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Potential Link Between Infectious Disease-induced Inflammation and Cardiovascular Disease: From Molecular Mechanisms to Clinical Translation

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ABSTRACT

Infectious diseases pose a significant health threat worldwide, while cardiovascular diseases remain among the leading causes of human mortality. Recent clinical and basic research has demonstrated that infectious diseases can induce or exacerbate cardiovascular complications, primarily through excessive or dysregulated inflammatory responses triggered by pathogen stimuli. Elevated levels of inflammatory factors not only directly damage cardiomyocytes and vascular endothelium but also accelerate the progression of cardiovascular pathology through various pathways, including immune imbalance and metabolic abnormalities.This review systematically describes the concept and molecular mechanisms of inflammation induced by infectious diseases. It discusses clinical translational strategies, ranging from biomarker detection to anti-inflammatory therapy and vaccine intervention, in the context of the clinical manifestations of cardiovascular and cerebrovascular complications caused by typical pathogens, such as viruses and bacteria. The review concludes with an outlook on current research challenges and future development directions. A deeper understanding of the inflammatory nexus between infectious diseases and cardiovascular and cerebrovascular diseases is crucial for developing more effective preventive and therapeutic programs, ultimately reducing the disease burden.

1. Introduction

Globally, infectious diseases (e.g., viral, bacterial, and parasitic infections) and cardiovascular diseases (e.g., coronary heart disease, hypertension, and stroke) are the leading causes of morbidity and mortality, respectively[1]. Growing evidence from clinical practice suggests a significant and close link between the two: deterioration of cardiovascular function or an increase in complications is often observed when an organism is infected by pathogens [2]. For instance, infections caused by the novel coronavirus (SARS-CoV-2) can result in severe complications such as myocarditis, thrombosis, and acute coronary syndromes, in addition to respiratory issues. Furthermore, populations infected with HIV are more likely to develop

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atherosclerosis and other cardiovascular complications at a younger age[3].

Behind this link, the central nexus: pathogens activate the host immune system, triggering a cascade of amplified inflammatory pathways that ultimately impact the structure and function of the cardiovascular system. In light of this, this article will focus on the critical role of disease-induced inflammation in the pathogenesis of cardiovascular complications. Firstly, we will summarize the fundamental concepts of inflammation and the primary mechanisms at the molecular level. Next, we will discuss the clinical impact of viruses, bacteria, and other typical pathogens on the cardiovascular system. We will then analyze how to translate these advancements in basic research into clinically feasible early diagnosis and intervention strategies, including biomarker detection, inflammation-targeted therapy, and vaccination. Finally, we will provide a brief overview of the challenges and future directions in this field.

2. Infectious Disease-Induced Inflammatory Response: Basic Concepts

2.1. Definition and Characterization of Systemic Inflammation

From a pathological and immunological perspective, inflammation serves as the body's fundamental defense mechanism against foreign pathogens and endogenous damage, playing a critical role in maintaining tissue homeostasis and facilitating repair processes. However, when this defense response becomes overactive or imbalanced, it can lead to severe consequences for the organism, potentially triggering multi-organ dysfunction. Research has demonstrated that for highly pathogenic or highly infectious agents, the intense inflammation they induce is frequently linked to increased rates of morbidity, mortality, and complications[4].

In clinical practice, extreme systemic inflammatory responses are often referred to as are characterized by significant elevations of pro-inflammatory cytokines (e.g., IL-1, IL-6, TNF-α, IFN-γ) in the circulation, as well as widespread activation of numerous immune cells, including neutrophils, macrophages, and T cells. This dramatic immune disorder can rapidly affect several key organs, including the heart, lungs, liver, kidneys, and central nervous system, leading to severe complications such as acute respiratory distress syndrome (ARDS), heart failure, and acute kidney injury[5]. For critically ill patients, failure to control the inflammatory storm in a timely and effective manner not only exacerbates tissue damage but may also result in shock or even death.

It is important to note that inflammation is not always “intense.” More often than not, the body experiences a chronic, low-grade inflammatory state. Although the symptoms may not be as apparent as in the acute phase, this chronic inflammation can also be detrimental, particularly when associated with underlying conditions such as diabetes, obesity, hypertension, or atherosclerosis. These conditions are more likely to predispose individuals to cardiovascular and cerebrovascular complications. Therefore, accurately identifying and managing the intensity of inflammation—so as to combat pathogens without causing excessive harm to the body—has become a focal point of both clinical and scientific research.

2.2. Main Mechanism: Pathogen Recognition and Immune Activation

When pathogens—such as viruses, bacteria, parasites, and fungi—enter the organism, the innate immune system is initially activated to recognize them. Pattern Recognition Receptors (PRRs) present on body cells play a crucial role in this process.

2.2.1. Toll-Like Receptors (TLRs)

Toll-like receptors (TLRs) are primarily located in cell membranes or endosomal membranes. They can detect pathogen-associated molecular patterns (PAMPs), such as bacterial lipopolysaccharides (LPS) or viral RNA fragments. Upon recognition of these PAMPs, TLRs activate signaling pathways, including MyD88 and TRIF, which facilitate the translocation of downstream transcription factors (e.g., NF-κB, IRF3) into the cell nucleus, leading to the production of a substantial quantity of pro-inflammatory cytokines.

2.2.2. RIG-I-Like Receptors (RLRs)

RIG-I-like receptors (RLRs) are located in the cytoplasm of cells and are specifically designed to recognize viral nucleic acids, such as double-stranded RNA and 5'-triphosphate RNA. The activation of RLRs typically initiates an antiviral response, including the production of type I interferons (IFN-alpha and IFN-beta), which bolster the host's resistance to viral replication and transmission.

2.2.3. NOD-Like Receptors (NLRs)

NLRs bind to specific molecular patterns and assemble into inflammasomes, such as the NLRP3 inflammasome. These complexes convert precursor forms of interleukin-1 beta (IL-1β) and interleukin-18 (IL-18) into their mature, active forms, significantly amplifying the intensity of inflammatory responses. NLRP3 inflammasomes have been implicated in a broad spectrum of infectious diseases and autoimmune disorders.

The massive release of pro-inflammatory factors and chemokines by the innate immune system can further attract and activate the adaptive immune system, including T cells and B cells. If pathogens are cleared promptly during this series of defenses, inflammation will subside, allowing the tissue repair phase to commence. However, if pathogens persist or if immune regulation cannot be efficiently activated, the response often evolves into systemic or chronic inflammation. This chronic process not only increases the risk of repeated tissue damage but also poses a significant threat to the cardiovascular system, creating an the development of atherosclerosis, myocardial damage, and other complications[6].

2.3. Potential Links Between Inflammatory Factors and the Cardiovascular System

In a systemic inflammatory context, substantial quantities of pro-inflammatory factors and activated immune cells

are not limited to the initial site of infection; rather, they can disseminate throughout the body via the circulatory system, affecting the vascular endothelium, myocardial tissue, and microcirculatory network [7]. The following mechanisms are particularly relevant to cardiovascular injury induced by infectious diseases:

2.3.1. Vascular Endothelial Cell Activation and Dysfunction

Endothelial cells serve as a crucial barrier that regulates vascular tension, permeability, and thrombosis. When stimulated by pro-inflammatory factors such as interleukin-1 beta (IL-1β) and tumor necrosis factor-alpha (TNF-α), endothelial cells overexpress adhesion molecules (including ICAM-1, VCAM-1, and E-selectin) on their surface. This overexpression facilitates the adhesion of immune cells and promotes their trans-endothelial migration, thereby triggering localized inflammation within the vessel wall. During this process, the synthesis of nitric oxide (NO) in endothelial cells decreases, while the generation of reactive oxygen species (ROS) increases. Consequently, the vasodilatory function is inhibited, leading to vasoconstriction, increased permeability, and hypercoagulability, which further elevates the risk of atherosclerosis and thrombosis.

2.3.2. Accelerated Development of Atherosclerosis

In a prolonged inflammatory environment, monocytes and macrophages accumulate beneath the endothelium and uptake oxidatively modified low-density lipoprotein (oxLDL), leading to the formation of foam cells and subsequently lipid plaques. If the NLRP3 inflammasome is activated during this process, it will continue to secrete potent pro-inflammatory factors such as IL-1β, which further exacerbates the inflammation within the plaque and increases the likelihood of plaque rupture and thrombosis.

2.3.3. Myocardial Damage and Cardiac Contractile Dysfunction

When the levels of inflammatory factors (e.g., TNF-α, IL-6) increase dramatically, the metabolism of cardiomyocytes, ion channels, and calcium homeostasis are adversely affected, leading to issues such as contractile weakness, diastolic dysfunction, and arrhythmias. If a pathogen can directly infect the myocardium or pericardium (for instance, certain viruses can bind to receptors on cardiomyocytes), it may induce myocarditis and potentially involve the pericardium, resulting in pericarditis. As inflammation persists, myocardial cells may undergo necrosis or apoptosis, thereby increasing the risk of heart failure.

2.3.4. Positive Feedback Loop Between the Coagulation Pathway and Inflammation

Inflammation activates the coagulation system, which in turn exacerbates the inflammatory response, creating a vicious cycle. Elevated levels of inflammatory factors upregulate the expression of tissue factor (TF), leading to platelet aggregation and fibrin deposition. The inflammatory mediators released by these coagulation factors and platelets subsequently stimulate additional immune cells, resulting in a continuous amplification of both inflammation and coagulation. If these processes occur in the coronary or cerebral arteries, there is a significant risk of fatal events such as acute myocardial infarction or stroke.

Overall, the intense inflammatory response triggered by infectious diseases is often more than a mere "immune clearance" process; it resembles a "systemic storm" involving various cell types and molecular signaling pathways, with potential damage to the cardiovascular system being of utmost significance. In the subsequent chapters, we will further investigate how different pathogens influence cardiovascular function through specific inflammatory pathways and offer insights for clinical prevention and treatment based on the latest research advancements.

3. Molecular Mechanisms: Effects of Inflammation on the Cardiovascular System

3.1. Inflammation and Endothelial Dysfunction

Vascular endothelial cells serve as a crucial and of the cardiovascular system. They not only maintain vasodilatory function by secreting nitric oxide (NO) and other reactive substances but also regulate the expression of various adhesion molecules and cytokines. These factors significantly influence the interactions between leukocytes, platelets, and the vascular wall.

However, when the organism is in a systemic inflammatory environment, the prolonged release of inflammatory factors (such as TNF-α and IL-1β) and reactive oxygen species (ROS) leads to the following damage [8]:

Excess reactive oxygen species (ROS) can reduce nitric oxide (NO) synthesis by reacting with NO to form harmful peroxynitrite (ONOO-). This reaction diminishes the biological activity of NO, leading to decreased vasodilatory function and impaired blood pressure regulation.

Impaired tight junction proteins: Endothelial intercellular junction proteins (e.g., VE-cadherin, claudin, occludin) can be easily degraded or rendered dysfunctional under inflammatory conditions. This degradation leads to increased vascular permeability, localized edema, and exudative inflammation.

Overexpression of Adhesion Molecules: Inflammatory factors can upregulate the gene expression of adhesion molecules such as VCAM-1, ICAM-1, and E-selectin, which promote leukocyte adhesion and their migration across the endothelial layer. The inflammatory microenvironment that develops within the arterial wall subsequently creates conditions conducive to atherosclerosis and plaque formation.

Since endothelial dysfunction is frequently regarded as an early indicator of atherosclerosis, thrombosis, and acute cardiovascular events, clinical monitoring and intervention—such as supplementation with antioxidants or the use of ACE inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) to enhance endothelial function—are crucial for preventing complications. Early identification of the deterioration of endothelial function and timely intervention can significantly reduce the incidence of cardiovascular and cerebrovascular events, particularly during severe infections or the recovery phase following infection.

3.2. Inflammation and Atherosclerosis

Atherosclerosis is not only a vascular lesion resulting from a disorder of lipid metabolism, but it is also considered a classic chronic inflammatory process. In the context of systemic inflammation induced by infectious diseases, various immune cells and inflammatory factors continuously stimulate vascular endothelial and smooth muscle cells, thereby accelerating the formation and progression of atherosclerotic plaques[9]. Its primary mechanisms include:

Foam Cell Formation: Under inflammatory conditions, a significant number of monocytes and macrophages are recruited to the subendothelial space to phagocytose oxidized low-density lipoproteins (oxLDL) and transform into foam cells. These foam cells are foundational to early atherosclerotic plaques and signify the onset of an inflammatory process that intensifies within the arterial wall.

Smooth muscle cell proliferation and migration: Certain pro-inflammatory factors (e.g., IL-1, TNF-α) and growth factors (e.g., PDGF) can stimulate vascular smooth muscle cells to proliferate or migrate abnormally to the intima-media layer. This process can result in the over-synthesis of extracellular matrix, ultimately leading to arterial wall hypertrophy and remodeling.

Continuous activation of inflammatory vesicles (such as NLRP3): NLRP3 inflammatory vesicles release potent inflammatory mediators, including IL-1β, which exacerbate the inflammatory response within and around the plaque, thereby increasing its instability and the risk of rupture. Once plaque rupture occurs, platelets and coagulation factors rapidly aggregate, potentially leading to acute coronary syndrome or stroke.

It is important to emphasize that when the underlying metabolic or immune status is already compromised (e.g., in patients with HIV or diabetes), the inflammation induced by infectious diseases tends to be more persistent and challenging to manage, significantly accelerating the progression of atherosclerosis. Enhanced inflammation testing (e.g., high-sensitivity C-reactive protein [hs-CRP], interleukin-6 [IL-6]) and imaging screening (e.g., carotid ultrasound, coronary computed tomography [CT]) are particularly essential for this vulnerable population.

3.3. Inflammation and Myocardial Injury

In a state of excessive inflammation, cardiomyocytes are subjected to multiple forms of attack, both directly and indirectly. Certain pathogens, such as the novel coronavirus (SARS-CoV-2), can directly induce cellular damage by binding to specific receptors on cardiomyocytes (e.g., ACE2) or disrupt the metabolic and electrophysiological activities of these cells through the release of elevated levels of cytokines[10].

Myocarditis is characterized by the infiltration of a significant number of neutrophils and macrophages into myocardial tissues due to viral or bacterial invasion and the subsequent immune response. This infiltration triggers degeneration of myocardial fibers, necrosis, and further inflammatory cell infiltration. Clinical symptoms may include chest pain, palpitations, and dyspnea. In severe cases, myocarditis can progress to dilated cardiomyopathy or life-threatening cardiac arrhythmias.

Cardiac systolic and diastolic disorders: Cytokines (e.g., TNF-α, IL-6) in the inflammatory environment can disrupt calcium ion homeostasis and mitochondrial function in cardiomyocytes. This disruption can lead to a decrease in cardiac output and a reduction in ejection fraction, clinically manifesting as heart failure or intractable hypotension.

Microcirculation disorders: Inflammation and coagulation abnormalities can further compromise myocardial blood supply, exacerbating myocardial cell hypoxia and metabolic dysfunction.

Against the backdrop of an imbalance between energy supply and demand in the body, cardiomyocytes often struggle to withstand multiple stresses, leading to apoptosis or necrosis. This phenomenon is a common lethal factor in patients with severe infectious diseases. Therefore, early recognition and effective management of the inflammatory response, combined with supportive therapies (e.g., mechanical ventilation, hemodynamic monitoring, and extracorporeal membrane oxygenation [ECMO]), are crucial for protecting against infection-induced acute cardiac injury.

3.4. Inflammation and Thrombosis

There is a effect between inflammation and coagulation, with each process activating the other and promoting the escalation of the pathological process.[11]

Inflammation promotes coagulation: Elevated levels of interleukin-1 (IL-1), tumor necrosis factor-alpha (TNF-α), and other pro-inflammatory cytokines stimulate vascular endothelial cells and monocytes to express tissue factor (TF), which serves as an initiator of the extrinsic coagulation pathway. Concurrently, inflammation inhibits the activity of natural anticoagulant proteins, such as protein C and protein S, leading the body to a hypercoagulable state.

Coagulation Amplifies Inflammation: During the coagulation process, platelets and thrombin release a variety of inflammatory mediators (e.g., platelet-activating factor [PAF] and thrombin), which recruit additional immune cells and initiate new inflammatory cascades. This establishes a positive feedback loop between inflammation and coagulation, potentially leading to acute myocardial infarction or stroke if embolization occurs in the coronary or cerebral arteries.

Disseminated Intravascular Coagulation (DIC): In severe infectious diseases such as sepsis and certain viral infections, inflammation and coagulation processes can become dysregulated and extensively affect the small vascular network. This dysregulation leads to the manifestation of DIC signs, including widespread systemic microthrombosis and significant consumption of coagulation factors and platelets. Consequently, the clinical mortality rate associated with DIC is exceedingly high.

In summary, inflammatory mediators and immune cells play a crucial role in cardiovascular and cerebrovascular pathology. They assist the body in combating pathogens at moderate levels; however, when their activity becomes excessive, they can transform into a that exacerbates cardiovascular and cerebrovascular injuries and complications. Therefore, investigating inflammatory pathways in basic research, along with monitoring and intervening on

inflammatory markers in clinical settings, can significantly enhance efforts to prevent and treat cardiovascular and cerebrovascular complications associated with infectious diseases.

4. Cardiovascular and Cerebrovascular Complications of Typical Infectious Diseases

Based on the mechanisms of inflammation and cardiovascular damage described in the previous section, this chapter will discuss the cardiovascular and cerebrovascular complications associated with common infectious diseases, as well as their clinical characteristics in relation to specific pathogens. These complications frequently involve inflammation, immune response, metabolic processes, and vascular endothelial function, resulting in diverse clinical manifestations and prognoses. To provide readers with a comprehensive overview of the characteristics of cardiovascular and cerebrovascular damage caused by various pathogens, the following table presents the types of complications, the range of incidence rates, and the primary mechanisms associated with several representative pathogens.

4.1. Viral Infections

4.1.1. New Coronavirus (SARS-CoV-2)

The outbreak of novel coronavirus pneumonia (COVID-19) since late 2019 has prompted a renewed academic focus on the relationship between infectious diseases and cardiovascular complications. The SARS-CoV-2 virus not only damages the lungs but also presents pathologies characterized by multi-system involvement[12].

Myocarditis and Myocardial Damage: The SARS-CoV-2 spike protein binds to the ACE2 receptor and may directly infect cardiomyocytes or vascular endothelial cells. In conjunction with a significant number of cytokines (e.g., IL-6, TNF-α) produced by the immune system, this can lead to the induction of acute myocarditis, myocardial fiber necrosis, and fibrosis.

Arrhythmic and Thrombotic Events: Some patients with COVID-19 develop intractable arrhythmias, such as ventricular tachycardia or atrial fibrillation, as well as thromboembolic conditions, including pulmonary embolism and deep vein thrombosis. There is a significant association between COVID-19 infections and hypercoagulable states, with contributing mechanisms that include inflammatory storms, endothelial injury, and abnormal platelet activation.

'Growing New Crowns' and Chronic Inflammation: A certain percentage of recovering patients exhibit symptoms such as fatigue, chest tightness, and palpitations. Recent evidence from large population-based follow-up studies suggests that these symptoms are associated with persistent low-grade inflammation and endothelial dysfunction, which may increase the long-term risk of heart failure and myocardial infarction in these patients.

4.1.2. HIV

The human immunodeficiency virus (HIV) is widely recognized for its capacity to progressively deplete the body's immune system. However, numerous epidemiological studies have demonstrated that HIV infection also significantly elevates the incidence of cardiovascular complications, including atherosclerosis and heart failure[13].

Chronic Immune Activation and Inflammation: Although effective antiretroviral therapy (ART) has significantly extended the lifespan of HIV-infected patients, chronic immune activation (e.g., IL-6, TNF-alpha) and markers of monocyte activation (such as sCD14) remain elevated. These persistent high levels can further accelerate atherosclerosis and myocardial damage.

Atherosclerosis and Coronary Heart Disease: Clinical data indicate that HIV-infected patients frequently experience an earlier onset of cardiovascular and cerebrovascular events. Additionally, imaging studies reveal that atherosclerotic plaques in these patients exhibit increased inflammatory activity.

Heart failure and cardiomyopathy: HIV-associated cardiomyopathy may be characterized by reduced contractility, enlargement of cardiac chambers, and arrhythmias. Direct viral toxicity, immunoinflammation, and comorbidities (e.g., tuberculosis) may exacerbate myocardial damage in this process.

4.2. Bacterial Infections

4.2.1. Streptococcus Pneumoniae

Streptococcus pneumoniae is a prevalent cause of community-acquired pneumonia, particularly affecting children and the elderly. It can also be associated with acute myocardial damage and myocardial infarction [14].

Inflammatory Factors and Toxins: Bacterial toxins can directly damage the mitochondrial function of cardiomyocytes. Additionally, the substantial release of inflammatory factors produced by the body to combat the pathogen can further deteriorate the metabolic environment of the myocardium.

Myocarditis and Arrhythmia: Studies have shown that patients infected with Streptococcus pneumoniae are at a higher risk of developing arrhythmias and acute myocarditis. The severity of these conditions is positively correlated with the extent of lung infection and the level of systemic inflammation.

Early monitoring and antimicrobial therapy: Implementing early pathogenetic testing and monitoring cardiac function in at-risk populations can significantly reduce the risk of acute myocardial injury.

4.2.2. Tuberculosis

Mycobacterium tuberculosis (TB) is primarily characterized by chronic infection and represents one of the significant public health challenges worldwide. In recent years, researchers have increasingly concentrated on clinical and mechanistic studies of the combined cardiovascular damage associated with tuberculosis[15].

Chronic Inflammation and Malnutrition: Tuberculosis (TB) induces chronic low-grade inflammation and malnutri-

tion, both of which contribute to the acceleration of atherosclerosis and other cardiovascular pathologies.

Direct invasion of the myocardium or pericardium: In certain instances, Mycobacterium tuberculosis can disseminate to the pericardium or myocardium, resulting in tuberculous pericarditis, myocarditis, and, in severe cases, pericardial tamponade or dilated cardiomyopathy.

A comprehensive treatment strategy is crucial for preventing the progression of cardiovascular complications. Early diagnosis and a standardized anti-tuberculosis regimen, which includes combined drug therapy and nutritional support, are essential components of this approach.

4.3. Other Pathogens

4.3.1. Malaria (Plasmodium Vivax)

Malaria is prevalent in tropical and subtropical regions and is transmitted by Plasmodium species through mosquito bites, with Plasmodium falciparum (P. falciparum) being the most lethal strain[16].

Microcirculatory Disorders: Plasmodium invades erythrocytes, leading to hemolysis and the release of significant amounts of free hemoglobin along with inflammatory mediators. This process results in local vascular obstruction and hypoxia, which subsequently impairs myocardial blood supply.

Elevated levels of inflammatory factors, such as IL-6 and TNF-α, can cause additional damage to the vascular endothelium and cardiomyocytes, potentially leading to heart failure or severe arrhythmias.

4.3.2. Spirochete Infections (E.G. Lyme Disease)

Lyme disease is caused by the tick-borne spirochete Borrelia burgdorferi and is predominantly found in temperate regions of the Northern Hemisphere [17].

Involvement of the myocardium and conduction system: Patients may experience myocarditis, atrioventricular block, and arrhythmias. If treatment is delayed, the resulting cardiac damage may be challenging to fully reverse.

Early and appropriate antibiotic therapy can significantly decrease the incidence of cardiac complications and enhance patient prognosis.

4.4. Summary

As illustrated in Table 1, although cardiovascular complications induced by various pathogens differ in their specific incidence and clinical manifestations, a common thread is that inflammation, immune dysregulation, and vascular endothelial dysfunction play crucial roles in the disease process. Some infections, such as neocollins, HIV, and tuberculosis, tend to cause more insidious and prolonged cardiovascular damage, while others, including Streptococcus pneumonia and Plasmodium vivax, can lead to fatal complications during the acute phase. These characteristics provide insights for early clinical identification and intervention, emphasizing the importance of monitoring and managing individuals with combined cardiovascular and cerebrovascular risks within the infectious disease prevention and control framework. Subsequent chapters will explore early diagnosis, therapeutic interventions, and prevention strategies for these complications, informed by research on molecular mechanisms and clinical practice.

5. From Molecular Mechanisms to Clinical Translation: Prevention and Treatment Strategies

Having systematically described the molecular mechanisms underlying inflammation and cardiovascular injury induced by infectious diseases, this chapter will focus on how these findings can be effectively translated into clinical applications. Overall, early detection and diagnosis, targeted anti-inflammatory treatments, and preventive interventions (e.g., vaccination and epidemiological surveillance) collectively represent the core strategies for preventing and treating cardiovascular complications associated with infectious diseases.

5.1. Biomarkers and Early Diagnosis

5.1.1. Conventional Markers of Inflammation and Myocardial Damage

Conventional inflammatory markers, such as high-sensitivity C-reactive protein (hs-CRP), white blood cell count, and erythrocyte sedimentation rate, are the most commonly used initial clinical screening tools. Among these, hs-CRP is often considered one of the most sensitive indicators of systemic inflammatory status and cardiovascular risk. It is particularly effective for assessing the risk of atherosclerosis, myocardial ischemia, and other cardiovascular and cerebrovascular events [18].

Troponin (cTnI, cTnT) and brain natriuretic peptide/amino-terminal brain natriuretic peptide (BNP/NT-proBNP) are important biochemical markers for identifying acute myocardial injury and heart failure. These markers can be utilized to assess the extent of myocardial damage and evaluate prognostic risk at an early stage.

5.1.2. Emerging Biomarkers and Multi-Omics Analysis

With the advancement of single-cell sequencing, high-throughput proteomics, and metabolomics technologies, an increasing number of novel biomarkers have been identified.

Cytokine profiles, such as IL-6, TNF-α, and IL-1β, play a crucial role in the inflammation induced by infectious diseases. However, fluctuations in individual cytokine levels are insufficient to capture the dynamic changes that occur throughout the course of the disease. By utilizing integrated multi-omics analysis, researchers can track the spatial and temporal distribution of multiple cytokines and immune cell subpopulations during infection. This approach provides a more nuanced foundation for clinical staging, diagnosis, and prognostic assessment.

Metabolomic markers, such as specific amino acids and lipid metabolites, can indicate the overall metabolic adaptations of an organism in response to infection and inflammation. These markers are highly relevant to pathological processes, including myocardial energy supply and vascular endothelial homeostasis.

Table 1 | Example of comparison of different pathogens and their cardiovascular complications

Pathogen	Common Cardiovascular Complications	Incidence/Incidence Range	Main Pathological Mechanisms	Reference
SARS-CoV-2	Myocarditis, thromboembolism, arrhythmia, heart failure, etc.	About 5 to 20 per cent (in severe cases)1	• Binding of viral sting proteins to ACE2 • Immune overactivation and inflammatory storms • Vascular endothelial dysfunction • Hypercoagulable state leading to microthrombosis	[10][11]
HIV	Atherosclerosis, heart failure, cardiomyopathy, etc.	Specific rates vary by population group[2]	• Chronic immune activation, upregulation of pro-inflammatory factors • Lipid metabolism disorders promote atherosclerotic process • Immune system fatigue and cytotoxic damage	[13]
Streptococcus pneumoniae	Acute myocardial damage, myocardial infarction	Strongly correlated with complication rate of severe pneumonia[3]	• Toxins disrupt mitochondrial function • Elevated systemic levels of inflammatory factors in pneumonia • Endothelial damage and impaired myocardial energy metabolism	[14]
Tubercle bacillus	Atherosclerosis, myocarditis, Pericarditis, heart failure	Up to 10-15 per cent in some areas[4]	• Long-term chronic inflammation • Malnutrition and lipid imbalance • Direct involvement of pathogens in the myocardium and pericardium	[15]
Plasmodium	Myocardial ischaemia, heart failure, Microcirculatory disorders	Mainly seen in falciparum malaria[5]	• Erythrocytolysis, microvascular blockage • High inflammatory factor levels • Tissue hypoxia and impaired energy supply	[16]
Lyme disease spirochete	Myocarditis, arrhythmia, Atrioventricular block	About 5-10 per cent of patients with Lyme disease [6]	• Direct invasion of myocardium and conduction system by spirochetes • Inflammatory response leading to tissue destruction • If not treated early, it can lead to persistent myocardial damage.	[17]

AI and Big Data-Assisted Screening: By employing machine learning algorithms, along with clustering and feature extraction techniques on extensive multi-omics databases, it is possible to identify more specific and sensitive early prediction and precise early warning of cardiovascular and cerebrovascular complications associated with infectious diseases.

In future clinical practice, the use of multi-marker associations and intelligent diagnostics will become a trend, offering more effective technical support for screening and individualized interventions for high-risk groups.

5.2. Therapeutic Strategies Targeting Inflammation

Inflammation caused by infectious diseases is a moderate inflammation can aid in clearing pathogens and initiating tissue repair, excessive or dysregulated inflammation can worsen cardiovascular damage. Therefore, targeted interventions aimed at addressing key inflammatory pathways are critical in clinical settings.

5.2.1. Inflammatory Factor Blockers

IL-6, IL-1β, and TNF-α Inhibitors/Monoclonal Antibodies: In chronic inflammatory diseases such as rheumatoid arthritis and inflammatory bowel disease, IL-6 receptor

blockers (e.g., tocilizumab), IL-1β inhibitors (e.g., canakinumab), and TNF-α inhibitors (e.g., infliximab) have demonstrated a significant degree of effectiveness. In recent years, studies have explored the application of these biologics in the treatment of infection-related severe inflammation (e.g., sepsis, severe COVID-19) and its cardiovascular complications, revealing some positive effects[19].

Potential Limitations: It is important to consider that the body requires moderate inflammation to combat pathogens during the early stages of infection. A complete blockade of certain cytokines may result in recurrent disease or the emergence of new secondary infections. Therefore, these medications should be used judiciously, based on pathogenetic testing, assessment of immune status, and multidisciplinary consultation.

5.2.2. Anti-Inflammatory Drugs and Immunomodulation

Non-steroidal anti-inflammatory drugs (NSAIDs) can effectively alleviate localized pain and inflammation; however, their influence on the risk of cardiovascular events remains controversial. Some NSAIDs may increase the risk of thrombosis or lead to renal insufficiency. Therefore, their use should be evaluated based on the patient's specific condition, type of infection, and underlying cardiovascular status.

Glucocorticoids: In certain instances of severe inflammation, such as the phase of SARS-CoV-2 infection, glucocorticoids may be administered for short durations to alleviate critical symptoms. However, prolonged use or high doses can suppress immune clearance and lead to metabolic side effects, necessitating strict therapeutic guidelines and a gradual dosage reduction strategy.

3Immune Cell Modulation and Cellular Therapies: Stem cell transplantation and stem cell exocytosis have demonstrated anti-inflammatory and tissue repair potential in animal models. Additionally, regulatory T-cell (Treg) therapy has been proposed as a means to balance excessive inflammation and autoimmune responses. However, these therapies require further validation of their safety and efficacy before they can be applied on a large scale in clinical settings.

5.2.3. Multimodal Intervention Strategies

In cases of severe infectious diseases accompanied by serious cardiovascular events, a combination of the following treatments is often necessary:

Anti-infective treatment: This includes antiviral, antibacterial, and antiparasitic medications, which should be used precisely according to the type of pathogen and the results of drug sensitivity tests.

Cardiovascular Support: This involves support for circulatory and organ function through various means, including the use of vasoactive drugs (which can raise or lower blood pressure), mechanical circulatory support (such as Intra-Aortic Balloon Pump (IABP) and Extracorporeal Membrane Oxygenation (ECMO)), and cardiac rhythm management (including pacemakers and Implantable Cardioverter-Defibrillators (ICDs)).

Nutritional and Metabolic Management: Control of blood glucose levels, optimization of lipid profiles, and supplementation of proteins and micronutrients are essential for enhancing the stability of the body's internal environment during states of infection and inflammation.

fLifestyle interventions should emphasize smoking cessation, alcohol moderation, a balanced diet, and regular exercise. These measures can significantly alleviate low-grade inflammation and reduce the risk of recurrent cardiovascular events during the chronic phase [20].

5.3. Vaccination and Infectious Disease Prevention and Control

5.3.1. The Centrality of Vaccines

Prevention is always the fundamental strategy for controlling infectious diseases. Vaccination not only decreases the incidence of infections but also indirectly reduces the risk of cardiovascular and cerebrovascular complications, as well as other serious consequences.

Novel Vaccine Technology: The successful application of mRNA vaccines during the COVID-19 pandemic has generated innovative approaches for the rapid development of immunoprophylactic strategies against novel or emerging pathogens. Compared to traditional inactivated or attenuated vaccines, mRNA vaccines offer advantages such as a shorter development cycle and easier scalability in production[21].

Priority for High-Risk Groups: Vaccination can significantly reduce the risk of endothelial damage and myocardial complications due to severe infections in high-risk populations, such as the elderly and patients with pre-existing cardiovascular and cerebrovascular diseases. Additionally, specific groups, such as immunosuppressed patients, require a more personalized immunization program.

5.3.2. Big Data and Precision Prevention and Control

Epidemiological Surveillance: Utilizing big data and artificial intelligence (AI) technology to conduct dynamic monitoring and early warning in regions with a high incidence of infectious diseases allows for the early identification of potential outbreaks. This proactive approach enables the implementation of targeted preventive and control measures, thereby reducing the incidence of severe illnesses and complications.

Individualized Risk Assessment: Utilizing machine learning models that integrate personal medical history, immune status, genomic data, and environmental factors, we can customize prevention and intervention strategies for individual patients. For instance, we may implement more intensive surveillance for patients with comorbid hypertension and coronary artery disease during the flu season, or provide enhanced vaccination and cardiac testing for the elderly during a new coronary epidemic.

5.3.3. Public Health Interventions

In addition to individual immunoprophylaxis, public health interventions—such as enhancing living conditions, providing health education, improving nutritional standards, and reducing avenues for disease transmission—can significantly impact the reduction of infectious diseases and their associated cardiovascular complications. In the context of globalization, the cross-border transmission of new

pathogens and drug-resistant strains has become increasingly frequent, necessitating the strengthening of international cooperation and multidisciplinary collaboration.

Summary

In conclusion, a comprehensive understanding of the mechanisms underlying inflammation and cardiovascular injury induced by infectious diseases highlights the importance of early diagnosis, targeted anti-inflammatory treatments, and preventive interventions. These strategies can significantly reduce the incidence of severe complications and enhance patient prognosis. With the rapid advancement of multi-omics and artificial intelligence technologies, personalized medicine and intelligent monitoring are poised to become major trends in the future, offering innovative and efficient solutions for infectious diseases as well as cardiovascular and cerebrovascular conditions. However, more rigorous clinical trials are necessary to validate the safety and efficacy of emerging therapies. Additionally, there is a need to strengthen the promotion of vaccines and enhance epidemiological surveillance at the public health level, ensuring that the principle of as the primary strategy, integrating prevention and treatment

6. Current Research Status, Challenges and Future Prospects

6.1. Limitations of Existing Research

6.1.1. Complex and Heterogeneous Mechanisms

Available evidence indicates that the chain linking infectious diseases, inflammation, and cardiovascular injury exhibits significant heterogeneity across various pathogens, host immune backgrounds, and comorbid chronic diseases. For instance, both the novel coronavirus and HIV can induce chronic inflammation; however, each virus possesses distinct characteristics regarding cellular invasion, patterns of inflammatory cell infiltration, and the resulting cardiovascular and cerebrovascular damage. For example, infections caused by Streptococcus pneumoniae often lead to rapid myocardial damage during the acute phase, whereas tuberculosis infections are characterized by prolonged chronic inflammation. These diverse pathogenic mechanisms have hindered researchers from establishing a universal, comprehensive model that accurately predicts and explains all processes related to infection, inflammation, and cardiovascular injury. Consequently, scholars frequently need to conduct targeted studies on specific pathogens or populations, resulting in fragmented and non-generalizable findings. This situation underscores the necessity for larger, multidimensional data integration in the future to uncover universal patterns and critical nodes.

6.1.2. Insufficient Evidence for Clinical Translation

Although a variety of anti-inflammatory drugs and molecular targets (e.g., IL-6, IL-1β, TNF-α) have shown potential in inhibiting inflammatory injury and protecting the myocardium and vascular endothelium in animal models and in vitro experiments, comprehensive and systematic validation of their efficacy and safety remains relatively scarce in actual clinical practice. On one hand, large-scale randomized controlled trials (RCTs) are expensive, time-consuming, and challenging in terms of patient recruitment. On the other hand, patients with infectious diseases often experience rapid disease progression and multi-organ damage, making it insufficient to merely block a specific inflammatory pathway to achieve significant clinical improvement. Therefore, there is a pressing need for more high-quality, multicenter RCTs to confirm the clinical value of these anti-inflammatory drugs and novel biologics, which will aid in the stratification and individualization of treatment.

6.1.3. Multidisciplinary Collaboration Needs To Be Strengthened

The boundaries between traditional disciplines such as epidemiology, cardiovascular science, immunology, and public health continue to limit, to some extent, the comprehensive study of disease processes and the development of effective prevention and treatment programs. Research teams with diverse professional backgrounds may vary in their experimental designs, selection of key indicators, and data analysis methods, which complicates the integration and comparison of results. Furthermore, in the field of public health, the emphasis is often placed on the transmission, prevention, and control of infectious diseases at the population level, while insufficient attention is given to the cardiovascular pathological mechanisms and clinical interventions at the individual level. To establish a clearer connection between infectious diseases and cardiovascular diseases and to propose effective prevention and control strategies, a robust interdisciplinary approach is required. This approach should integrate molecular mechanism research with large-scale epidemiological investigations and facilitate the sharing of data and resources.

6.2. Future Research Directions

6.2.1. High-Throughput Genomics and Multi-Dimensional Data Integration

The rapid advancement of genomics, transcriptomics, proteomics, metabolomics, and single-cell sequencing technologies has equipped researchers with powerful tools for the in-depth investigation of the relationship between inflammation, infectious diseases, and cardiovascular injury. Multi-omics data not only aids in identifying new inflammatory factors and regulatory molecules but also elucidates the complex interactions between various pathogens and host immune cells, tissues, and organs across different temporal and spatial contexts. By integrating these high-dimensional data with clinical information (e.g., disease progression, complication status, prognostic indicators), it is anticipated that more specific and predictive biomarkers can be discovered, thereby providing scientific support for personalized diagnosis and treatment.

6.2.2. Precision Medicine and Big Data Assistance

Based on extensive clinical databases and population cohorts, the application of artificial intelligence and bioinformatics algorithms for clustering and risk assessment of patient characteristics has emerged as a prominent focus in contemporary medical research. By integrating electron-

ic medical records, genomic data, imaging information, and lifestyle factors, clinicians and researchers can effectively stratify and manage high-risk populations for infectious diseases. This approach enables the timely identification of specific subgroups vulnerable to cardiovascular and cerebrovascular complications, allowing for the development of personalized intervention plans. With advancements in cloud computing, the Internet of Things, and wearable device technology, the capabilities for remote monitoring and real-time early warning functions are expected to expand further in the future, facilitating the implementation of the warning - precise intervention.

6.2.3. Research and Development of Novel Drugs and Vaccines

Fine regulation and targeted treatment of inflammatory pathways are essential for preventing and managing cardiovascular and cerebrovascular complications associated with infectious diseases. Emerging strategies, such as gene editing technologies (CRISPR/Cas), small nucleic acid therapies (siRNA, ASO), nanocarrier drugs, and peptide or mRNA vaccines, offer expanded opportunities for targeting inflammatory responses and safeguarding cardiovascular function. In the event of emerging infectious diseases or outbreaks, these rapid and scalable research and development (R&D) and production technologies can provide effective vaccines or therapeutic drugs promptly, thereby mitigating the impact of widespread outbreaks on human health and socio-economic stability.

6.3. Importance of Interdisciplinary Collaboration

The traditional unidisciplinary research model often struggles to address the multi-system damage caused by infectious diseases and the complexities arising from the interplay of various chronic disease complications. Only through in-depth collaboration among immunology, pathobiology, cardiovascular medicine, public health, epidemiology, and various clinical specialties can the connection between infectious diseases and cardiovascular diseases be fully elucidated, from the molecular level to the population level. This collaborative approach will facilitate the development of more effective integrated prevention and control strategies.

With the rise of globalization, the risk of trans-regional epidemics caused by novel and drug-resistant pathogens has significantly increased. This situation necessitates collaborative research and information sharing across countries and disciplines. For instance, in the early detection of emerging pathogens, the integration of resources such as gene sequencing, international outbreak notifications, and clinical surveillance networks is crucial for the timely assessment of their potential cardiovascular and cerebrovascular damage, as well as for the development of targeted vaccines and drug programs. Multidisciplinary collaboration and international cooperation will be essential in the future to tackle the dual challenges posed by infectious diseases and cardiovascular and cerebrovascular conditions.

Conclusion

The close association between inflammation induced by infectious diseases and cardiovascular and cerebrovascular diseases has increasingly become a prominent research topic and a significant clinical challenge in contemporary medicine and public health. Numerous studies have demonstrated that a series of pathological processes, including vascular endothelial dysfunction, accelerated atherosclerosis, myocardial injury, and thrombosis, all of which substantially elevate the risk of cardiovascular and cerebrovascular complications. Although there is a preliminary understanding of the mechanisms by which typical pathogens, such as the novel coronavirus, HIV, Streptococcus pneumoniae, and Mycobacterium tuberculosis, cause cardiovascular injury, there is no complete consensus on when and how to precisely intervene in inflammation to effectively balance the removal of pathogens with the protection of cardiovascular function.

In the future, with the comprehensive application of molecular biology, multi-omics technology, artificial intelligence, and big data in the medical field, it is anticipated that the network structure of disease-inflammation-cardiovascular injury can be depicted more systematically. This advancement will facilitate the research and development of new anti-inflammatory drugs, the identification of specific biomarkers, and the formulation of individualized prevention and treatment strategies. Such progress will establish a more robust scientific foundation for the development of novel anti-inflammatory drugs and biomarkers. Particularly in the context of emerging infectious diseases, the ability to rapidly identify inflammatory pathways induced by viral or bacterial infections, as well as to monitor and intervene in cardiovascular complications promptly, will directly influence patient clinical outcomes and the efficiency of healthcare resource allocation.

In this process, multidisciplinary collaboration and international cooperation are essential, along with the need for more large-scale clinical trials and real-world studies to provide high-quality evidence for treatment and control options. Through the concerted efforts of experts from various fields and the support of all sectors of society, the dual threat posed by infectious diseases and cardiovascular and cerebrovascular diseases to public health and socio-economic development can be significantly mitigated. This collective action will contribute to the establishment of a healthier and more resilient public health system.

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