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"CARDIAC SEQUELAE OF SEPSIS: MECHANISTIC INSIGHTS AND FUTURE DIRECTIONS: A REVIEW"

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ABSTRACT

Sepsis is a life-threatening syndrome characterized by dysregulated host response to infection, resulting in widespread inflammation, microcirculatory dysfunction, and multi-organ failure. Among affected organs, the heart is particularly vulnerable, with sepsis-induced cardiac dysfunction emerging as a major determinant of prognosis. Epidemiological data suggest that 30–60% of septic patients develop septic cardiomyopathy, a reversible but often fatal condition marked by global biventricular dysfunction, reduced ejection fraction, and ventricular dilatation. The underlying mechanisms involve inflammatory cytokine storms, nitric oxide overproduction, mitochondrial dysfunction, endothelial injury, and microcirculatory impairment, which collectively depress contractility and impair myocardial responsiveness.Clinical manifestations include hypotension, tachycardia, dyspnea, arrhythmias, and signs of heart failure, often requiring advanced hemodynamic monitoring. Both systolic and diastolic dysfunction of the left ventricle are common, while right ventricular dysfunction results from increased afterload due to pulmonary hypertension. Arrhythmias, particularly atrial fibrillation, further destabilize hemodynamics. Additionally, Type II myocardial infarction arises from oxygen supply–demand mismatch rather than plaque rupture. Diagnosis relies on biomarkers (troponins, natriuretic peptides), echocardiography, and advanced imaging, though no specific marker for septic cardiomyopathy exists. Management is largely supportive, focusing on fluid resuscitation, vasopressors, inotropes, infection control, and antimicrobial therapy, with mechanical support

reserved for refractory cases. Emerging therapies targeting inflammatory mediators, oxidative stress, and mitochondrial protection are under investigation. Despite its reversible nature, septic cardiomyopathy is associated with 40–50% mortality, prolonged ICU stays, and long-term cardiovascular risk. Advances in precision medicine, novel biomarkers, and artificial intelligence hold promise for improving diagnosis and tailoring therapy in the future.

KEYWORDS: Sepsis, septic cardiomyopathy, cardiac dysfunction, Inflammatory cytokines, Biomarkers, Critical care.

1. INTRODUCTION

Sepsis is a life-threatening condition that arises when the body's response to infection becomes dysregulated, leading to systemic inflammation, tissue damage, and multi-organ dysfunct(1). Among the organs involved, the heart is particularly vulnerable, as septic cardiomyopathy—a reversible but often fatal form of cardiac dysfunction—plays a central role in the morbidity and mortality of septic patients. Understanding the relationship between sepsis and the heart requires an exploration of epidemiology, etiology, pathophysiology, clinical manifestations, diagnostics, and management strategies(2). Globally, sepsis remains one of the leading causes of critical illness, accounting for nearly one in every five deaths, with an especially heavy burden in low- and middle-income countries where resources for early detection and treatment are limited. The introduction of sepsis as a cardiovascular entity reflects a paradigm shift from viewing sepsis as a generalized syndrome of infection toward recognizing its organ-specific effects, particularly on myocardial function(3). The bacterial infections account for the majority of cases, followed by fungal, viral, and parasitic causes(4). Pathogens trigger an overwhelming immune response, marked by cytokine storms, oxidative stress, and mitochondrial dysfunction, all of which depress myocardial contractility. Cardiac involvement is not limited to direct infection but arises through systemic pathways that disrupt calcium handling, impair energy production, and damage endothelial and microvascular integrity(5). Epidemiological data indicate that 30–60% of septic patients develop cardiac dysfunction, with elderly individuals and those with pre-existing cardiovascular disease being disproportionately affected. Importantly, while septic cardiomyopathy is usually reversible in survivors within 7–10 days, its presence is strongly associated with higher short-term mortality, prolonged ICU stay, and long-term cardiovascular complications(6). The interaction between inflammatory mediators such as TNF-α, IL-1β, and IL-6 with myocardial cells is pivotal(7). These cytokines interfere with

calcium signaling and β-adrenergic pathways, while nitric oxide overproduction leads to vasodilation, hypotension, and impaired contractility. Simultaneously, mitochondrial dysfunction reduces ATP generation and triggers the release of damage-associated molecular patterns (DAMPs), amplifying inflammation(8). Endothelial dysfunction and microcirculatory impairment further compromise coronary perfusion, producing a mismatch between oxygen delivery and demand despite adequate systemic circulation. Collectively, these mechanisms culminate in reversible myocardial depression, clinically observed as reduced ejection fraction, ventricular dilatation, arrhythmias, and increased vulnerability to shock(9).

Clinically, septic cardiomyopathy manifests with persistent hypotension, tachycardia, dyspnea, and signs of poor perfusion, often requiring advanced hemodynamic monitoring and supportive therapy(10). Diagnostic tools include biomarkers such as troponins and natriuretic peptides, which reflect myocardial stress but lack specificity, as well as echocardiography, which reveals global hypokinesia and biventricular dysfunction. Advanced modalities like cardiac MRI and PET-CT are increasingly useful for characterizing myocardial involvement but remain limited in critically ill populations. Risk stratification is often aided by scoring systems such as SOFA and qSOFA, although these primarily assess global sepsis severity rather than cardiac-specific dysfunction(11). Septic cardiomyopathy focuses on hemodynamic stabilization, infection control, and supportive care. Fluid resuscitation remains the cornerstone but requires careful balance to avoid pulmonary edema in patients with impaired cardiac reserve. Vasopressors such as norepinephrine are first-line agents, with vasopressin and epinephrine used in refractory cases(12). Inotropes like dobutamine may improve contractility in low-output states, though their role remains controversial due to pro-arrhythmic potential. In severe, refractory cases, mechanical circulatory support (e.g., ECMO, Impella devices) may be employed as a bridge to recovery. Antimicrobial therapy is critical, with prompt broad-spectrum coverage followed by targeted de-escalation(13). Emerging adjuncts such as β-blockers, antioxidants, mitochondrial protectors, and immunomodulators offer experimental promise but lack definitive clinical validation. pre-existing heart failure, coronary artery disease, post-cardiac surgery status, cardiac implantable devices, and elderly patients are particularly vulnerable to the interplay of sepsis and cardiac dysfunction(14). In these groups, fluid management becomes more complex, arrhythmic risks are heightened, and prognosis is often worse. Device-related infections, such as those

involving pacemakers or LVADs, represent unique challenges due to the difficulty of eradicating biofilm-associated pathogens without device removal(15).

Despite extensive research, major challenges persist. The lack of specific biomarkers for septic cardiomyopathy hampers early recognition, and diagnostic overlap with acute coronary syndrome complicates management. Additionally, controversies remain regarding optimal fluid strategies, the use of adjunctive therapies, and the long-term prognosis of survivors(16). Importantly, while septic cardiomyopathy is considered reversible, many survivors experience persistent cardiac dysfunction, reduced exercise tolerance, and increased cardiovascular risk.

2. Etiology of sepsis

2.1 Bacterial Causes

Bacterial infections remain the most frequent cause of sepsis and, by extension, septic cardiomyopathy(17). Gram-positive bacteria such as *Staphylococcus aureus* (including MRSA), *Streptococcus pneumoniae*, and *Enterococcus* species are responsible for 30–50% of cases, while Gram-negative organisms such as *Escherichia coli*, *Klebsiella*, *Pseudomonas aeruginosa*, *Neisseria meningitidis*, *Salmonella*, and *Acinetobacter* account for 25–40%. Polymicrobial infections, particularly in abdominal and surgical sites, are also common(18). In the context of cardiac sepsis, bacterial toxins and pathogen-associated molecular patterns (PAMPs) stimulate a massive cytokine release, leading to inflammation, nitric oxide overproduction, and mitochondrial dysfunction, all of which contribute to myocardial depression.

2.2. Fungal Causes

Fungal pathogens, particularly *Candida* species, are important causes of sepsis in immunocompromised and critically ill patients, especially those with central venous catheters(19). *Aspergillus* and other molds, though less common, can cause severe invasive infections in neutropenic or transplant patients. In septic cardiomyopathy, fungal sepsis is linked to persistent systemic inflammation and microvascular injury, impairing coronary perfusion and directly affecting myocardial contractility(20).

2.3. Viral Causes

Viral infections are less frequent but clinically significant triggers of sepsis, particularly in immunosuppressed patients. Influenza, SARS-CoV-2 (COVID-19), cytomegalovirus (CMV),

Epstein-Barr virus (EBV), and hemorrhagic fever viruses such as Ebola and Dengue have all been implicated(4). Viral sepsis can lead to cardiac involvement not only through the systemic septic response but also via direct viral invasion of cardiomyocytes, as seen in viral myocarditis(21). This dual mechanism exacerbates septic cardiomyopathy by combining systemic inflammation with direct myocardial injury.

2.4. Parasitic Causes

Parasitic infections, while less common globally, remain significant in endemic regions. *Plasmodium falciparum* malaria can cause a septic-like syndrome with profound systemic inflammation, while *Leishmania donovani* (visceral leishmaniasis) and *Trypanosoma cruzi* (Chagas disease) are also implicated(22). These parasites contribute to sepsis-induced cardiac dysfunction through microvascular obstruction, systemic immune activation, and in some cases, direct myocardial damage, compounding the risk of septic cardiomyopathy(23).

2.5. Common Sites of Infection Leading to Cardiac Sepsis

The respiratory tract is the most common source of sepsis (40–50%), typically due to pneumonia, followed by urinary tract infections (20–25%), abdominal infections (10–20%), and skin and soft tissue infections such as cellulitis or necrotizing fasciitis. Central nervous system infections like meningitis or encephalitis, and device-related infections involving catheters, ventilators, or prosthetic devices are also key contributors. Regardless of the source, the systemic inflammatory response triggered by these infections drives endothelial dysfunction(24), impaired oxygen delivery, and mitochondrial injury, ultimately predisposing the heart to septic cardiomyopathy.

2.6. Risk Factors for Cardiac Sepsis

Certain populations are at higher risk of developing both sepsis and cardiac involvement. Extremes of age, particularly neonates and the elderly, are highly vulnerable due to immature or weakened immune responses. Chronic conditions such as diabetes, chronic kidney disease, COPD(25), heart failure, and cancer further predispose individuals to infection and sepsis-related myocardial dysfunction. Immunosuppression from HIV/AIDS, chemotherapy, corticosteroids, or organ transplantation also heightens susceptibility. Additionally, ICU-related factors such as prolonged mechanical ventilation, invasive catheters, and major surgery increase the risk of bloodstream infections and septic cardiomyopathy. In these groups, once sepsis develops, the likelihood of cardiac dysfunction is amplified by reduced myocardial reserve and an exaggerated inflammatory response(26).

3. Epidemiology of cardiac sepsis

Sepsis-induced cardiac dysfunction, commonly referred to as septic cardiomyopathy, is increasingly recognized as a critical determinant of morbidity and mortality in patients with severe sepsis and septic shock. Epidemiological studies suggest that cardiac involvement occurs in 30–60% of septic patients, though reported prevalence varies depending on the diagnostic criteria, patient population, and methods used to assess cardiac function(27). The condition is characterized by reversible global systolic and diastolic dysfunction, ventricular dilatation, and impaired myocardial contractility, often resolving within 7–10 days in survivors. Despite this reversibility, septic cardiomyopathy is associated with poor short-term outcomes, as affected patients have higher rates of hemodynamic instability, prolonged need for vasopressors, and increased risk of multi-organ failure compared to those without cardiac involvement. Mortality rates in patients with sepsis-induced myocardial dysfunction remain high, ranging from 40% to over 70%, with outcomes particularly poor in those who progress to septic shock.

Demographic patterns show that elderly patients, who already have reduced cardiac reserve and higher prevalence of comorbidities such as hypertension, diabetes, and coronary artery disease, are disproportionately affected(28). Similarly, patients with pre-existing heart failure or structural heart disease are at greater risk of developing severe myocardial dysfunction during sepsis. Epidemiological data also indicate a sex-related difference, with some studies suggesting that men are more likely to develop septic cardiomyopathy, although outcomes may be worse in women, possibly due to differences in immune response and hormonal regulation. Children and neonates can also develop sepsis-related cardiac dysfunction, which is a major contributor to pediatric sepsis mortality, particularly in low- and middle-income countries where timely diagnosis and advanced supportive care may be lacking.

From a healthcare perspective, the epidemiological impact of septic cardiomyopathy is significant, as it increases intensive care unit (ICU) length of stay, resource utilization, and long-term healthcare costs. Many survivors continue to experience persistent symptoms such as exercise intolerance, fatigue, and increased susceptibility to recurrent cardiovascular events(29). Given that sepsis accounts for nearly one in five global deaths, the burden of cardiac involvement is substantial, yet often underrecognized due to the absence of standardized diagnostic criteria. Improving epidemiological surveillance, incorporating advanced imaging modalities, and applying biomarkers in large population-based studies are

essential to accurately define the incidence, risk factors, and outcomes of sepsis-induced cardiac dysfunction.

4. Symptoms of septic cardiomyopathy

Septic cardiomyopathy, or cardiac sepsis, manifests with a range of symptoms that overlap with general sepsis but reflect direct impairment of the heart. Patients often present with persistent hypotension that does not improve with fluid resuscitation, owing to reduced myocardial contractility **Fig.1** . Dyspnea and shortness of breath are common due to low cardiac output and pulmonary congestion, while tachycardia frequently persists despite resuscitation efforts, reflecting diminished cardiac reserve(30). Cardiac rhythm disturbances, particularly atrial fibrillation and other arrhythmias, may develop as a result of systemic inflammation, electrolyte imbalances, and autonomic dysfunction. Some patients may report chest discomfort or pressure, although this is less specific than in ischemic heart disease. Clinically, septic cardiomyopathy leads to fatigue, weakness, and signs of heart failure, such as cool extremities, oliguria, and pulmonary edema. Diagnostic investigations often reveal reduced ejection fraction, biventricular dilatation, and impaired diastolic function on echocardiography, alongside elevated troponins and BNP/NT-proBNP, which suggest myocardial injury and ventricular strain but are not specific to sepsis(31). Collectively, these symptoms highlight the profound but often reversible myocardial depression that characterizes cardiac involvement in sepsis.

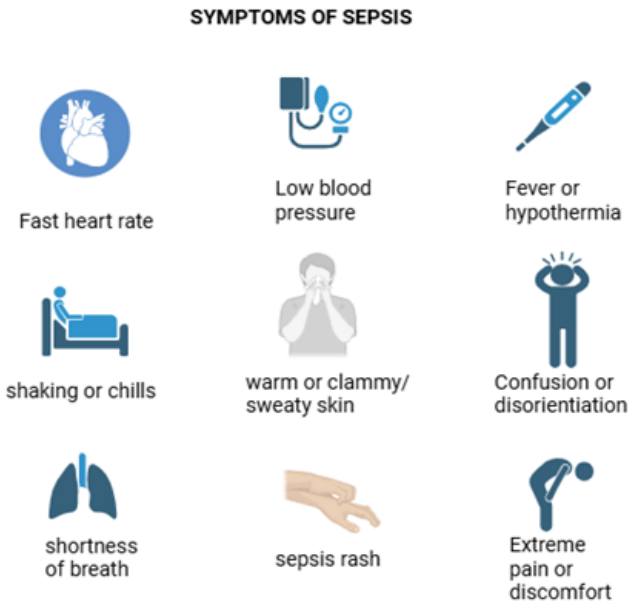

FIG No: 1 SYMPTOMS OF SEPSIS.

5. Pathophysiology of Sepsis-Induced Cardiac Dysfunction

5.1 Inflammatory cytokines (TNF-α, IL-1β, IL-6 → depress myocardial contractility):

Proinflammatory cytokines such as TNF-α, IL-1β, and IL-6 are major mediators in septic cardiomyopathy(32). TNF-α and IL-1β directly impair myocardial contractility by altering calcium handling and depressing β-adrenergic signaling pathways. These cytokines also induce secondary mediators, including nitric oxide, which amplify their cardiodepressant effects. Studies have shown that recombinant TNF-α reproduces the hemodynamic features of septic shock, including reduced ejection fraction and hypotension. In both animal models and human sepsis, high levels of TNF-α and IL-1β correlate with myocardial depression and poor outcomes. Although anti-TNF therapies improve cardiovascular parameters, they have not consistently reduced mortality, suggesting a multifactorial process. IL-6 further sustains inflammation and augments cardiac dysfunction by promoting systemic inflammatory response and myocardial depressant factors(33). Together, these cytokines form part of a "cytokine storm," driving reversible but often severe myocardial depression during septic shock **Fig : 2** .

5.2 Nitric oxide overproduction (vasodilation, hypotension, impaired contractility):

During sepsis, the expression of inducible nitric oxide synthase (iNOS) in the myocardium leads to excessive nitric oxide (NO) production. NO causes profound vasodilation and systemic hypotension, hallmarks of septic shock. Beyond vascular effects, high NO levels also impair myocardial contractility by modifying calcium sensitivity of myofilaments and interacting with reactive oxygen species (ROS) to form peroxynitrite, a cytotoxic radical that damages cardiomyocytes(34). While constitutive isoforms of NO (eNOS, nNOS) have physiological roles in regulating vascular tone and cardiac function, uncontrolled iNOS-derived NO overwhelms protective mechanisms. Inhibitors of NO pathways, such as methylene blue or guanylate cyclase inhibitors, transiently restore blood pressure and contractility, but without clear survival benefits. This paradox highlights the dual role of NO as both protective at baseline and deleterious when dysregulated. In septic shock, its overproduction contributes to vasoplegia, impaired coronary perfusion, and decreased myocardial responsiveness to catecholamines.

5.3 Mitochondrial dysfunction (reduced ATP, impaired calcium handling, myocardial energy failure):

Mitochondria are crucial for cardiac energy supply and calcium regulation, and their dysfunction plays a central role in sepsis-induced myocardial depression(35). In septic hearts, activities of mitochondrial respiratory chain complexes I and II are markedly reduced, impairing ATP production. Proinflammatory mediators such as NO, TNF-α, and IL-1β, along with ROS, disrupt oxidative phosphorylation and promote mitochondrial permeability transition, further compromising energy generation. Damaged mitochondria also release DAMPs such as mitochondrial DNA, cytochrome c, and ROS, which amplify inflammatory responses and tissue injury. The resultant "cytopathic hypoxia" reflects impaired oxygen utilization despite adequate oxygen supply, leading to contractile failure. Additionally, altered calcium handling within mitochondria disturbs excitation–contraction coupling, impairing systolic and diastolic function(36). Some studies suggest that myocardial dysfunction in sepsis may represent a protective "hibernating state," reducing energy demand during stress. However, persistent mitochondrial injury contributes to long-term dysfunction and higher mortality in septic shock patients.

5.4 Endothelial dysfunction (leaky vessels, impaired coronary perfusion):

Endothelial cells are critical regulators of vascular tone, permeability, and coagulation, and their dysfunction in sepsis has widespread cardiac consequences. Inflammatory cytokines and ROS disrupt endothelial integrity, leading to increased vascular permeability and interstitial edema. This reduces effective circulating volume and impairs preload, limiting cardiac output(37). Endothelial injury also alters nitric oxide bioavailability, resulting in disordered coronary blood flow regulation and impaired perfusion of myocardial tissue. Endothelial dysfunction further contributes to microvascular thrombosis through activation of coagulation pathways, worsening perfusion mismatch. The resultant myocardial edema and impaired oxygen delivery exacerbate diastolic and systolic dysfunction. Moreover, endothelial cells produce vasoactive mediators, such as endothelin and prostacyclin, whose imbalance contributes to vasoplegia and hypoperfusion. These processes collectively weaken myocardial resilience in septic shock, reducing adaptive capacity and worsening patient prognosis.

5.5 Microcirculatory impairment (mismatch between oxygen delivery and demand):

In septic shock, global coronary flow is often preserved or even increased, yet microcirculatory dysfunction leads to heterogeneous perfusion within the myocardium. Capillary shunting, endothelial swelling, and fibrin deposition disrupt local oxygen delivery, producing regions of ischemia amidst adequate macrocirculation. This mismatch between oxygen supply and demand explains why elevated lactate levels persist despite apparently normal hemodynamic parameters. Microvascular injury also facilitates neutrophil infiltration, edema, and oxidative stress, further impairing cardiomyocyte function(38). Studies show that troponin elevations in sepsis reflect microcirculatory ischemia rather than global hypoperfusion. The impaired autoregulation of myocardial microcirculation resembles patterns seen in peripheral tissues, highlighting systemic endothelial and microvascular injury. Ultimately, microcirculatory impairment limits oxygen extraction, perpetuates metabolic failure, and contributes to contractile dysfunction, even when systemic oxygen delivery appears sufficient.

5.6 Oxidative stress & apoptosis of cardiomyocytes:

Reactive oxygen species (ROS) and reactive nitrogen species (RNS) accumulate during sepsis as a result of cytokine activation, mitochondrial dysfunction, and excessive nitric oxide production. These radicals damage cellular membranes, proteins, and DNA within cardiomyocytes, leading to impaired excitation–contraction coupling and energy failure. Peroxynitrite, formed by the interaction of NO with superoxide, is particularly cytotoxic, inducing lipid peroxidation and calcium handling defects. In addition to oxidative stress, apoptotic pathways are activated, with mitochondrial release of cytochrome c and activation of caspases driving programmed cell death(39). Extracellular histones and HMGB1 amplify oxidative damage and calcium dysregulation, worsening cardiomyocyte injury. Together, oxidative stress and apoptosis not only cause acute contractile dysfunction but also contribute to long-term structural remodeling and reduced cardiac reserve in sepsis survivors. Antioxidant therapies have shown experimental promise, but clinical benefits remain unproven.

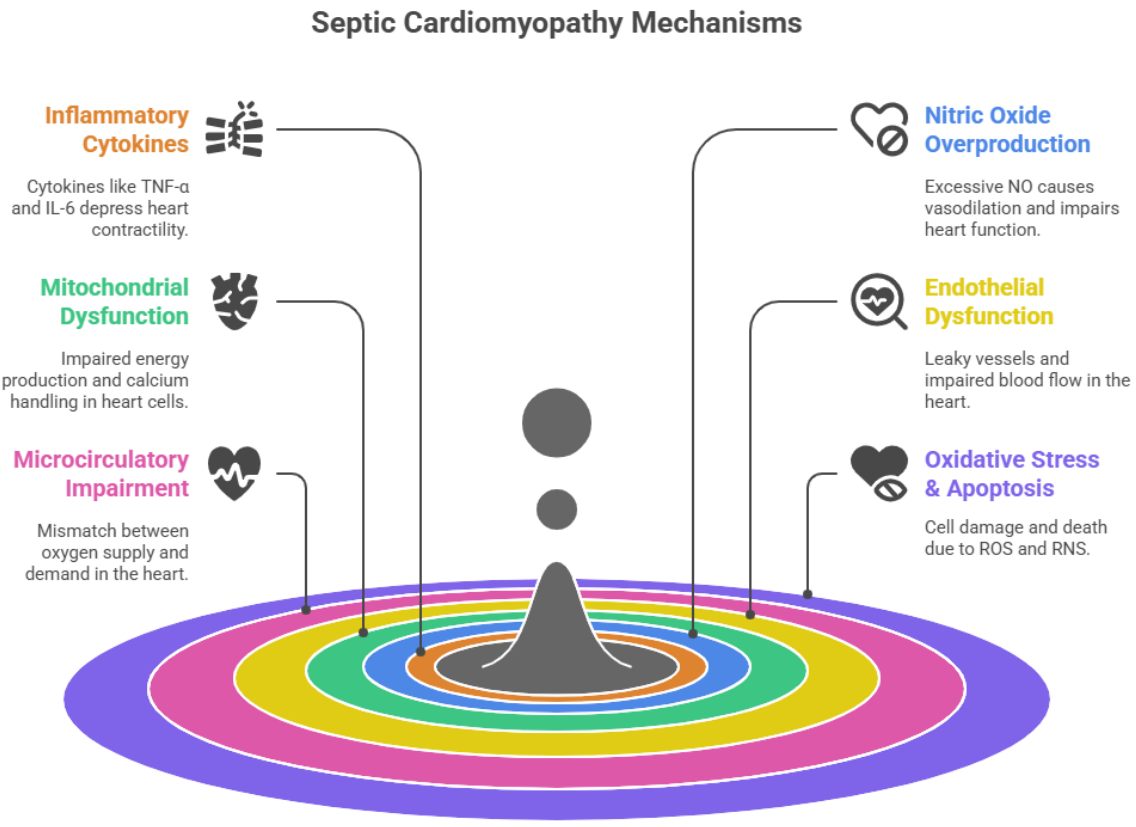

Fig no: 2 septic cardiomyopathy mechanism.

6. Cardiac Manifestations of Sepsis

6.1 Septic Cardiomyopathy

A hallmark of sepsis, septic cardiomyopathy is a reversible, global biventricular dysfunction. Unlike chronic cardiomyopathies, it develops acutely during infection and resolves within 7–10 days in survivors. It is driven by inflammatory cytokines, nitric oxide, mitochondrial dysfunction, and impaired calcium handling in cardiomyocytes, which collectively depress contractility and blunt responsiveness to catecholamines **Fig 2** . Clinically, patients show low ejection fraction (LVEF <45%), ventricular dilation, and low stroke volume, despite often elevated cardiac output. Importantly, the dysfunction represents myocardial stunning rather than irreversible necrosis. Its presence, however, signals a higher mortality risk, emphasizing its prognostic importance(40).

6.2 Left Ventricular Dysfunction

Systolic and diastolic impairment of the left ventricle (LV) is a frequent manifestation of sepsis.

6.2.1 Systolic dysfunction:

In septic patients, systolic LV dysfunction presents as reduced contractility and a decline in ejection fraction, often accompanied by ventricular dilatation. This phenomenon is paradoxical, as septic patients may still display a hyperdynamic circulation with elevated cardiac output, yet contractile reserve is impaired. Cytokines such as TNF-α and IL-1β, nitric oxide, and mitochondrial injury directly suppress contractility. Troponin elevations, observed in many septic patients, reflect either reversible myocyte injury or microcirculatory ischemia rather than classic myocardial infarction(41).

6.2.2 Diastolic dysfunction:

Diastolic abnormalities are also common and include impaired relaxation and increased ventricular stiffness. Elevated filling pressures and delayed relaxation impair stroke volume and worsen pulmonary congestion. Echocardiography often reveals reduced tissue Doppler velocities and abnormal transmitral flow patterns. Unlike systolic dysfunction, which is often transient, diastolic dysfunction may persist longer and has been linked with poorer outcomes(42). Together, these impairments lead to reduced LV stroke volume, impaired systemic perfusion, and inadequate oxygen delivery to tissues, despite aggressive fluid resuscitation and vasopressor therapy **Fig.3**.

6.3 Right Ventricular Dysfunction

The right ventricle (RV) is particularly vulnerable during sepsis due to pulmonary hypertension caused by ARDS, hypoxia, microthrombi, and ventilator-induced pressures(43).The thin-walled RV is not designed for high afterload, leading to dilatation, impaired function, and worsening systemic hypoperfusion. This dysfunction complicates fluid management and predisposes to hemodynamic instability(44).

6.4 Arrhythmias

Arrhythmias are common in sepsis due to inflammation, autonomic imbalance, electrolyte disturbances, and catecholamine surges. Atrial fibrillation (AF) is the most frequent, affecting up to 25% of septic shock patients and worsening hemodynamic instability. Less common are ventricular tachyarrhythmias, linked with electrolyte derangements and ischemia, and bradyarrhythmias, caused by autonomic dysfunction or conduction block. Management focuses on correcting triggers and applying rate or rhythm control.

6.5 Myocardial Ischemia (Type II MI)

Unlike Type I MI, sepsis usually causes Type II myocardial infarction, driven by oxygen supply–demand imbalance and microcirculatory dysfunction. Contributing factors include tachycardia, fever, hypotension, hypoxemia, and anemia. Endothelial injury and impaired coronary autoregulation worsen perfusion. Troponin elevation is common but reflects reversible injury rather than thrombosis. Elevated troponins strongly predict adverse outcomes, making them both diagnostic and prognostic(45).

6.6 Clinical Implications and Outcomes

Cardiac dysfunction in sepsis complicates fluid resuscitation and vasopressor therapy, as impaired contractility reduces treatment effectiveness. Echocardiography is critical for differentiating septic cardiomyopathy from primary cardiac disease. Biomarkers like troponin and natriuretic peptides enhance diagnosis and risk prediction. Current therapy remains supportive—including antibiotics, fluids, vasopressors, and inotropes—while targeted interventions against inflammatory mediators and mitochondrial dysfunction are still under study. Despite reversibility, septic cardiomyopathy carries a 40–50% mortality rate, and survivors often experience reduced exercise capacity, arrhythmias, and impaired quality of life(46).

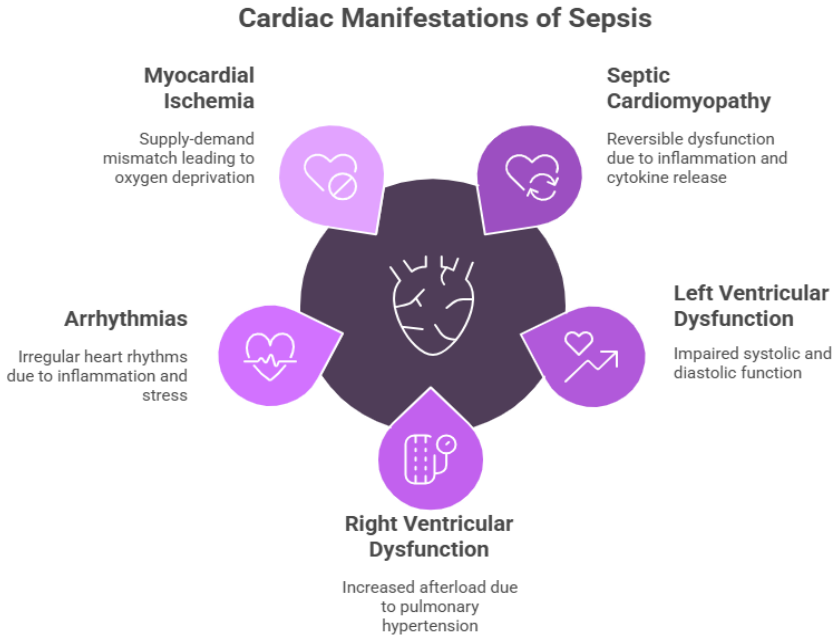

Fig. no: 3 cardiac Manifestations of Sepsis.

7. Diagnostic Approaches

7.1 Clinical Features

Cardiac dysfunction in sepsis often manifests through a cluster of systemic signs that reflect impaired perfusion and hemodynamic compromise. The most prominent clinical feature is hypotension(47), which arises from systemic vasodilation, capillary leakage, and reduced myocardial contractility. Despite aggressive fluid resuscitation, blood pressure frequently remains low, requiring vasopressor support to maintain adequate tissue perfusion. Tachycardia is another common finding, functioning as a compensatory mechanism to sustain cardiac output in the face of low stroke volume. However, persistent tachycardia can be deleterious, increasing myocardial oxygen demand and reducing diastolic filling time, which further compromises cardiac efficiency. Signs of poor perfusion**,** such as cold extremities, mottled skin, and delayed capillary refill are typical indicators of impaired systemic circulation. These changes reflect inadequate oxygen delivery to tissues, which in severe cases progresses to multi-organ dysfunction. Neurological features such as confusion or delirium emerge due to cerebral hypoperfusion and systemic inflammation. Similarly, oliguria, or reduced urine output, signals compromised renal perfusion and the onset of acute kidney injury. Taken together, these clinical features highlight the systemic impact of septic shock on the cardiovascular system and emphasize the need for early recognition and intervention **Fig. 4** .

7.2 Biomarkers

Troponins

Cardiac troponins are highly sensitive markers of myocardial injury, and their elevation is frequently observed in septic patients. Unlike classic acute coronary syndromes, where troponin elevation usually reflects coronary occlusion, in sepsis the mechanism is multifactorial. It may result from microvascular ischemia, cytokine-induced cardiotoxicity, mitochondrial dysfunction, or demand–supply mismatch, rather than plaque rupture. Elevated troponin levels in septic patients correlate with the presence of septic cardiomyopathy and predict higher mortality rates(48). Importantly, troponin elevation in sepsis should not automatically be interpreted as an acute coronary syndrome, though it warrants careful evaluation to exclude concomitant cardiac pathology. Clinically, troponin measurement serves as a valuable prognostic tool, helping stratify risk and guide the intensity of monitoring and therapy.

BNP and NT-proBNP

Brain natriuretic peptide (BNP) and its inactive precursor NT-proBNP are markers of myocardial wall stress and ventricular dysfunction. In sepsis, their levels are often elevated due to ventricular dilatation, impaired relaxation, and increased filling pressures. While these markers are not specific to septic cardiomyopathy, they provide additional evidence of cardiac involvement when interpreted alongside clinical and imaging findings. Elevated BNP/NT-proBNP levels are associated with worse outcomes and may help identify patients at risk of hemodynamic instability(49). Together with troponins, natriuretic peptides offer complementary insights into myocardial injury and stress, supporting a more comprehensive assessment of cardiac function during sepsis.

Echocardiography

Echocardiography is the cornerstone tool for diagnosing and monitoring septic cardiomyopathy. It provides non-invasive, real-time insights into cardiac structure and function, making it indispensable in critically ill patients(50).

The most consistent echocardiographic finding in septic cardiomyopathy is a reduced left ventricular ejection fraction (LVEF), often accompanied by global hypokinesia rather than regional wall motion abnormalities. This distinguishes septic cardiomyopathy from ischemic heart disease, where dysfunction is typically localized. Additionally, septic patients frequently display ventricular dilatation, which acts as a compensatory mechanism to maintain stroke volume despite depressed contractility. Right ventricular (RV) dysfunction is also common, often caused by increased afterload due to pulmonary hypertension, hypoxia, or acute respiratory distress syndrome (ARDS). RV dilatation and impaired contractility worsen systemic perfusion and complicate fluid management strategies. Advanced echocardiographic techniques such as speckle-tracking strain imaging provide a more sensitive assessment of myocardial function. Reductions in global longitudinal strain may identify subclinical dysfunction even when ejection fraction appears preserved. Echocardiography is also invaluable for guiding resuscitation, differentiating septic cardiomyopathy from hypovolemia, and ruling out alternative cardiac causes of instability, such as tamponade or valvular disease.

7.3 Advanced Imaging

Cardiac MRI

Cardiac magnetic resonance imaging (MRI) is a powerful modality for characterizing myocardial tissue and detecting structural or functional changes not visible on echocardiography. In septic cardiomyopathy, cardiac MRI may reveal myocardial edema, diffuse hypokinesia, and reversible ventricular dysfunction, reflecting inflammatory and metabolic alterations. Unlike myocarditis or ischemic cardiomyopathy, septic cardiomyopathy rarely demonstrates late gadolinium enhancement, indicating the absence of significant fibrosis or necrosis. These findings support the notion that septic cardiomyopathy is primarily a functional and reversible process rather than a structural injury(51). However, the use of MRI in critically ill septic patients is limited by feasibility, patient stability, and logistical constraints.

PET-CT

Positron emission tomography–computed tomography (PET-CT) provides unique insights into myocardial metabolism and inflammation. Using tracers such as fluorodeoxyglucose (FDG), PET-CT can detect altered glucose uptake in septic myocardium, consistent with mitochondrial dysfunction and inflammatory activity. This imaging approach highlights the metabolic derangements underlying septic cardiomyopathy and may prove useful in future research or in selected clinical cases where differentiation from other cardiomyopathies is essential(52). Despite its promise, PET-CT is not widely used in routine practice due to cost, complexity, and limited availability in intensive care settings.

Scoring Systems

Scoring systems provide structured and standardized methods for assessing disease severity in sepsis, offering valuable support in prognostication and clinical decision-making. The Sequential Organ Failure Assessment (SOFA) score evaluates dysfunction across six organ systems, with the cardiovascular component reflecting the severity of hypotension and vasopressor requirements; higher SOFA scores are strongly associated with increased mortality, and septic cardiomyopathy often contributes to elevated cardiovascular subscores. The Quick SOFA (qSOFA) score, although less comprehensive, serves as a practical bedside tool based on three simple criteria—systolic blood pressure ≤100 mmHg, respiratory rate ≥22/min, and altered mentation—helping to rapidly identify patients at higher risk who require urgent intervention. Furthermore, combining these scoring systems with cardiac-

specific assessments, such as echocardiographic findings and biomarkers like troponins and BNP, enhances both diagnostic accuracy and prognostic value. Patients with elevated cardiac biomarkers and echocardiographic evidence of myocardial dysfunction, alongside high SOFA scores, typically exhibit particularly poor outcomes. This integrated approach allows for more precise risk stratification, supports individualized treatment strategies, and improves consistency in clinical research comparison(53).

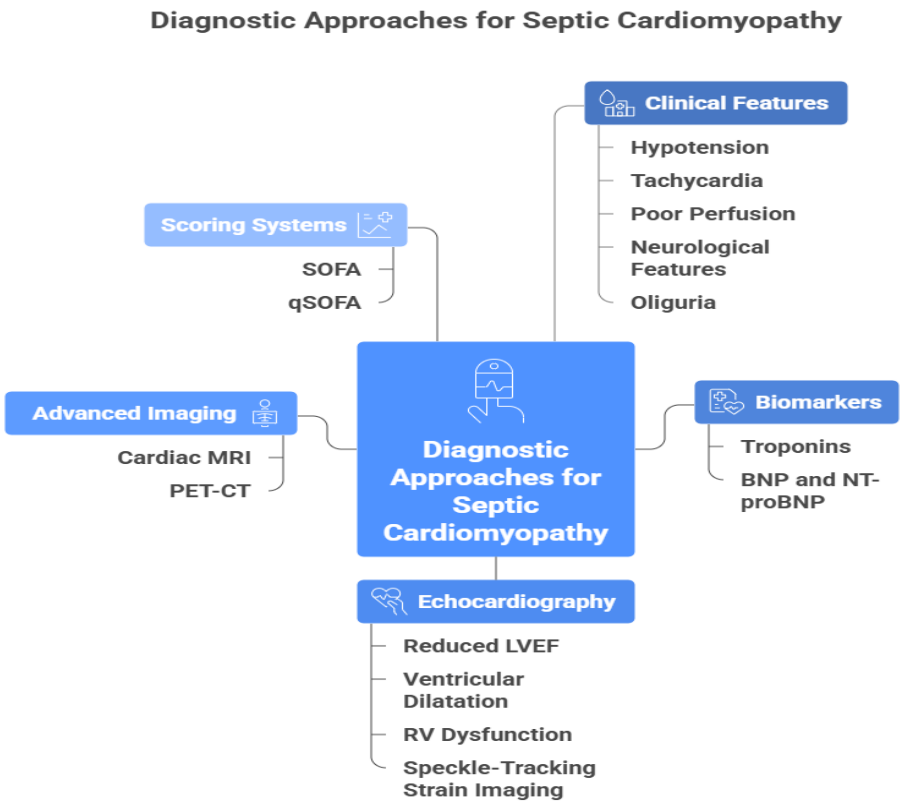

Fig.no: 4 Diagnostic Approaches for Septic Cardiacmyopathy

8. Management Strategies

8.1 Hemodynamic Support

8.1.1 Careful Fluid Resuscitation

The cornerstone of early sepsis management is adequate hemodynamic stabilization through fluid resuscitation. In septic shock, profound vasodilation and capillary leak lead to intravascular volume depletion, making fluids essential for restoring perfusion(53). However, in patients with septic cardiomyopathy or pre-existing cardiac disease, aggressive fluid administration may worsen pulmonary edema, increase filling pressures, and impair

myocardial function. Current guidelines advocate for a conservative and individualized fluid strategy, often beginning with 30 mL/kg of crystalloids, followed by frequent reassessment using dynamic parameters such as stroke volume variation, passive leg raise tests, and echocardiographic measurements(54). The goal is to optimize preload without precipitating fluid overload, striking a balance between improving tissue perfusion and preventing secondary cardiac injury.

8.1.2 Vasopressors

When hypotension persists despite adequate fluid resuscitation, vasopressors are required to maintain mean arterial pressure (MAP) ≥65 mmHg. Norepinephrine is the first-line agent, as it provides potent α-adrenergic vasoconstriction with modest β-adrenergic effects, raising systemic vascular resistance without excessively increasing heart rate(55). Clinical studies consistently demonstrate norepinephrine's superiority over dopamine, with lower rates of arrhythmias and improved survival. Vasopressin is considered a second-line agent, often added to norepinephrine in refractory shock to reduce catecholamine requirements **Fig. 5**. Low-dose vasopressin targets vasoplegia through non-adrenergic pathways, improving vascular tone without additional tachycardia(56). Other vasopressors, such as epinephrine, are reserved for selected cases but are associated with increased lactate levels and arrhythmogenic potential. The choice and titration of vasopressors require continuous hemodynamic monitoring, emphasizing the dynamic and individualized nature of therapy.

8.1.3 Inotropes

In cases where septic shock is complicated by persistent low cardiac output despite adequate fluid resuscitation and vasopressor support, inotropes are indicated. Dobutamine is the most commonly used inotrope, enhancing myocardial contractility through β-adrenergic stimulation(57). It can improve stroke volume and oxygen delivery in patients with septic cardiomyopathy, but must be used cautiously due to the risk of tachyarrhythmias and increased myocardial oxygen demand. Alternative inotropes such as milrinone may be considered, particularly in patients with right ventricular dysfunction, though hypotension is a limiting factor. The decision to initiate inotropic therapy is guided by echocardiography, hemodynamic monitoring, and biomarkers of tissue perfusion such as lactate clearance.

8.1.4 Mechanical Support

In patients with refractory septic shock and severe myocardial dysfunction, mechanical circulatory support (MCS) may serve as a bridge to recovery when medical therapy fails.

Veno-arterial ECMO offers full cardiopulmonary support and is increasingly used in severe septic cardiomyopathy, though it carries risks such as bleeding, thrombosis, and infection. The Impella device, while less common in sepsis, can unload the left ventricle and maintain perfusion in cases of severe dysfunction, and intra-aortic balloon pump (IABP) may provide limited benefit through afterload reduction and improved coronary perfusion(58). Overall, MCS is a rescue strategy reserved for specialized centers with expertise and multidisciplinary management.

8.2 Antimicrobial Therapy

Prompt initiation of effective antimicrobial therapy is central to all sepsis management and directly impacts cardiac outcomes(59). Delays in antibiotic administration correlate with higher mortality, as ongoing infection perpetuates systemic inflammation, cytokine release, and myocardial injury. Initial therapy should be broad-spectrum, covering both Gram-positive and Gram-negative pathogens, and tailored to local resistance patterns and infection sources. Once culture and sensitivity results are available, therapy should be de-escalated to narrower-spectrum agents to reduce the risk of resistance and toxicity. Source control, including drainage of abscesses, removal of infected devices, or surgical intervention, is equally critical for infection eradication(60). For cardiac patients, special attention is needed to minimize nephrotoxic and cardiotoxic drug interactions, particularly when concomitant organ dysfunction is present. Effective infection control not only halts the progression of septic shock but also allows myocardial function to recover, underscoring the interdependence of antimicrobial therapy and cardiac outcomes.

8.3 Adjunctive Therapies

8.3.1 Beta-Blockers

The role of beta-blockers in septic shock is an evolving area of research. Sepsis is associated with a hyperadrenergic state characterized by elevated catecholamines, which contribute to tachycardia, arrhythmias, and increased myocardial oxygen demand. Experimental and early clinical studies suggest that short-acting beta-blockers such as esmolol can reduce heart rate, improve diastolic filling, enhance stroke volume, and potentially reduce mortality(61). By modulating sympathetic overdrive, beta-blockers may restore a more physiologic hemodynamic profile. However, careful titration is essential to avoid excessive bradycardia or hypotension. While promising, beta-blocker therapy in septic shock remains experimental and requires further validation in large randomized trials.

8.3.2 Antioxidants and Mitochondrial Protectors

Oxidative stress and mitochondrial dysfunction are central to the pathogenesis of septic cardiomyopathy. Excessive production of reactive oxygen and nitrogen species damages cardiomyocytes and impairs ATP generation(62). This has spurred interest in antioxidants and mitochondrial protectors as adjunctive therapies. Agents such as N-acetylcysteine, coenzyme Q10, and mitochondria-targeted antioxidants (e.g., MitoQ) have shown potential in experimental models by reducing oxidative damage and preserving mitochondrial function. Similarly, drugs that stabilize mitochondrial membranes or enhance biogenesis may improve energy metabolism and contractility. Despite encouraging preclinical findings, translation into clinical benefit remains unproven, and ongoing trials are investigating their therapeutic potential.

8.3.3 Immunomodulators and Corticosteroids

The use of **immunomodulatory agents and corticosteroids** in sepsis remains highly debated. Corticosteroids, particularly hydrocortisone, are sometimes employed in refractory septic shock to reduce vasopressor requirements by addressing relative adrenal insufficiency. Their benefits on cardiac function, however, are less clear. Some studies suggest modest improvements in hemodynamics, while others report no significant mortality benefit(63). Immunomodulators such as anti-TNF agents, IL-6 inhibitors, and other biologics have shown promise in targeting the cytokine storm underlying septic cardiomyopathy. Yet, clinical trials have yielded mixed results, with concerns about increased susceptibility to secondary infections. Thus, while immunomodulation holds theoretical appeal, its routine use in septic cardiomyopathy remains limited to research settings.

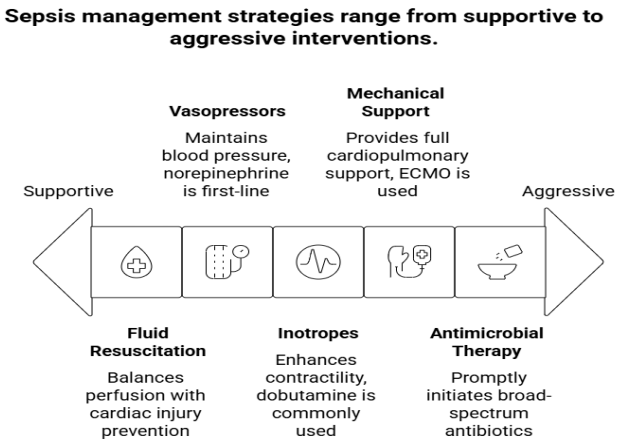

Fig.no 5: Sepsis management strategies

9. Sepsis in Special Cardiac Populations

9.1 Pre-existing Heart Failure

Patients with pre-existing heart failure (HF) are among the most vulnerable when sepsis develops. Heart failure is marked by impaired contractility or diastolic dysfunction, reduced cardiac reserve, and neurohormonal activation. The vasodilation, capillary leakage, and increased metabolic demands of sepsis further compromise cardiovascular function(64). Fluid resuscitation, a cornerstone of sepsis treatment, becomes particularly challenging in this group: while aggressive early fluids are needed to restore perfusion, excessive volumes may precipitate pulmonary edema and respiratory failure. Careful, individualized fluid management guided by echocardiography or dynamic assessments is essential. Arrhythmias such as atrial fibrillation and ventricular tachyarrhythmias are also more common due to sepsis-related sympathetic activation, electrolyte imbalances, and inflammation(65). These further destabilize hemodynamics, and outcomes are generally poorer in septic patients with HF, reflecting their limited compensatory capacity.

9.2 Coronary Artery Disease

Patients with coronary artery disease (CAD) face a different but equally serious set of challenges. Sepsis increases myocardial oxygen demand while simultaneously reducing oxygen delivery through hypotension, anemia, and hypoxemia, often leading to Type II myocardial infarction. Microvascular dysfunction and endothelial injury further impair tissue-level perfusion. Elevated troponins are frequent, but their interpretation is complex, as they may indicate demand–supply mismatch rather than acute thrombosis(66). Importantly, CAD patients are less able to increase coronary blood flow during stress, leaving them more vulnerable to ischemia. Management must balance standard sepsis protocols with measures to protect coronary perfusion, particularly cautious vasopressor use. Mortality and complication rates remain higher in septic patients with CAD than in those without.

9.3 Post–Cardiac Surgery Patients

Post–cardiac surgery patients are another high-risk population. These individuals are predisposed to infection due to prolonged hospitalization, surgical wounds, and invasive monitoring. When sepsis occurs, it amplifies systemic inflammation, coagulation abnormalities, and myocardial depression, severely impairing recovery(67). Distinguishing between sepsis and normal post-operative inflammatory responses can be difficult, delaying diagnosis. Once established, sepsis in this setting significantly increases ICU stay, mortality,

and long-term complications such as renal failure, underscoring the importance of preventive strategies including strict asepsis and early infection control.

9.4 Patients with Cardiac Devices (ICD, Pacemakers, LVADs)

Patients with cardiac devices, such as pacemakers, implantable cardioverter-defibrillators (ICDs), or left ventricular assist devices (LVADs), face additional risks. These devices can act as sources of infection, supporting bacterial colonization and biofilm formation(68). Infections may progress from local sites to systemic sepsis or endocarditis, and in LVAD patients, driveline infections are a major cause of septic shock. Management often requires both antibiotics and device removal, but this is technically challenging and risky in unstable patients. Outcomes are particularly poor, especially for LVAD recipients awaiting transplantation.

9.5 Elderly patients

Elderly patients form another vulnerable group, as aging reduces cardiac reserve, increases arterial stiffness, and impairs diastolic relaxation. They often carry multiple comorbidities such as diabetes, CAD, and chronic kidney disease, which compound vulnerability(68). Sepsis-induced myocardial depression, arrhythmias, and hypotension are less well tolerated, leading to rapid progression to multi-organ failure. Atypical presentations, such as confusion without fever, delay recognition and treatment. Prognosis is particularly poor, with higher mortality and significant long-term functional decline among survivors.

10. Challenges and Controversies

10.1 Distinguishing Septic Cardiomyopathy from Acute Coronary Syndrome

A major diagnostic challenge is differentiating SCM from acute coronary syndrome (ACS). Both can present with chest discomfort, hemodynamic instability, elevated troponins, and reduced ventricular function(69). In sepsis, however, troponin elevations are often due to cytokine-mediated injury, microvascular dysfunction, and Type II myocardial infarction (supply–demand mismatch) rather than the plaque rupture typical of Type I ACS. Echocardiography may help: SCM usually shows global biventricular hypokinesia with dilated ventricles, whereas ACS often reveals regional wall motion abnormalities. Yet image quality in critically ill patients is often limited. Misclassification has serious implications—overdiagnosis of ACS risks unnecessary invasive procedures, while underdiagnosis delays reperfusion therapy(70). Currently, clinicians must rely on clinical judgment, serial imaging, and dynamic biomarker trends, reflecting a major gap in sepsis cardiology.

10.2 Lack of Specific Biomarkers

Another controversy is the absence of reliable biomarkers for SCM. Troponins and natriuretic peptides (BNP, NT-proBNP) indicate myocardial injury or strain but lack specificity, as elevations may stem from sepsis itself or comorbid conditions like chronic kidney disease. Novel candidates, including pro-adrenomedullin, sST2, and GDF-15, show promise but remain experimental. The dynamic and reversible nature of SCM complicates biomarker interpretation, limiting their role in early recognition, risk stratification, and monitoring therapy(71). This lack also hampers clinical trials, as inconsistent diagnostic criteria reduce comparability and enrollment accuracy.

10.3 Limited Clinical Trial Evidence

Progress is further constrained by the scarcity of randomized controlled trials (RCTs) focused on SCM. Most evidence comes from observational cohorts or post hoc analyses, with limited statistical power. Investigations into β-blockers, antioxidants, and immunomodulators show physiologic benefits but inconsistent outcomes. The heterogeneity of septic populations—different infection sources, comorbidities, and treatment responses—further reduces generalizability(72). Ethical constraints also limit invasive monitoring. Consequently, many therapeutic strategies rely on expert consensus rather than robust trial evidence**.**

10.4 Fluid Resuscitation vs. Pulmonary Edema

Early aggressive fluid resuscitation is central to sepsis care, but in patients with cardiac disease or SCM, this creates controversy. Excess fluids risk pulmonary edema, RV overload, and impaired gas exchange, while inadequate resuscitation worsens tissue hypoperfusion. Static measures like central venous pressure (CVP) are unreliable; dynamic tools such as passive leg raise, stroke volume variation, and echocardiography provide better guidance but require expertise(73). The debate centers on whether restrictive fluid strategies should replace standard aggressive protocols in high-risk patients. Emerging data favor individualized, goal-directed therapy, but guidelines remain generalized.

10.5 Additional Controversies

Vasopressors and inotropes represent another area of debate. While norepinephrine is the first-line vasopressor, the roles of vasopressin, epinephrine, and dobutamine are controversial due to risks of arrhythmia and uncertain effects on coronary perfusion. Similarly, adjunctive therapies like β-blockers, immunomodulators, and mitochondrial protectors show potential but lack strong evidence. The prognosis and reversibility of SCM remain contentious.

Although often described as reversible within 7–10 days, many survivors develop persistent cardiac dysfunction, reduced exercise tolerance, and long-term cardiovascular risk(74). Whether this represents incomplete recovery, unmasking of pre-existing disease, or new pathology triggered by sepsis remains unclear.

11. Future Perspectives

11.1 Precision Medicine

The application of precision medicine offers a promising approach to septic cardiomyopathy. Current management typically follows standardized sepsis protocols, such as aggressive fluid resuscitation and vasopressor therapy, but these strategies may not suit all patients. Sepsis is a heterogeneous syndrome shaped by genetic variation, comorbidities, pathogen type, and host immune responses, all of which influence cardiac involvement. While some patients develop severe myocardial depression, others retain preserved cardiac function. Genomic and transcriptomic studies are now identifying host-response patterns that could stratify patients into specific endotypes with distinct pathophysiology. For example, those with strong pro-inflammatory signatures may benefit from immunomodulation, while immunosuppressed patients may require stimulatory therapies. Precision medicine could also help tailor fluid resuscitation in patients with pre-existing cardiac disease, minimizing the risk of pulmonary edema or ischemia. Ultimately, integrating genomic, proteomic, and metabolomic data may allow clinicians to predict which patients are most vulnerable to septic cardiomyopathy and guide them toward the most effective therapies.

11.2 Novel Biomarkers

One of the greatest limitations in current practice is the absence of specific biomarkers for septic cardiomyopathy. Traditional markers such as troponins and natriuretic peptides are widely used but lack specificity, as they are elevated in a range of cardiac and systemic conditions. Emerging research has identified novel biomarkers with greater diagnostic and prognostic potential. Circulating microRNAs (miRNAs), particularly miR-21 and miR-146a, have shown strong links to inflammation, apoptosis, and myocardial dysfunction during sepsis. Their stability and disease-specific expression make them attractive for clinical use. Similarly, mitochondrial biomarkers such as mitochondrial DNA (mtDNA), cytochrome c, and oxidative phosphorylation indicators offer insight into the central role of energy failure in septic cardiomyopathy. Elevated mtDNA levels, in particular, correlate with worse outcomes. In the future, multi-marker panels combining miRNAs, mitochondrial indicators, and

classical cardiac proteins may allow earlier detection, improved risk stratification, and better monitoring of treatment responses.

11.3 Artificial Intelligence and Big Data

The rapid growth of electronic health records, bedside monitoring devices, and large clinical databases has enabled the integration of AI and big data into sepsis care. Machine learning algorithms are capable of processing complex datasets—including laboratory values, hemodynamic parameters, imaging, and biomarker fluctuations—to predict septic cardiomyopathy before overt clinical deterioration. For example, AI can identify subtle changes in heart rate variability, echocardiographic strain, or biomarker trends that precede myocardial dysfunction. Predictive models may help stratify patients into risk categories, optimizing the timing and intensity of interventions. AI-assisted echocardiography also holds promise for automated detection of ventricular dysfunction, particularly in resource-limited settings. While challenges such as data standardization, interoperability, and ethical concerns persist, AI has the potential to transform sepsis cardiology by enabling personalized, real-time decision-making.

11.4 Innovative Therapies

Beyond diagnostics, several therapeutic innovations are being investigated. Stem cell therapy, particularly with mesenchymal stem cells (MSCs), has shown preclinical benefits through paracrine effects that reduce apoptosis, dampen inflammation, promote angiogenesis, and enhance mitochondrial function. Immunotherapy is another exciting frontier, aimed at regulating the dysregulated immune response that drives myocardial depression. While monoclonal antibodies against cytokines like TNF-α, IL-1β, and IL-6 have shown mixed outcomes, checkpoint modulators such as PD-1/PD-L1 inhibitors may help restore immune balance. Additionally, mitochondrial protection strategies directly address the energy failure central to septic cardiomyopathy. Antioxidants like N-acetylcysteine, mitochondria-targeted drugs such as MitoQ and SS-31, and metabolic modulators that enhance mitochondrial biogenesis or efficiency have demonstrated promise in preclinical studies. Together, these therapies may one day move treatment from supportive care toward targeted, disease-modifying interventions**.**

CONCLUSION

Sepsis represents a global health crisis, and its impact on the heart highlights the intricate relationship between systemic infection, immune dysregulation, and cardiovascular function.

Septic cardiomyopathy has emerged as a critical determinant of outcomes, characterized by reversible yet often fatal myocardial depression. Its prevalence—affecting up to half of septic patients—underscores the need for heightened awareness, early detection, and tailored management strategies. The burden is particularly high among elderly patients, those with pre-existing cardiac conditions, and populations in resource-limited settings, where timely intervention remains a challenge. The pathophysiological complexity of septic cardiomyopathy involves multiple overlapping mechanisms: inflammatory cytokine storms, nitric oxide overproduction, mitochondrial dysfunction, endothelial injury, microcirculatory impairment, oxidative stress, and apoptosis. Together, these pathways depress myocardial contractility and impair hemodynamic stability. While these changes are often reversible, their occurrence signals higher mortality, prolonged ICU stays, and greater healthcare costs. Clinically, patients present with refractory hypotension, tachycardia, arrhythmias, and features of both systolic and diastolic dysfunction. Troponin and BNP elevations, along with echocardiographic findings of ventricular dilatation and reduced ejection fraction, aid diagnosis, though no biomarker is yet specific to septic cardiomyopathy. Management remains largely supportive. Early infection control with antibiotics and source management is essential, while hemodynamic stabilization requires careful titration of fluids, vasopressors, and inotropes. Advanced therapies such as ECMO offer life-saving potential in refractory cases, but their use is limited to specialized centers. Adjunctive strategies—including β-blockers, antioxidants, mitochondrial protectors, and immunomodulatory agents—show promise in experimental models but lack robust clinical validation. This therapeutic uncertainty reflects broader challenges in the field, including diagnostic ambiguity, limited trial evidence, and heterogeneity among septic patients. Despite these limitations, progress is being made. The integration of echocardiography, biomarker assessment, and risk scores into routine sepsis care has improved recognition of cardiac involvement. Future directions, including precision medicine, novel biomarkers, artificial intelligence, and innovative therapies like stem cell therapy, hold the potential to transform outcomes. Importantly, sepsis survivors require long-term follow-up, as persistent cardiac dysfunction, recurrent arrhythmias, and increased cardiovascular risk are increasingly recognized. septic cardiomyopathy exemplifies the systemic and devastating impact of sepsis on the heart. While often reversible, it remains a major contributor to sepsis-related mortality. Addressing this challenge requires a comprehensive approach that spans early recognition, individualized management, and long-term rehabilitation. Continued research into targeted therapies and improved diagnostics is essential for advancing care. Ultimately, a better understanding of

sepsis-induced cardiac dysfunction will not only improve survival but also enhance quality of life for millions of patients worldwide, reaffirming the need to place the heart at the center of sepsis management and research.

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