REVIEW ARTICLE

Antibiotics in Heart Failure: A Narrative Review

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Abstract

Infections commonly cause acute decompensation and poor outcomes in heart failure (HF), a major global health burden. Patients with heart failure are particularly vulnerable to infections related to the respiratory, urinary, skin, and devices because of systemic inflammation, immune dysfunction, changes in the gut barrier, and repeated exposure to healthcare facilities. The use of empirical antibiotics without confirmation due to overlapping symptoms between infection and heart failure is frequently associated with extended hospital stays, drug toxicity, and antibiotic resistance. While early targeted therapy improves outcomes in confirmed infections, evidence points to limited benefit and possible harm from unnecessary antibiotics. To maximize management in this susceptible population, careful diagnostic evaluation, stewardship, and customized prescribing are crucial.

Keywords: Acute decompensated heart failure, Acute heart failure, Acute respiratory infections, Lower respiratory tract infections, Nonresolving pneumonia.

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Introduction

Heart failure (HF) is becoming a bigger problem for public health around the world. It affects more than 26 million people and is a major cause of hospitalizations and deaths, especially among older people.[1,2] Even though drug- and device-based treatments have come a long way, heart failure (HF) still causes a lot of illness and death, mostly because of recurrent decompensations and other health problems that come with them.

One of the biggest problems for people with HF is that they are more likely to get infections. These infections generally cause acute decompensation, which means longer hospital stays, higher healthcare expenses, and worse clinical outcomes.[3,4] Patients with HF are more likely to have infections because they have a systemic inflammatory state, their important organs do not get enough blood flow, their intestines swell, and their gut permeability changes.[3,5]

Respiratory tract infections, urinary tract infections, and sepsis are frequently observed in HF patients and are commonly treated with empirical or broad-spectrum antibiotics.[4] While antibiotics are essential in managing infections, their widespread and sometimes inappropriate use in HF patients—often without robust diagnostic confirmation—raises several concerns. These include increased risk of antibiotic-associated complications such as *C. difficile* infection, drug interactions with heart failure medications, and the broader public health threat of antimicrobial resistance.[6,7]

Recent clinical guidelines emphasize a careful and evidence-based approach to the management of HF, highlighting the need to differentiate between cardiac and infectious causes of symptoms such as fever, dyspnea, and elevated biomarkers.[1,4] Simultaneously, the global threat of antimicrobial resistance necessitates judicious antibiotic prescribing practices, particularly in vulnerable populations like those with HF.[7]

Given the clinical complexity and overlapping symptomatology in HF, this review aims to explore the use of antibiotics in patients with heart failure, the common infections encountered, diagnostic challenges, and stewardship strategies to optimize care while minimizing harm.

Methods (For Structured Narrative Reviews)

We did a detailed literature review of the existing information on treatment of heart failure, pneumonia, and protocols on management of patients with presentation of clinical features resembling both these conditions but diagnosis yet not confirmed from multiple sources, including research articles and narrative reviews from PubMed, Cochrane, NCBI, NEJM, EJCM, and textbooks (Harrison, Braunwald, etc.). We found the available data based on search keywords such as heart failure, pneumonia, LRTI, ADHF, and based on the collected data, we did a systematic interpretation and tabulated and summarized all the data with the intent to draw a draft that summarizes the available information on the topic. Based on this data, we summarized a working impression on the best management protocol for management of this clinical scenario.

Association between Heart Failure, Infection and Antibiotics

Pathophysiological Link between Heart Failure and Infection

Heart failure is a complex clinical syndrome characterized by impaired cardiac output and systemic congestion, which contributes to a cascade of physiological disturbances that increase susceptibility to infections. Several interrelated mechanisms underlie this heightened vulnerability in HF patients, including immune dysfunction, altered gut permeability, systemic inflammation, and neurohormonal activation.

Chronic heart failure induces a persistent pro-inflammatory state, marked by elevated levels of tumor necrosis factor-alpha (TNF-α), interleukins (e.g., IL-1, IL-6), and other cytokines that compromise immune surveillance and cellular immunity.[3,6] This immune dysregulation impairs the host's ability to respond adequately to bacterial and viral pathogens, increasing the risk and severity of infections.

A particularly critical mechanism is gut translocation. In HF, mesenteric hypoperfusion and intestinal congestion lead to ischemia of the intestinal mucosa and disruption of tight junctions. This results in increased intestinal permeability and translocation of bacteria and endotoxins into systemic circulation—a phenomenon referred to as the "gut hypothesis" of heart failure.[3] Niebauer et al. first demonstrated elevated circulating endotoxins and monocyte activation markers in patients

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with advanced HF, highlighting the role of gut-derived inflammation in disease progression.[8]

Systemic inflammation is also worse when the liver and kidneys are congested and cannot eliminate inflammatory mediators as well. Neurohormonal activation, which happens when the renin–angiotensin–aldosterone system (RAAS) and the sympathetic nervous system are turned up, further lowers immune function, making it easier for infections to spread.[5,6]

Another thing that is often missed is how many times HF patients must go to the hospital, have invasive procedures, and be in healthcare environments, all of which raise their risk of getting infections while they are getting care. These places often have indwelling catheters, IV lines, and a lot of exposure to antibiotics, which makes people more likely to get infections and makes antibiotics less effective.

Patients with heart failure are at a uniquely high risk of getting infections because of the combination of systemic inflammation, immune suppression, mucosal barrier dysfunction, and healthcare exposures. To come up with focused preventative and treatment plans, it is important to understand these pathophysiological linkages.

Common Infections in Heart Failure Patients

People with heart failure are more likely to get several infections because their immune systems are weak, they are often in the hospital, they have invasive operations, and they have other health problems such as diabetes, chronic renal disease, and chronic obstructive pulmonary disease (COPD). These infections generally cause severe decompensation and are linked to more illness, longer hospital admissions, and death.

Respiratory Tract Infections

Respiratory infections, including community-acquired pneumonia (CAP) and hospital-acquired pneumonia (HAP), are among the most frequently encountered infections in patients with HF. The clinical overlap between symptoms of pneumonia and HF—such as dyspnea, fatigue, and crackles—often complicates the diagnosis and may lead to either delayed antibiotic therapy or unnecessary antibiotic use.[9] Pneumonia is a major precipitating factor for acute decompensated heart failure and is associated with worse short- and long-term outcomes.[10]

Urinary Tract Infections

Urinary tract infections (UTIs) are also common in HF patients, especially among the elderly, those with indwelling catheters, and patients with diabetes or fluid overload. They often present with nonspecific symptoms such as confusion or malaise, which may be mistaken for worsening heart failure. Empirical antibiotic therapy is frequently initiated based on urinalysis findings, though asymptomatic bacteriuria remains a diagnostic challenge in this group.[10]

Skin and Soft Tissue Infections

Patients with chronic edema, venous insufficiency, and reduced mobility are predisposed to cellulitis and other skin infections. Diuretics used in HF management can lead to electrolyte imbalances and dehydration, which further impair skin integrity. These infections may also be complicated by resistant organisms, especially in those with repeated antibiotic exposure.[6]

Sepsis and Bloodstream Infections

Sepsis is a serious consequence of HF that is often not identified. It may show low blood pressure and high lactate levels, which are also signs of cardiogenic shock, making it hard to tell what is wrong. Once sepsis is diagnosed, it is very important to start the right antibiotics right once. However, HF patients may need to have their doses changed if their organs are not working properly.[5]

Device-associated Infections

People who have pacemakers or implantable cardioverter-defibrillators (ICDs) are at risk for infections that can happen with these devices. These infections can be as mild as a pocket infection or as serious as infective endocarditis. These infections are hard to treat and may need the removal of the device along with long-term antibiotic therapy.[11]

In all of these situations, infection not only makes the clinical picture more complicated, but it also strongly triggers decompensated heart failure. So, it is important to recognize the problem early and give the right antibiotics, but this should be done in a way that avoids overuse and resistance.

Challenges in Diagnosing Infections in Heart Failure

It might be hard to tell if a patient with heart failure (HF) has an infection because the symptoms and lab results for both illnesses are quite similar. Misunderstanding can cause a diagnosis to be delayed, antibiotics to be used incorrectly, and bad results. Older people, people with several comorbidities, and people with acute decompensated heart failure (ADHF) make things even more complicated.

Overlapping Clinical Features

Fever, shortness of breath, exhaustion, and a fast heart rate are all common indications of infection. These are also common signs of HF exacerbation. For example, chest X-rays of people with HF may show lung congestion that looks like pneumonia, and peripheral edema may hide indications of a soft tissue infection. Also, symptoms like changes in mental state or general malaise, especially in older people, can be vague and misleading.[12]

Biomarker Limitations

Commonly used biomarkers, such as white blood cell count and C-reactive protein (CRP), may be elevated in HF even in the absence of infection due to chronic systemic inflammation. Although procalcitonin (PCT) has emerged as a potentially more specific marker for bacterial infection, its interpretation in HF is still evolving. Maisel et al. suggest that low PCT levels can safely exclude bacterial infection in patients with ADHF, but Scolletta et al. highlighted in their study that even modest elevations may be associated with increased mortality, independent of infection status.[12,13]

Imaging and Diagnostic Tools

Radiological imaging can be inconclusive in HF patients. Pulmonary edema can mask or mimic infiltrates, and the interpretation of chest X-rays or CT scans is often complicated by volume overload. Similarly, findings on urinalysis or blood cultures may reflect colonization or contamination rather than true infection, especially in patients with indwelling devices or frequent hospitalizations.[9]

Diagnostic Stewardship in Heart Failure

The risk of diagnostic inertia—relying on suggestive but non-definitive signs—may result in the overuse of empiric antibiotics. This is particularly relevant in emergency and intensive care settings, where time pressures often drive early antibiotic initiation. Studies have shown that up to 30%–40% of patients hospitalized with ADHF receive antibiotics without a confirmed infection, which contributes to increased healthcare costs and adverse events, including antimicrobial resistance and *C. difficile* infection.[9]

Role of Clinical Judgment and Serial Assessment

Given these diagnostic ambiguities, clinical judgment remains critical. Serial evaluation of symptoms, biomarker trends, imaging findings, and therapeutic response can help refine diagnosis. Multidisciplinary collaboration—especially involving infectious disease specialists and heart failure teams—can enhance diagnostic accuracy and prevent unnecessary antibiotic use.

Patterns and Indications for Antibiotic Use in Heart Failure

Doctors commonly provide antibiotics to people with heart failure (HF) as a first line of defense against infections that could make their condition worse. When a person has a confirmed or highly suspected infection, they should get antibiotics right away. However, new evidence suggests that many HF patients get antibiotics when they do not need them or when they should not, which raises concerns about antimicrobial resistance, bad drug reactions, and costs.

Empirical Antibiotic Use in Decompensated HF

In HF patients, respiratory tract infections are still the most common reason for getting antibiotics. Because pneumonia and acute decompensated heart failure (ADHF) have similar clinical signs, antibiotics are routinely prescribed before a definitive diagnosis is made. Studies have revealed that more than 30% of hospitalized HF patients start taking antibiotics, especially beta-lactams and macrolides, without any proof that they have an infection.[9] People do this because they think it is better to be safe than sorry, especially for elderly patients and those with high inflammatory markers.

Urinary Tract Infections and Overdiagnosis

Asymptomatic bacteriuria is frequently misinterpreted as urinary tract infection (UTI) in hospitalized HF patients. Positive urine cultures, in the absence of clinical signs of infection, often lead to unnecessary antibiotic initiation. This is especially prevalent in older adults and patients with indwelling catheters or urinary retention—common scenarios in advanced HF.[6]

Skin and Device-related Infections

In patients with chronic edema or implanted cardiac devices (e.g., pacemakers, ICDs), antibiotics are appropriately used for documented cellulitis, pocket infections, or endocarditis. These typically require longer durations of therapy and careful antimicrobial selection to cover resistant pathogens such as *Staphylococcus aureus*.[11] However, the threshold for suspecting and treating these infections varies widely across institutions.

Commonly Used Antibiotic Classes

The most frequently used antibiotic classes in HF patients include:

- *Beta-lactams (e.g., amoxicillin-clavulanate, ceftriaxone)*—used for pneumonia and urinary infections.
- *Macrolides (e.g., azithromycin)*—often added empirically for atypical respiratory coverage.
- *Fluoroquinolones (e.g., levofloxacin, ciprofloxacin)*—used for broad-spectrum coverage, though associated with increased cardiovascular risk in HF.
- *Vancomycin and Linezolid*—reserved for MRSA or device-related infections.

These agents must be used with caution, especially in the context of altered pharmacokinetics, potential QT prolongation, and renal dysfunction common in HF patients.[14]

Risks Associated with Inappropriate Use

When antibiotics are prescribed incorrectly, they can cause drug-related toxicity, longer hospital stays, the growth of multidrug-resistant organisms, and a higher risk of *C. difficile* infection. Also, antibiotics such as fluoroquinolones and macrolides have been linked to arrhythmias and worsening heart failure in people who are already at risk, which makes it even more important to carefully weigh the risks and benefits.[15] Antibiotics are an important part of treating infections in HF, but they should only be used when there are clear clinical reasons, diagnostic proof, and a grasp of the patient's individual situation to avoid harm and keep the antibiotics effective.

Antibiotic Pharmacokinetics and Pharmacodynamics in Heart Failure

Heart failure (HF), particularly in its acute decompensated form, significantly alters the pharmacokinetics (PK) and pharmacodynamics (PD) of antibiotics, affecting their efficacy and safety (Fig. 1).

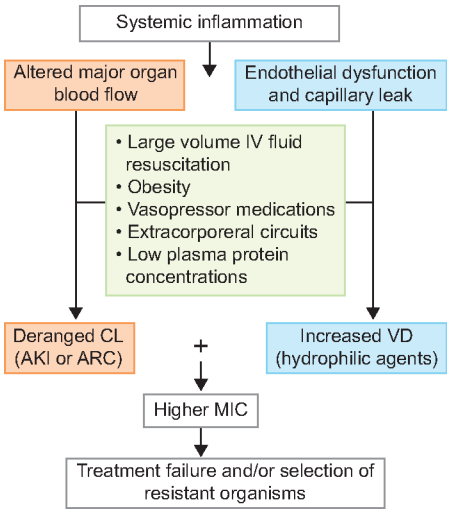

Fig. 1: Proposed pathway linking systemic inflammation to altered antibiotic pharmacokinetics and treatment outcomes

Pharmacokinetic Changes in HF

The state of systemic arterial hypoperfusion, venous congestion, and neurohormonal activation occurring in HF negatively affects the integrity and the function of key organs, particularly the gastrointestinal tract, the liver, and the kidney. Pathophysiological changes of heart failure in systemic organs can potentially affect drug absorption, first-pass metabolism, protein binding, volume of distribution, and clearance; there is significant inter-individual variability in the presence and severity of hepatic and renal dysfunction, singly or in combination, in the HF population.[16] The presence of significant fluid overload can lead to modifications of specific compartments, such as the pleural space (pleural effusion) and the peritoneal cavity (ascites), and/or a systemic expansion of the interstitial fluid volume (anasarca), with significant effects on the distribution of water-soluble drugs.[17]

Review of Literature and Discussion

Studies

Here is a tabulated representation of available studies from various resources addressing the above-discussed clinical dilemma of managing the clinical scenario of using empirical antibiotics in patients of heart failure with presentation resembling both ADHF and pneumonia, and the diagnosis of pneumonia has not yet been confirmed (Table 1).

Discussion

We noted that most studies done in the past indicate that irrational use of empirical antibiotics in unconfirmed infections leads to poor outcomes, including prolonged hospital stay and higher intermediate mortality. The benefit of empirical antibiotics in heart failure with unconfirmed pneumonia is limited to a high likelihood of infections with biomarker correlates. Irrational or aggressive antibiotic use is not supported by any of the existing literature. However, the benefit of early antibiotics is noted as the clinical evidence of infection becomes stronger in favor of infection even before final confirmation.

Gaps in Knowledge

Most of the studies done on antibiotic use in empirical therapy in heart failure are based on very small data sets, with limited inclusion of various ethnic and regional groups. Very limited data is available on tropical region protocols where the burden of infection is very high, and the potential of antibiotic use in patient benefit is possible. Studies in the Indian scenario, where the burden on Heart

Table 1: Summary of recent studies evaluating antibiotic use in heart failure

Study	*Design and population*	*Antibiotic use*	*Primary outcome(s)*	*Key results*	*Conclusions*
Katherine Schojan et al. (2023)[18]	Retrospective cohort (2018–2022), 161 patients with ADHF without confirmed infections	≥48 hours of IV antibiotics vs no antibiotics	Hospital length of stay (LOS)	LOS significantly longer in antibiotic group (matched: 5 vs 4 days, $p < 0.01$); increased sodium/fluid exposure	Avoid empiric antibiotics unless infection is confirmed; risk of fluid overload and prolonged hospitalization
Loosen et al. (2023)[19]	Retrospective case-control study, 162,188 outpatients (Germany)	Analyzed total dose and class over 5 years	Incidence of HF	Low antibiotic use (≤6000 mg) associated with lower HF risk (OR = 0.87); high cephalosporin use increased risk (OR = 1.16)	Antibiotic use linked to HF risk in a dose- and class-dependent manner; may involve gut microbiome alterations
Rohini Pawar et al. (2025)[20]	Prospective observational study, 100 patients with AHF (India)	All received antibiotics on admission	Duration and rationality of use	Mean duration, 5.37 ± 2.62 days; only 10% had antibiotics stopped at 48 hours	Highlights overuse of antibiotics; calls for rational use and de-escalation in suspected cardiac dyspnea
PAPRICA-3 study	Multicenter observational study, 6,727 patients with AHF (Spain)	Early antibiotic administration in infection-triggered AHF	13-week mortality and readmission	Higher early mortality in infection-triggered AHF (unadjusted); lower postdischarge mortality after adjustment	Infection-triggered AHF not linked to worse midterm outcomes; early antibiotic use and hospitalization may help
Frisbee et al. (2024)[21]	Retrospective review, 144 patients with ADHF with low pneumonia risk	IV antibiotics vs no antibiotics	LOS, diuretic use, readmission, mortality	IV antibiotic group had longer LOS (6.6 vs 3.0 days), more diuretic use (930 vs 320 mg), and higher readmission (OR = 2.51)	IV antibiotics without infection worsen ADHF outcomes; reinforce stewardship to avoid fluid/sodium overload

failure patients is on an exponential rise, but the infection prevalence in the population is still high, are very few. The various antibiotic combinations, use of alternative antibiotics, and interantibiotic comparison in this scenario have also not been studied extensively. Therefore, the exact verdict on the scenario can only be drafted after more comparative studies in the future, giving us potential research topics which need to be answered and may be considered in future analysis.

Conclusion

Heart failure (HF) is a major global health issue marked by high morbidity and mortality, with frequent infections acting as common precipitants of acute decompensation. Patients with HF are particularly susceptible to infections due to systemic inflammation, impaired organ perfusion, gut barrier dysfunction, and immune dysregulation. Common infections in HF include respiratory tract infections, urinary tract infections, skin infections, sepsis, and device-related infections, many of which overlap symptomatically with HF itself—making diagnosis and treatment particularly challenging. Empirical antibiotic use is common but often unjustified, driven by diagnostic uncertainty, leading to potential harm such as prolonged hospitalization, drug toxicity, and increased antimicrobial resistance. Studies show that inappropriate antibiotic administration in patients with unconfirmed infections correlates with worse outcomes, highlighting the urgent need for diagnostic stewardship, individualized clinical assessment, and careful antibiotic selection. This review underscores the pathophysiological links between HF and infection, common infectious patterns, diagnostic dilemmas, pharmacological considerations, and evidence-based approaches for judicious antibiotic use in this vulnerable population.

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Conflict of Interest

None.

Authors' Contributions

TK and R contributed to conception, study design, supervision, funding, material collection, data collection and/or processing, analysis and/or interpretation, literature review, writing, and critical review. PK and SA contributed to material collection, data collection and/or processing, and critical review. BDM and KK contributed to material collection, data collection and/or processing, and analysis and/or interpretation.

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