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REVIEW ARTICLE

Impact of respiratory infections and vaccination on heart failure outcomes – a comprehensive review

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Abstract

Introduction and Objective. Heart failure (HF) is a clinical syndrome resulting from structural or functional cardiac abnormalities that impair circulation. COVID-19, pneumococcal disease, and influenza exacerbate HF, increasing morbidity and mortality. Vaccination has been shown to mitigate these risks. The aim of the review is to assess the impact of influenza, pneumococcal, and COVID-19 vaccinations on HF patients, and their role in HF management.

Review Methods. A literature review was conducted using PubMed and Google Scholar. Search terms included 'heart failure', 'vaccination', 'influenza', 'pneumococcal infection', 'COVID-19', and related variations.

Brief description of the state of knowledge. Airborne infections such as influenza, pneumococcal disease, and COVID-19, negatively impact HF outcomes, increasing mortality through myocardial injury, inflammation, and decompensation. Vaccination alleviates these effects: influenza vaccines lower hospitalization and mortality, pneumococcal vaccines reduce pneumonia-related complications and cardiovascular events, and COVID-19 vaccines decrease severe infections and improve survival. Combined vaccination strategies provide additional benefits, highlighting their essential role in HF management.

Summary. HF patients benefit significantly from vaccination against influenza, pneumococcal infections, and COVID-19, which reduces hospitalization and mortality. However, further randomized clinical trials are needed to confirm the effectiveness of COVID-19 and pneumococcal vaccines in HF patients, as promising outcomes have been observed in broader cardiovascular populations.

Key words

influenza, pneumococcal infections, COVID-19, vaccination, heart failure

INTRODUCTION

Heart failure (HF) is a clinical syndrome characterised by cardinal symptoms, such as breathlessness, fatigue, and ankle swelling, often accompanied by signs like pulmonary crackles and peripheral oedema. It results from structural or functional cardiac abnormalities that lead to elevated intracardiac pressures or inadequate cardiac output. HF is categorised based on left ventricular ejection fraction (LVEF) into 3 phenotypes: heart failure with reduced ejection fraction (HFrEF, LVEF ≤40%), mildly reduced ejection fraction (HFmrEF, LVEF 41%-49%), and preserved ejection fraction (HFpEF, LVEF ≥50%). It can also be divided into chronic heart failure, characterised by a gradual onset of symptoms, and acute heart failure, which may arise suddenly or as decompensation of chronic HF. The incidence of HF in Europe is approximately 3 per 1,000 person-years across all age groups, with prevalence increasing significantly with age. Coronary artery disease (CAD) and hypertension are the leading causes in developed countries, with ischaemic aetiology more common in HFrEF and HFmrEF, compared to HFpEF. Ageing populations and increasing comorbidities suggest a rising burden of HF in the coming decades.

Infections, such as influenza, pneumococcal disease, and Coronavirus Disease 2019 (COVID-19), place a high burden on patients with heart failure, often serving as major precipitants of cardiac decompensation and thus increasing hospitalizations. Cardiovascular conditions are further compromised by such infections, leading to serious complications and even death, especially in those over the age of 65 or suffering from comorbidities. Myocarditis, pericarditis, or exacerbation of pre-existing conditions are common complications of influenza in HF patients, including increased in-hospital mortality [1]. Pneumococcal infections, the major cause of pneumonia, disproportionately affect HF patients, significantly increasing mortality in those

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with concomitant pneumonia [2]. Likewise, COVID-19 is a separate risk factor for cardiovascular disease related to complications, such as myocardial injury, pericarditis, coagulopathy, myocardial infarction, heart failure, and arrhythmias. Consequently, COVID-19 patients hospitalized with HF have poor prognoses [3]. In the management of heart failure, these data emphasize the importance of preventing respiratory infections, especially via vaccination.

According to leading cardiovascular guidelines, vaccinations can improve outcomes for patients with heart failure. The 2022 recommendations of the American Heart Association (AHA), American College of Cardiology (ACC), and Heart Failure Society of America (HFSA) indicate that vaccinating against influenza, COVID-19, and pneumococcal infections is a reasonable approach to reducing mortality in HF patients [4]. Additionally, the COVID-19 vaccination, when available, should be considered in patients with HF [5]. Similarly, the 2021 European Society of Cardiology (ESC) guidelines indicate that influenza and pneumococcal vaccinations should be considered to prevent HF hospitalizations. Despite standard pharmacological and non-pharmacological treatment, vaccinations play a crucial role in preventing life-threatening complications in heart failure.

OBJECTIVE

The aim of the review is to examine the role of vaccination against influenza virus, pneumococcal infection, and COVID-19 in the management of heart failure patients. A further aim is to outlines how these vaccinations influence cardiovascular and all-cause mortality of HF patients by analyzing current evidence, as well as showing the impact of these infections on cardiovascular events. Moreover, the review shows existing gaps and limitations of current data.

Review methods. A literature review was conducted using the PubMed and Google Scholar databases with search terms such as 'vaccination', 'influenza,' 'pneumococcal infection', 'COVID-19', 'heart failure', and all variations related to these terms. The review focused on clinical trials, randomized controlled trials, meta-analyses, systematic reviews, and other review articles. To ensure a deep understanding of the topic and maintain up-to-date results of the research, priority was given to articles published within the last 8 years. The literature search did not include case reports.

BRIEF DESCRIPTION OF THE STATE OF KNOWLEDGE

Influenza. Analysis of data from the PARADIGM-HF trial evaluated influenza vaccination prevalence and its impact on outcomes in 8,099 cases heart failure with reduced ejection fraction patients. Only 21% of participants were vaccinated, with significant regional variation: the highest rates were in The Netherlands (77.5%), while the lowest were in Asia (2.6%). Influenza vaccination was associated with a reduced risk of all-cause mortality with a Hazard Ratio (HR) of 0.81 [6]. Following this, the analysis of 4,243 patients with acute heart failure (AHF) showed that influenza vaccination, statistically significantly reduced hospitalisation rates in in-hospital mortality, and 90-day and 1-year mortality. On the other hand, COVID-19 vaccination was associated with higher hospitalisation rates, but lower 90-day mortality without a significant impact on 1-year mortality. Finally, full vaccination achieved the largest reductions in in-hospital mortality (HR 0.638), 90-day mortality (HR 0.702), and 1-year mortality (HR 0.815). Among the cohort, 43% received influenza vaccinations, 74% received COVID-19 vaccinations, and 41.8% received all recommended vaccinations.

These findings highlight the benefits of influenza and full vaccination in AHF patients, though COVID-19 vaccination alone is less clear [7]. According to the same authors, vaccination was also associated with a reduced probability of hospitalization in 6,147 decompensated heart failure patients with 19% of vaccinated patients (OR 0.823, 95% CI: 0.709–0.955) [8]. On the contrary, alternative evidence emerged from study conducted by Bhat et al, which evaluated influenza vaccination rates in 313,761 heart failure patients discharged from 392 U.S. hospitals. Despite being a low-cost and widely accessible intervention, influenza vaccination uptake, which averaged 68%, showed increasing refusal rates, raising significant public health concerns. Interestingly, influenza vaccination was not significantly associated with differences in 1-year all-cause mortality compared to non-vaccinated (adjusted HR: 0.96; 95% CI: 0.89–1.03) [9]. Conversely, conflicting results to those obtained by Ghat were presented by a study by Gotsman et al. with total of 6,435 heart failure patients being evaluated and 69% vaccinated. There was a lower mortality rate associated with vaccination (HR 0.77) and fewer cardiovascular hospitalizations associated with vaccination (HR 0.83). Additionally, it was found that survival was improved (HR 0.80) and deaths were reduced (HR 0.86) [10].

Table 1. Impact of influenza infection on cardiovascular events in heart failure patients

Effect of Influenza Infection	Description	Consequences
Increased Pro-Inflammatory Cytokines	IL-6, C-reactive proteins, TNF-alpha	Arterial and venous thrombotic events, coagulopathy
Reduced Beta-Adrenergic Responsiveness	Alters cardiac myocyte contractility	Impaired heart function
Cardiac Tissue Remodelling	Chronic cytokine production	Left ventricular dilation, increased collagen content
Myocarditis and Pericarditis	Acute myocarditis, cardiogenic shock	Increased risk of death
Exacerbation of Pre-existing Conditions	Chronic heart failure, ischemic heart disease	Worsened outcomes
Arrhythmias	Ventricular arrhythmias, conduction disorders	Increased risk of cardiac complications
Myocardial Infarction Risk	Six-fold increase within 1-week post-infection [11]	Increased risk of acute myocardial infarction
Myocarditis Rate	Up to 10% [12]	Significant cardiac involvement
Hospital Outcomes	Higher in-hospital mortality (6.2% vs. 5.4%), longer hospital stays (5.9 vs. 5.2 days) [13]	Poorer patient outcomes
Excess Mortality and Hospitalizations	Annual excess of 250 all-cause deaths, 115 cardiovascular deaths, and 251 excess hospitalizations [14]	Increased morbidity and mortality

Furthermore, this placebo-controlled, double-blind, randomised trial evaluated the impact of influenza vaccination on 5,129 patients with heart failure across 30 clinics in 10 countries between 2015–2021. A 3-year study was conducted in which participants were randomly assigned to receive either a placebo or an annual influenza vaccine. Vaccination significantly reduced the number of hospitalizations for all causes (HR 0.84), including pneumonias (HR 0.58). Additionally, vaccinations were associated with significant reductions in cardiovascular events, all-cause mortality, and cardiovascular mortality during peak influenza periods [15]. A systematic review and meta-analysis of 179,158 patients with heart failure found that influenza vaccination significantly reduced all-cause mortality (HR 0.83), but not cardiovascular mortality or all-cause hospitalizations [16]. Beyond that, one of the latest meta-analysis of 6 randomised controlled trials (RCTs) involving 9,340 patients (4,211 with ischaemic heart disease and 5,129 with heart failure), demonstrated that influenza vaccination significantly reduced major adverse cardiovascular events (MACE), including cardiovascular death, acute coronary syndrome, stent thrombosis or coronary revascularization, stroke, and heart failure hospitalisation (HR: 0.740). In addition to reducing cardiovascular mortality (HR: 0.63), vaccination also reduced overall mortality (HR: 0.72) [17].

In the INVESTED trial and its subsequent analysis, influenza vaccination was compared in high-risk cardiovascular (CV) populations, including those with heart failure and previous myocardial infarction. Primary study objectives included evaluating vaccine-related adverse reactions (ARs) and their association with clinical outcomes. It was found that mild-to-moderate ARs, experienced by 37.8% of 5,260 participants, reduced mortality and cardiopulmonary hospitalizations. whereas severe ARs increased the risk, suggesting that ARs reflect the intensity of the immune response and should not refrain from vaccinations in the future [18]. A secondary analysis showed a significant correlation between increased influenza-like illness (ILI) activity and higher cardiopulmonary events. However, high-dose vaccines did not outperform standard doses in terms of reducing these events, even during peak ILI periods [19]. Moreover, among 658 participants in an immune response sub-study, humoral responses were correlated with clinical outcomes. The high-dose vaccines produced higher antibody titres and seroconversion rates, but seroconversion was not associated with a reduction in cardiopulmonary hospitalizations or mortality [20].

In alignment with the above-mentioned results, Vardeny et al. also demonstrated that in patients with high-risk cardiovascular disease, high-dose trivalent inactivated influenza vaccine did not significantly reduce all-cause mortality or cardiopulmonary hospitalizations compared to standard-dose quadrivalent inactivated influenza vaccine [21]. Based on these studies, influenza vaccination reduces mortality and cardiopulmonary hospitalizations in high-risk CV patients. However, vaccine doses and antibody responses may not predict clinical outcomes, underscoring the importance of broader vaccination efforts rather than dose-specific strategies.

The DANFLU-1 trial found that the high-dose quadrivalent influenza vaccine (QIV-HD) reduced hospitalizations for pneumonia or influenza and all-cause mortality in older adults with cardiovascular disease, including heart failure. However, QIV-HD did not significantly out-perform standard-dose vaccine (QIV-SD) in reducing all-cause hospitalizations among those with chronic cardiovascular conditions [22].

As part of the ongoing DANFLU-2 trial (NCT05517174), over 200,000 adults over the age of 65 in Denmark will be evaluated for their relative effectiveness against severe influenza outcomes when given a high-dose quadrivalent vaccine as compared to a standard dose quadrivalent vaccine in a multi-season, fully-powered study [23]. As none of these studies specifically targeted heart failure patients, further dedicated randomized controlled trials are needed to determine whether high dose quadrivalent influenza vaccination is beneficial to this high-risk group.

Pneumococcal infection. Patients with heart failure face significantly heightened mortality risks when pneumonia is present. In the OPTIMIZE-HF study, 15% of 48 612 patients had pneumonia or another respiratory condition. neumonia (OR, 1.60) was associated with higher in-hospital mortality [2]. In the PARADIGM-HF and PARAGON-HF trials sub-analysis, Shen et al. found an increased incidence of pneumonia in heart failure patients, especially those with preserved ejection fractions. The incidence rate was 29 per 1,000 patient-years and 39 per 1,000 patient-years, approximately 3 times higher than expected. It was also shown that the mortality rate was 4-fold higher after a first episode of pneumonia [24]. Interesting evidence emerged on examining a large cohort study of 4,988 adults with CAP and no prior history of heart failure, which was matched to 23,060 controls. It demonstrated a significant increase in the risk of incident HF following CAP. Over a median follow-up of 9.9 years, 11.9% of pneumonia patients developed HF compared with 7.4% of controls. The heightened risk was observed regardless of treatment setting, and persisted in the short term (90 days) and intermediate term (1 year) [25]. An additional meta-analysis of 39 observational studies involving 92,188 patients found that 9.2% of patients developed new or exhibited worsening of a pre-existed heart failure after CAP [26]. Consequently, pneumonia and heart failure have a bilateral connection that increases their risk of occurrence.

Table 2. Mechanisms of cardiac damage by pneumococcal infections [27]

Mechanism	Description	Consequences
Cardiotoxic effects of Pneumolysin	Immunocompromise, cardiotoxicity, necroptosis of cardiac macrophages	Myocardial dysfunction, intracardiac microlesions, biofilm formation
Pneumococcal Adhesins	Interaction with cardiomyocytes, exposure to pneumolysin	Cardiomyocyte death, severe myocardial dysfunction
Prothrombotic and Pro-Inflammatory Processes	Activation of platelets and neutrophils, intravascular thrombosis	Increased intravascular coagulation, cardiac damage

Evidence for the effectiveness of pneumococcal vaccination specifically in heart failure patients is still limited, though promising studies in cardiovascular populations have shown its potential to reduce the incidence of cardiovascular events and mortality. A meta-analysis of 18 studies encompassing 716,108 participants, demonstrated that the 23-valent polysaccharide pneumococcal vaccine PPV23 was associated with a reduced risk of any cardiovascular event (Relative Risk (RR): 0.91) and myocardial infarction (RR: 0.88), with the strongest protective effect observed in individuals aged ≥65

years. Additionally, PPV23 significantly reduced all-cause mortality in all age groups, particularly in those aged ≥65 years [28]. In agreement with prior findings, a systematic review and meta-analysis of 7 observational studies involving 163,756 participants, showed a significant 22% reduction in all-cause mortality. However, no randomized controlled trials (RCTs) were identified, and 3 studies exhibited a serious risk of bias, lowering the confidence in these findings.

Despite these limitations, the evidence suggests pneumococcal vaccination offers substantial survival benefits for individuals with CVD or elevated cardiovascular risk, supporting its recommendation in this population [29]. Jaiswal et al. created a meta-analysis of 15 studies involving 347,444 patients, in which 32% received pneumococcal vaccine, while 68% were not vaccinated. Vaccination was associated with a significant reduction in all-cause mortality (HR: 0.76) and incidence of myocardial infarction (HR: 0.73). However, no significant reductions were observed in CV or stroke risk [30]. In contrast to previous findings, as mentioned above, Ghat et al. showed that pneumococcal vaccination was also not associated with significant differences in 1-year all-cause mortality compared to non-vaccinated (adjusted HR: 0.95; 95% CI: 0.89–1.01) [9].

The Australian Study for the Prevention through Immunisation of Cardiovascular Events investigated whether the pneumococcal polysaccharide vaccine reduces such cardiovascular events as myocardial infarction and stroke. While vaccination induced sustained increases in anti-pneumococcal IgG and IgG2 levels at 4 years, no significant differences were observed in surrogate markers of cardiovascular disease, such as c-reactive protein, carotid intima-media thickness, and pulse wave velocity. Final results are awaited to clarify whether these immunological responses translate into clinical cardiovascular benefits [31, 32].

It has been shown that pneumococcal and influenza vaccine exhibit additive benefits when administered together. This was highlighted in a retrospective cohort study in Taiwan in individuals aged 75 years and older. Among 24,426 propensity-matched participants who received both vaccines, all-cause mortality was significantly reduced (RR: 0.74), as well as hospitalizations for conditions such as pneumonia, chronic obstructive pulmonary disease, and heart failure (RR: 0.77). Additionally, in-patient expenditures for all diseases decreased by 13%, compared with influenza vaccination alone [33]. Correspondingly, a study involving 258,754 individuals aged ≥65, indicated that dual vaccination with influenza and pneumococcal vaccines significantly reduced hospitalizations for influenza (37%), pneumonia (29%), and invasive pneumococcal disease (44%), compared to unvaccinated individuals. Among the vaccinated, 72,107 received both vaccines, resulting in lower in-hospital pneumonia mortality [34]. Moreover, a prospective cohort study of 36,636 elderly patients (≥65 years) with chronic illnesses showed that dual vaccination statistically significantly reduced risks of death, pneumonia, ischemic stroke, and acute myocardial infarction. Coronary and intensive care admissions were also statistically lowered. However, as compared to the unvaccinated group, subjects who received only the pneumococcal vaccination did not have a significant reduction in chronic heart failure [35].

The above- mentioned findings highlight the superior benefits of combined vaccination in reducing respiratory-related hospitalizations and deaths in older adults.

COVID-19. This disease is an independent risk factor for cardiovascular disease, with complications including myocardial injury, pericarditis, coagulopathy, myocardial infarction, heart failure, arrhythmias, and persistent post-acute cardiovascular risk [3]. Acute heart failure occurred in 20.2% of hospitalized COVID-19 patients, as shown in a meta-analysis of 6 studies involving 1,064 individuals (mean age 66 years, 58% male). This complication was associated with a significantly increased risk of in-hospital mortality (OR 9.36) [36]. A study of 3,080 COVID-19 patients with at least 30 days of follow-up, revealed a significant impact on heart failure outcomes. Patients with chronic heart failure, 4.9% of the cohort, had a markedly higher risk of acute heart failure development, 11.2% vs. 2.1%, and mortality, 48.7% vs. 19.0%, compared to those without CHF. Overall, 2.5% of patients developed AHF, most of whom (77.9%) had no prior HF history. AHF was strongly associated with mortality, 46.8% vs. 19.7% with arrhythmias, and CHF identified as key predictors. Importantly, the withdrawal of guideline-directed medical therapy, significantly increased in-hospital mortality [37]. Additionally, meta-analysis of 27 studies examining patients with pre-existing heart failure infected by COVID-19, revealed significantly worse outcomes. HF patients had a statistically significant higher risk of mortality and an increased need for mechanical ventilation [38]. In the DELIVER trial, involving 6,263 participants with heart failure, COVID-19 was reported in 9.4% of participants, with over half requiring or prolonging hospitalization, and 15% of all deaths adjudicated as definitely or possibly COVID-19-related. The mortality rate within 12 months following a COVID-19 diagnosis was significantly higher, 8.6-fold, particularly in the first 3 months. Even when excluding COVID-19-related deaths, survivors had a 2.46-fold increased risk of all-cause mortality compared to the broader trial cohort [39]. Similarly, in 132,312 HF patients hospitalized 6.4% were admitted with COVID-19. Hospitalization for COVID-19 was associated with significantly higher in-hospital mortality (24.2%) than hospitalization for acute HF (2.6%) [40].

Regarding long-term complication of COVID-19, including cardiovascular impairment, a study using healthcare data analysed 153,760 COVID-19 survivors assessed long-term cardiovascular risks. At 1-year post-infection, patients with COVID-19 demonstrated increased risks of cerebrovascular disorders, dysrhythmias, ischemic and non-ischemic heart disease, pericarditis, myocarditis, heart failure, and thromboembolic disease. These risks were present even among non-hospitalized patients and escalated with the severity of the acute phase, including hospitalization and intensive care admission [41]. A meta-analysis of 21,463,173 individuals revealed that 1.1% of COVID-19 survivors developed heart failure during a mean follow-up of 9.2 months. COVID-19 recovery was associated with a 90% increased risk of incident HF, particularly in the early post-acute phase. These findings highlight the need for targeted cardiovascular monitoring and management in COVID-19 survivors [42].

Benefits of COVID-19 vaccination in heart failure patients remain understudied. At the ESC Heart Failure Event in May 2024, Chun et al. presented a retrospective analysis of 651,127 HF patients in Korea (mean age 69.5 years, 50% male), and demonstrated significant protective effects of vaccination. Vaccinated patients (82.7%) experienced a 32% lower risk of hospitalization for HF (HR 0.68) and a 27% lower risk of COVID-19 infection (HR 0.73), compared to unvaccinated

Table 3. Mechanisms of Myocardial Injury in COVID-19 [43]

Mechanism	Description	Consequences
Indirect Mechanisms	Fever, hypoxaemia, inflammation	Increased oxygen demand, cardiomyocyte death, coagulation disorders
Cytokine Storm	IL-1, IL-6, TNF-alpha, VEGF release	Acute lung injury, endothelial damage, cardiac injury
Direct Mechanisms	SARS-CoV-2 entry via ACE2	Direct cardiomyocyte infection
	ACE2 down-regulation	Increased angiotensin II, vasoconstriction, fibrosis, inflammation

patients. Moreover, vaccination reduced the risk of critical COVID-19 infection requiring intensive care or ventilatory support by 73% (HR 0.27). Vaccinated HF patients also had significantly lower risks of stroke, myocardial infarction, myocarditis/pericarditis, and venous thromboembolism. The above information is based on the abstract of the original paper, which has not yet been published.

These findings highlight the critical role of vaccination in mitigating both COVID-19-related and cardiovascular risks in HF patients [44]. Supporting these results, an analysis of 165,453 HF patients revealed that vaccination significantly reduced the severity of COVID-19 outcomes. Among 9,728 HF patients infected with COVID-19, ICU hospitalization rates were higher in the unvaccinated group (7.6%), decreasing to 4.8% in vaccinated individuals and 2.9% in those who received a booster. The effectiveness of the vaccine in preventing ICU hospitalization was 41.9% in vaccinated HF patients and 76.6% in those who received a booster. It is evident from these findings that both initial vaccination as well as booster doses of COVID-19 can mitigate severe outcomes in patients with HF [45]. Johnson et al. created a retrospective cohort study of 7,094 heart failure patients among whom 9.1% were partially vaccinated, 31.0% were fully vaccinated, 14.8% were boosted, and 45.1% were unvaccinated. Over an average follow-up period of 276.5 days, boosted and fully vaccinated patients experienced markedly lower mortality rates, HR 0.33 and HR 0.36, respectively, compared to the unvaccinated individuals. No mortality benefit was observed in partially vaccinated individuals [46].

Considering more general cohorts, a study using the National COVID Cohort Collaborative database examined the association between COVID-19 vaccination and major adverse cardiac events (MACE) in 1,934,294 patients aged 18–90 years, with confirmed SARS-CoV-2 infection. Among the patients, 0.7% experienced MACE, with rates of 0.7% in unvaccinated individuals, 0.7% in partially vaccinated, and 0.5% in fully vaccinated patients. Both full vaccination and partial vaccination significantly reduced the risk of MACE. Median time to MACE was 17 days post-infection, with a median of 212 days from last vaccination to MACE [47]. Reinforcing previous conclusions, in a cohort of 167 hospitalized COVID-19 patients, vaccination significantly reduced the risk of acute cardiac events (RR: 0.33) and lowered troponin T levels. Type 2 diabetes (OR: 2.99) and pre-existing cardiac disease (OR: 4.31) were key risk factors for cardiac events [48]. Ultimately, full COVID-19 vaccination was significantly associated with reduction of the risk of acute myocardial infarction (aHR, 0.48) and ischemic stroke (aHR, 0.40) between 31–120 days post-infection, compared to unvaccinated patients [49].

CONCLUSIONS

Vaccination against influenza, pneumococcal infections, and COVID-19 is another important factor in reducing the risk of adverse outcomes in patients with HF. The influenza vaccine has been shown to reduce all-cause mortality, HF decompensations, and hospitalization rates, underlining its protective role against systemic inflammation and cardiovascular stress. The pneumococcal vaccines decrease the rates of invasive pneumococcal disease, cardiovascular events, and all-cause mortality in CVD population. Though COVID-19 vaccination can cause myocarditis in younger populations, its safety has been confirmed in HF regarding venous thromboembolism or myocarditis [50]. Additionally, it has been shown to decrease the incidence of severe COVID-19 infections that can exacerbate HF. The combination of influenza and pneumococcal vaccinations offers additive benefits that reduce hospitalizations and mortality further. As part of a comprehensive HF management strategy, these vaccinations play an important role in improving not only cardiovascular outcomes, but also overall health outcomes for this vulnerable population.

Although many observational studies and meta-analyses have supported vaccination for cardio-protection, randomized controlled trials in HF patients are needed, especially in terms of pneumococcal and COVID-19 vaccines. In future studies, it would be useful to examine the comparative effectiveness of different types and dosages of vaccines on long-term cardiovascular outcomes, and the possible mechanisms behind vaccination-associated reductions in cardiovascular events. The complex interplay between vaccination timing, immune response, and clinical outcomes in HF patients requires further research.

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