cardiac surgery, reaching a peak between 48 and 72 hours, as a reflection of sterile inflammation induced by CPB and surgical trauma (Arkader *et al.*, 2004).

Although the initial increase is expected, no reduction or a second peak of CRP after the third postoperative day (PO) may be an indicator of an exacerbated inflammatory response or, more critically, of the development of an infectious focus or sepsis (Póvoa *et al.*, 1998).

Procalcitonin (PCT) is a more specific biomarker for bacterial infection/sepsis. In patients with post-CPB SIRS, PCT levels may be transiently elevated due to the sterile inflammatory response itself. However, values higher than 0.5 ng/mL or progressive ascent after the second postoperative day may be indicative of infectious complication, helping to distinguish between SIRS and sepsis (Meisner, 2010).

The blood count provides crucial data on the cellular immune response and hemostasis.

The leukocyte count, especially neutrophils, usually increases during and after CPB, reflecting the activation and release of these cells, which release cytotoxic enzymes, such as neutrophil elastase. Left-shift leukocytosis is one of the diagnostic criteria for SIRS (white blood cell count > 12,000/uL or < 4,000/uL or > 10% of immature forms). Monitoring the

absolute neutrophil and lymphocyte count is vital (Moura; Pomerantzeff; Gomes, 2001).

Thrombocytopenia and platelet dysfunction are common post-CPB, due to hemodilution and platelet activation in the artificial circuit. Reduced platelet count increases the risk of bleeding and is a component of multiorgan dysfunction (Moura; Pomerantzeff; Gomes, 2001).

Platelets undergo activation in the CPB circuit, resulting in thrombocytopenia and platelet dysfunction, which contributes to increased postoperative bleeding and the need for transfusion (Lobo Filho *et al.*, 2005).

Activation of the coagulation and fibrinolysis system is intrinsic to CPB, and dysregulation can lead to coagulopathy, evidenced in the laboratory by changes in Prothrombin Time (PT), Activated Partial Thromboplastin Time (APTT), and D-dimer levels.

Recently, the Systemic Immunoinflammation Index (IBS), calculated from platelet, neutrophil and lymphocyte counts (Neutrophils X Platelets/Lymphocytes), has been shown to be an independent predictor of in-hospital mortality in post-CPB patients. High preoperative IBS scores, with cut-off values above 811.93, were associated with worse outcomes and longer hospital stays (Güntürk *et al.*, 2024).

Monitoring of creatinine and urea is the gold standard for the diagnosis of Acute Kidney Injury (AKI). The progressive increase in creatinine, even if slight, requires immediate intervention to avoid the need for renal replacement therapy (Dias *et al.*, 2021).

Increased lactate levels (hyperlactatemia) is a sensitive indicator of tissue hypoperfusion and anaerobic metabolism, often present in SIRS and shock. Persistently elevated lactate levels (reduced clearance) correlate with higher morbidity and mortality.

The relationship between the partial pressure of oxygen in the arterial blood and the fraction of inspired oxygen is a key parameter for monitoring pulmonary dysfunction, which can progress to Acute Respiratory Distress Syndrome (ARDS), one of the most serious manifestations of SIRS (Silva *et al.*, 2017).

3.6 THE ROLE OF THE PERFUSIONIST IN THE MANAGEMENT OF CEC AND RISK MITIGATION

The perfusionist is the driver of CPB and, therefore, the manager of the risks inherent to the procedure. In Brazil, a health or biology professional (such as biomedicine, nursing, pharmacy, physiotherapy, biology or medicine) who has completed a Lato Sensu postgraduate course in the area can be a perfusionist. Their responsibilities and clinical practice (Moreira; Silva, 2020), are comprehensive:

Preparation and assembly – Plan, order and assemble the CEC circuit. Perform

priming (filling the circuit with solution), ensuring the absence of air and testing the operation of all components (pump, oxygenator, heat exchanger and filters).

Physiological support – Replace cardiac and pulmonary function (Pump and Oxygenator). Control blood flow (artificial output), oxygenation, ventilation and body temperature (controlled hypothermia).

Pharmacological control – Prepare and administer, under medical guidance, solutions such as cardioplegia (to paralyze and protect the myocardium) and other drugs (heparin, protamine, vasodilators, etc.) in the circuit.

Laboratory Monitoring – Perform and interpret, in real time, intraoperative laboratory parameters, such as Blood Gas Tests and Activated Coagulation Time (ACT), correcting acidosis, alkalosis, electrolyte and hemostatic disturbances.

Advanced Assistance – Assist in the installation and maintenance of long-term circulatory and respiratory support devices, such as ECMO (Extracorporeal Membrane Oxygenation) and the intra-aortic balloon (Moreira; Silva, 2020).

3.6.1 Role of the Biomedical Perfusionist

The Biomedical Perfusionist is the higher level professional who specializes in the management of CPB, being vital for the cardiovascular surgery team. Its performance is recognized by the Federal Council of Biomedicine (CFBM) and regulated by the Brazilian Society of Extracorporeal Circulation (SBCEC), which attests to the complexity and importance of its responsibilities (Matos, 2021).

The Perfusionist's role is to temporarily replace the patient's cardiac and pulmonary functions, maintaining physiological balance during highly complex surgical procedures (Matos, 2021). The performance is divided into three critical phases: Assembly, Conduction and Maintenance of the Circuit.

3.6.2 Strategies to minimize the inflammatory response

In order to minimize the undesirable effects of the inflammatory response caused by CPB, some strategies are implemented during the procedure, including:

3.6.2.1 Circuit Hemocompatibility Techniques:

The contact of the blood with the synthetic material of the CPB circuit is the initial factor for the activation of the coagulation pathways and the complement system (Souza; Elias, 2006; Mesquita *et al.*, 2010).

3.6.2.2 Biocompatible coatings (hemocompatible surfaces):

The use of circuits coated with materials that mimic the vascular endothelium (such as heparin or specific polymers) is an active strategy to reduce the interaction of blood with synthetic surfaces.

According to Mesquita *et al.* (2010, p. 66), "in order to prevent blood clotting in the infusion system, it is imperative to administer adequate doses of heparin before the initiation of CPB."

Although heparin is administered directly to the patient, the use of heparin-coated circuits aims to increase the hemocompatibility of the circuit itself.

3.6.2.3 Circuit Miniaturization and Priming Reduction:

SCC systems with reduced fill (prime) volumes, often referred to as Mini-SCC, minimize hemodilution and exposure of blood to non-biological surfaces.

Reducing the volume of the prime and using equipment such as hemoconcentrators are strategies adopted during cardiac surgery to minimize bleeding and the need for blood transfusion, factors interlinked to the inflammatory response (Souza; Moitinho., 2008).

3.6.2.4 Choice of Pump Type:

Blood pump selection is an important technical decision. Studies have already compared the use of roller pumps and centrifugal pumps, indicating that the use of centrifugal pumps can induce a lower inflammatory response by causing less shear stress and mechanical injury to the figurative elements of the blood (Braulio, 2009).

3.6.2.5 Use of Filters and Mediator Removal Devices:

The Perfusionist employs specific devices to remove inflammatory mediators and excess fluids, preventing the accumulation of pro-inflammatory cytokines.

3.6.2.6 Ultrafiltration (UF) and Hemofiltration:

UF is a fundamental technique used by the Perfusionist to control water balance and remove cytokines, which are low and medium molecular weight molecules. The removal of inflammatory mediators such as TNF-α and interleukins can be achieved through modified ultrafiltration (MUF), performed at the end of or during CPB.

For Antunes *et al.* (2009, p. 67). "Ultrafiltration to remove mediators of the inflammatory response is one more possibility in strategies to minimize this organic response."

3.6.2.7 Arterial Filters and Leucorrection:

Arterial filters are incorporated into the circuit to trap microparticles and microbubbles of air (prevention of gas embolism). In addition, the use of leukoreductive filters may be indicated to remove activated leukocytes, which are responsible for the release of cytotoxic enzymes and inflammatory mediators (Mesquita *et al.*, 2010).

3.6.2.8 Control of Temperature (Hypothermia) and Perfusion

Strict control of temperature and blood flow is managed by the Perfusionist and has a direct impact on the inflammatory response and organic protection. The induction of controlled hypothermia (reduced body temperature, typically between 28°C and 35°C, depending on the procedure) is crucial to decrease cellular metabolism and, consequently, the oxygen consumption of tissues, protecting noble organs such as the brain. According to Menasche, et. al. (1995 apud Mesquita *et al.*, 2010, p. 71), "performing CPB in hypothermia reduces the release of inflammatory response markers, but does not abolish it entirely."

The Perfusionist monitors the temperature in real time (nasopharynx, rectal) and uses the oxygenator's heat exchanger to control the cooling and reheating speed, avoiding sudden temperature gradients. Adequate blood flow to the patient's body surface and temperature should be maintained (adequate flow and adequate temperature are factors that have reduced the inflammatory response in animal models). Insufficient flow (hypoperfusion) can lead to ischemia and acidosis (increased lactate), potentiating SIRS and organic damage (Silva, 2020), so the perfusionist is responsible for calculating and adjusting the perfusion flow to maintain hemodynamic stability and acid-base balance in all areas of CPB (Mesquita *et al.*, 2010).

4 DISCUSSION

The analysis of the literature shows that Cardiopulmonary Bypass (CPB), although consolidated as an indispensable life support technology for modern cardiac surgery because it provides a bloodless and immobile operative field, as described by Souza and Elias (2006) and corroborated by Machado *et al*. (2011), presents itself as a physiological paradox. The results indicate that the interaction of blood with the non-endothelial surfaces of the artificial circuit acts as a potent trigger for Systemic Inflammatory Response Syndrome (SIRS). Moura, Pomerantzeff and Gomes (2001) explain that this condition transcends the local response to surgical trauma, manifesting itself as a generalized immune dysregulation. It is observed, in agreement with Rodrigues (2018), that the pathophysiology of this response is multifactorial and occurs in two distinct phases: the initial phase, mediated by direct contact with the

synthetic material that activates the contact and complement systems (Souza; Elias, 2006); and the late phase, exacerbated by ischemia and reperfusion injury after aortic declamping, generating massive oxidative stress, according to Moura *et al.* (2001).

With regard to chemical mediators, Brasil *et al.* (1999) characterize the response induced by CPB as a true "cytokine storm", where bioactive molecules compromise homeostasis. Interleukin-6 (IL-6) and Tumor Necrosis Factor-alpha (TNF-α) stand out as the main pro-inflammatory markers; Cardoso *et al.* (2021) reinforce that high and prolonged levels of IL-6 are directly correlated with longer hospital stay and clinical severity. The activation of the complement system, with the production of anaphylatoxins C3a and C5a described by Souza and Elias (2006), recruits leukocytes and increases vascular permeability. At the same time, Moura *et al.* (2001) indicate that the activation of kallikrein-kinin releases bradykinin, contributing to vasoplegia. Such biochemical mechanisms explain complications such as pulmonary dysfunction cited by Luz and Junior (2002) and acute kidney injury, which, according to Paulitsch (2009) and Alves (2022), is aggravated by hypoperfusion and hemolysis associated with mechanical trauma from the pumps.

In view of this inflammatory scenario, the discussion about laboratory monitoring is crucial. The data compiled indicate that traditional markers, such as C-Reactive Protein (CRP), have limitations. Arkader *et al.* (2004) observe that CRP suffers nonspecific elevation due to surgical trauma, which, according to Póvoa *et al.* (1998), makes it difficult to distinguish between sterile SIRS inflammation and infectious processes in the immediate postoperative period. On the other hand, Meisner (2010) points to Procalcitonin (PCT) as a biomarker with greater specificity; the persistence of its high levels or secondary peaks strongly signal the presence of sepsis, aiding in the differential diagnosis (Arkader *et al.*, 2004). Additionally, serum lactate monitoring and intraoperative blood gas analysis, emphasized by Moreira and Silva (2020) and Silva *et al.* (2017), are indispensable tools to assess tissue perfusion and acid-base balance, allowing the immediate correction of metabolic disorders (Alcantara *et al.*, 2025).

Finally, the results underline the decisive role of the biomedical perfusionist not only as an operator, but as a manager of the inflammatory response. The literature confirms that the application of mitigation strategies is the responsibility of this professional. Mesquita *et al.* (2010) highlight the use of circuits with biocompatible coatings (such as heparin) to reduce complement activation and the induction of controlled hypothermia to reduce metabolic demand. Braulio (2009) suggests that centrifugal pumps may induce a lower inflammatory response by reducing mechanical trauma. In addition, Antunes *et al.* (2009) demonstrate the effectiveness of ultrafiltration in the removal of circulating cytokines. Therefore, the

specialized performance of the perfusionist, based on strict coagulation monitoring (TCA) and the maintenance of hemodynamic stability (Silva, 2020), is the key factor to attenuate the magnitude of SIRS and improve the prognosis of patients.

5 FINAL CONSIDERATIONS

This study aimed to document the fundamentals of Cardiopulmonary Bypass (CPB) and its complex relationship with Systemic Inflammatory Response Syndrome (SIRS), analyzing the pathophysiology, clinical and laboratory implications, and the central role of the biomedical perfusionist in the management of this process.

The literature review confirmed that SIRS is an intrinsic and paradoxical pathophysiological consequence of CPB, being the main vector of postoperative morbidity. The findings demonstrated that inflammation is triggered by two main and synergistic mechanisms: the activation of the complement and kallikrein-kinin system by the contact of blood with the non-endothelial surfaces of the circuit and ischemia-reperfusion injury, which generates reactive oxygen species.

This activation results in a "cytokine storm", with release of mediators such as IL-6 and TNF-alpha, whose direct clinical implications include pulmonary, renal and cardiovascular dysfunction. In the laboratory sphere, the importance of monitoring biomarkers such as C-reactive protein (CRP) and, with greater specificity, procalcitonin (PCT) was highlighted for the differential diagnosis between sterile SIRS and sepsis.

The contribution of this study to the contextualization of the biomedical perfusionist as an active manager of the inflammatory response, and not just a circuit operator, is very significant. It was evidenced that proactive management, through intraoperative laboratory monitoring (such as blood gas analysis and TCA) and the application of mitigation strategies — such as the use of biocompatible circuits, ultrafiltration to remove mediators, and control of hypothermia — is fundamental.

Therefore, it is concluded that the detailed understanding of the biochemical cascade that mediates CPB-induced SIRS and the specialized performance of the biomedical perfusionist are decisive factors to minimize the inflammatory response, reduce organ dysfunction and, consequently, improve the patient's prognosis in the postoperative period of cardiac surgery.

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