World Journal of Cardiovascular Diseases, 2026, 16(8), 509-518
https://www.scirp.org/journal/wjcd
ISSN Online: 2164-5337
ISSN Print: 2164-5329

Vericiguat in the Management of De Novo Acute Decompensated Heart Failure after Acute Myocardial Infarction: A Single-Center Pilot Cohort Study

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How to cite this paper: Patra, S., Deb, S., Ahuja, S., Bhauwala, A. and Sarkar, D. (2026) Vericiguat in the Management of De Novo Acute Decompensated Heart Failure after Acute Myocardial Infarction: A Single-Center Pilot Cohort Study. *World Journal of Cardiovascular Diseases*, **16**, 509-518.
https://doi.org/10.4236/wjcd.2026.168049

Received: June 1, 2026
Accepted: August 10, 2026
Published: August 13, 2026

Abstract

Background: The role of vericiguat in worsening chronic heart failure with reduced ejection fraction (HFrEF) is well established. However, its safety and role in managing de novo acute decompensated heart failure (ADHF) immediately following acute myocardial infarction (AMI) remain largely unknown. **Methods:** In this single-center, retrospective pilot cohort study conducted from November 2023 till December 2025, we screened 145 patients admitted with de novo ADHF following AMI. A total of 106 consecutive patients who received early oral vericiguat within 48 hours of admission alongside guideline-directed medical therapy (GDMT) were enrolled. After excluding 5 patients who died during the index admission or follow-up, 101 survivors were evaluated at 7 days and 3 months post-discharge for clinical, echocardiographic, and laboratory changes. **Results:** The analytic survivor cohort (n = 101) had a mean age of 56 ± 10 years and 85% were male. All had severe ADHF (100% requiring intravenous diuretics, 80% cardiogenic shock requiring inotropes). Over 3 months of vericiguat and GDMT administration, New York Heart Association (NYHA) functional class improved significantly (class III/IV at baseline down to 10% class III and 90% class II; $P < 0.01$). Mean left ventricular ejection fraction (LVEF) increased from 30.5% ± 8.5% to 36.6% ± 6.4% ($P < 0.05$). Prevalence of hypotension decreased from 80% to 10% ($P < 0.01$). Renal function (eGFR) improved over time. No adverse effects leading to vericiguat withdrawal were observed. **Conclusions:** In this pilot cohort, vericiguat administered with GDMT was well tolerated in patients with post-AMI de novo ADHF and was associated with short-term clinical and hemodynamic improvement.

Keywords

Vericiguat, Acute Decompensated Heart Failure, Acute Myocardial Infarction, Heart Failure with Reduced Ejection Fraction, Guideline-Directed Medical Therapy, Pilot Cohort Study

1. Introduction

The pathophysiology of acute decompensated heart failure (ADHF) remains complex, and optimal therapeutic management for patients in the acute setting is limited [1]. ADHF is associated with an elevated risk of multiorgan failure, recurrent hospitalizations, and poor overall prognosis [2]. Following acute myocardial infarction (AMI), the risk for de novo ADHF increases markedly, bringing profound morbidity, mortality, and financial burden [3]. Although guideline-directed medical therapies (GDMT) form the cornerstone of management for chronic heart failure with reduced ejection fraction (HFrEF) [4]-[7], their prompt initiation in the setting of ADHF—particularly when complicated by cardiogenic shock or pulmonary edema post-AMI—is often hindered by hemodynamic instability.

Vericiguat, a novel oral soluble guanylate cyclase stimulator, has emerged as a critical therapy for HFrEF, especially in the context of worsening heart failure [4] [6]. The VICTORIA trial confirmed the safety and efficacy of vericiguat in reducing cardiovascular death or heart failure hospitalization in patients with chronic HFrEF who experienced a recent decompensation [6]. Consequently, vericiguat currently carries a Class 2b recommendation in contemporary ACC/AHA/HFSA guidance for selected patients with high-risk HFrEF despite GDMT [4].

Despite these advances, the clinical trajectory and safety profile of vericiguat in the treatment of de novo ADHF occurring acutely after an AMI remain largely unstudied. Addressing this evidence gap, we conducted a single-center pilot cohort study to explore the short-term clinical parameters of patients receiving early vericiguat therapy for de novo post-AMI ADHF.

2. Methods

2.1. Study Design and Population

This single-center retrospective pilot cohort study was conducted at a tertiary care hospital between November 1, 2023 and September 30, 2025. To ensure complete follow-up for all included patients, enrollment was censored on September 30, 2025, allowing a minimum of 3 months of follow-up through December 31, 2025.

The study protocol was reviewed and approved by the Institutional Ethics Committee. Given the retrospective nature of the study, the Ethics Committee approved the collection of clinical data from hospital records. Surviving patients were contacted during follow-up and consent was obtained for use of their clinical information whenever feasible. Consent status did not influence inclusion in the

retrospective analysis.

We screened 145 patients admitted with de novo ADHF following an AMI. ADHF was diagnosed via clinical evaluation using the Framingham criteria and confirmed by elevated N-terminal pro-B-type natriuretic peptide (NT-proBNP) standardized for age, alongside echocardiographic evidence of an LVEF < 50%. AMI was defined according to the Fourth Universal Definition of Myocardial Infarction [5].

Patients were excluded if they had a previous diagnosis of heart failure, primary valvular heart disease requiring intervention, significant uncorrected valvular disease, secondary cardiomyopathies (rheumatic, alcoholic, or dilated), autoimmune diseases, advanced tumors, severe sepsis, primary functional disorders of vital organs (brain, liver, lungs), abnormal thyroid function, mental disorders impeding communication, or were on ventilatory support.

Of 145 patients screened with de novo acute decompensated heart failure following acute myocardial infarction, 39 were excluded. Reasons for exclusion included prior history of heart failure (n = 12), significant valvular heart disease (n = 6), secondary cardiomyopathy (n = 5), severe sepsis or advanced systemic illness (n = 7), requirement for prolonged mechanical ventilatory support (n = 4), and incomplete clinical records or loss to follow-up before discharge (n = 5). The remaining 106 consecutive eligible patients received vericiguat and comprised the study cohort.

2.2. Treatment Protocol

Among the eligible cohort, 106 consecutive patients were treated with oral vericiguat initiated within 48 hours of hospital admission. All patients were managed with guideline-directed medical therapy (GDMT) for heart failure—including angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB), beta-blockers, mineralocorticoid receptor antagonists (MRA), and sodium-glucose cotransporter-2 (SGLT2) inhibitors—as tolerated based on blood pressure, renal function, and electrolyte status. Acute management included intravenous diuretics, and, tailored to hemodynamic status, intravenous inotropes or vasodilators. Revascularization via percutaneous coronary intervention (PCI) and secondary prevention with dual antiplatelet therapy and statins were provided per ACC/AHA guidelines.

Vericiguat was initiated within 48 hours of admission at a dose of 2.5 mg once daily. Dose escalation followed standard prescribing recommendations as tolerated, with uptitration to 5 mg and subsequently 10 mg once daily at approximately 2-week intervals based on blood pressure, renal function, and clinical stability. Drug tolerability was assessed during follow-up visits through review of symptoms, blood pressure measurements, renal function, and treatment continuation.

2.3. Outcomes and Statistical Analysis

The primary endpoint was change in NYHA functional class from baseline to 3

months.

Secondary endpoints included changes in left ventricular ejection fraction, estimated glomerular filtration rate and vericiguat discontinuation due to adverse effects.

Repeated measurements across baseline, 7 days, and 3 months were analyzed using repeated-measures analysis of variance (ANOVA) for continuous variables and Cochran's Q test for categorical variables, followed by pairwise comparisons where appropriate.

Patients were systematically evaluated during the index admission, at 7 days post-discharge, and at 3 months post-discharge. Assessments included NYHA functional classification, blood pressure, renal function, serum electrolytes, and LVEF estimation via echocardiography.

Statistical analysis was performed using SPSS version 22.0. Categorical data were reported as counts and percentages, and comparisons were made using chi-square tests. Continuous variables were presented as mean ± standard deviation (SD). For normally distributed data exhibiting homogeneity of variance, paired sample t-tests were utilized for within-patient comparisons across timepoints. A two-sided P-value < 0.05 was considered statistically significant. Because 5 patients died prior to the 3-month follow-up, they were excluded from the longitudinal paired comparative analysis, leaving a final analytic cohort of 101 survivors.

3. Results

3.1. Baseline Characteristics

Of the 106 patients enrolled and treated with vericiguat, 5 patients died during the index admission or follow-up period and were excluded from the 3-month comparative outcomes analysis. The final baseline characteristics for the remaining 101 patients are detailed in **Table 1**. The cohort was predominantly male (85%) with a mean age of 56 ± 10 years. Comorbidities were common, including chronic kidney disease (CKD stage III-V) in 78%, diabetes in 67%, and hypertension in 45%. All 101 patients (100%) in the analytic cohort underwent PCI. The severity of decompensation was high: all patients presented with NYHA class III (69%) or IV (31%) symptoms, 80% experienced cardiogenic shock requiring inotropic support, and 100% required intravenous diuretics. Echocardiography indicated HFrEF in 85% and mildly reduced EF (HFmrEF) in 15%. All 101 patients (100%) in the analytic cohort underwent PCI. The severity of decompensation was high: all patients presented with NYHA class III (69%) or IV (31%) symptoms, 80% experienced cardiogenic shock requiring inotropic support, and 100% required intravenous diuretics. Echocardiography indicated HFrEF in 85% and mildly reduced EF (HFmrEF) in 15%.

145 patients screened De novo ADHF following AMI 106 consecutive patients Enrolled & treated with vericiguat 5 patients died (Excluded from comparison) 101 survivors Included in 3-month follow-up.

Table 1. Baseline characteristics.

Characteristics	Heart failure following MI
Cases	101
Gender (male %)	85 (85%)
Age (years)	56 ± 10
Systolic BP	106 ± 15
Diastolic BP	70 ± 9
Heart Rate	110 ± 18
Medical History	
Hypertension	45 (45%)
Diabetes	67 (67%)
CKD (III-V)	78 (78%)
Cardiogenic shock requiring inotropic support	80 (80%)
Patient on injectable vasodilator	20 (20%)
Patient on intravenous diuretics	101 (100%)
Percutaneous coronary angioplasty (PCI)	101 (100%)
NYHA functional class	
III	69 (69%)
IV	32 (31%)
Hear failure classification by ejection fraction	
HFrEF	85 (85%)
HFmrEF	16 (15%)
Medication	
Angiotensin receptor-neprilysin inhibitor (ARNI)	20 (20%)
Beta blockers	60 (60%)
Mineralocorticoid receptor antagonist (MRA)	70 (70%)
SGLTi	90 (90%)
Ivabradine	80 (80%)
Vericiguat	101(100%)
Intravenous inotropic	80 (80%)
Intravenous vasodilator	26 (26%)
Inravenous diuretics	101 (100%)

3.2. Clinical and Laboratory Changes over Follow-Up

Table 2 summarizes the clinical and laboratory trajectories of the 101 survivors. Vericiguat therapy was well-tolerated over the follow-up period, with no reported adverse effects necessitating drug withdrawal. In the total enrolled cohort of 106 patients, there were 4 deaths (4%) observed by 7 days post-discharge and 1 additional death by 3 months.

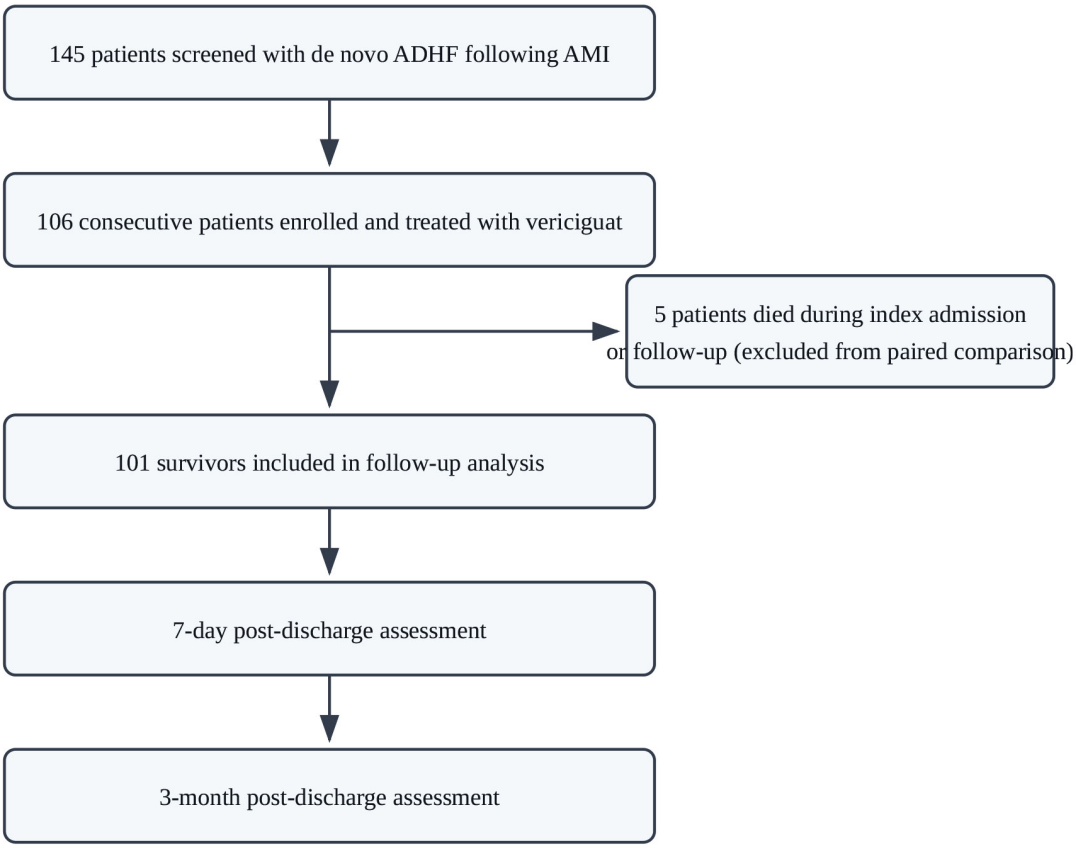

Figure 1. Study flow diagram. Depicting the selection, treatment, and final analytic inclusion of patients presenting with de novo acute decompensated heart failure (ADHF) after acute myocardial infarction (AMI).

Table 2. Effect of vericiguat on post AMI de novo ADHF.

Variables	Prior to medications	At 7 days after discharge	At 3 months after discharge	P value
NYHA STATUS				P < 0.01
I			90 (90%)	
II		90 (90%)	11 (10%)	
III	69 (69%)	11 (10%)		
IV	32 (31%)			
Hypotension	80 (80%)	35 (35%)	10 (10%)	P < 0.01
Ejection fraction (%)	30.5 ± 8.5	32 ± 6.8	36.6 ± 6.4	P < 0.05
eGFR	45 ± 14	50 ± 12	66 ± 18	P < 0.05
Serum sodium	131 ± 8	133 ± 5	135 ± 7	P = ns
Serum potassium	3.6 ± 1.8	3.4 ± 1.9	3.9 ± 1.7	P = ns
Adverse effects leading to vericiguat withdrawal	N/A	Nil	Nil	P = ns

*P values denote comparisons between baseline and 3 months. NS = not significant. Dashes indicate data not reported at that time point. Deaths (n = 5) were reported among the initial 106 treated patients but excluded from these paired comparisons.

Among the survivors, significant improvement was observed in functional capacity; baseline NYHA classes were exclusively III and IV, transitioning to predominantly class II (90%) by both 7 days and 3 months ($P < 0.01$). The incidence of clinical hypotension diminished markedly from 80% at admission to 35% at 7 days, and 10% by 3 months ($P < 0.01$).

Echocardiographic and laboratory assessments also demonstrated improvement. Mean LVEF improved from 30.5% ± 8.5% at baseline to 36.6% ± 6.4% at 3 months ($P < 0.05$), and renal function, assessed by estimated glomerular filtration rate (eGFR), increased from 45 ± 14 to 66 ± 18 ($P < 0.05$). Serum sodium and potassium levels remained broadly stable without statistically significant changes. Correspondingly, reliance on diuretics diminished substantially, with active diuretic prescriptions dropping from 100% at baseline to 22% at 3 months ($P < 0.01$), while ACEI/ARNI use increased from 20% to 90% ($P < 0.01$). These temporal trends are illustrated in Figure 2 and the additional laboratory and treatment visualizations in Figure 3.

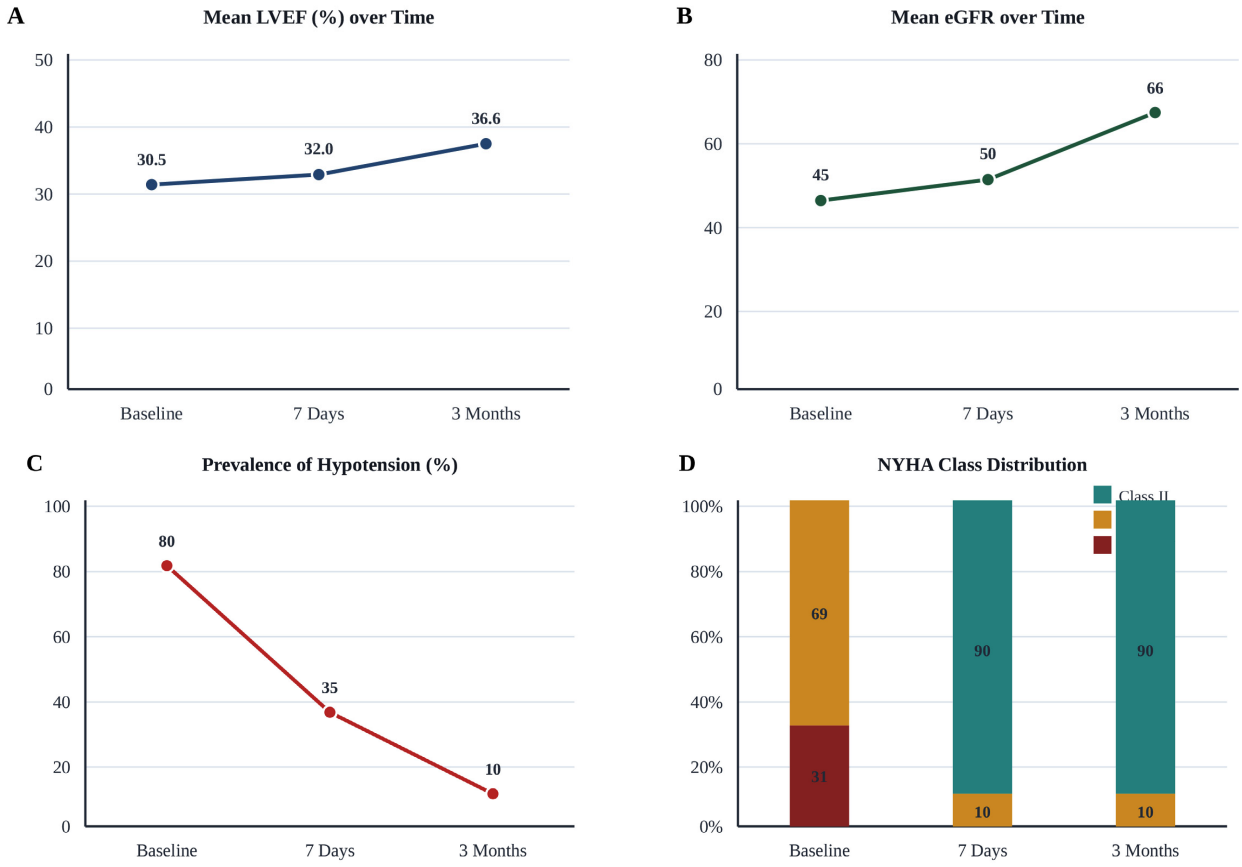

Figure 2. Clinical and Hemodynamic Changes over Time. Shown are trends across baseline, 7 days post-discharge, and 3 months post-discharge in the analytic survivor cohort (n = 101) receiving vericiguat and standard GDMT.

4. Discussion

This pilot cohort suggests that early vericiguat use in de novo ADHF after AMI is

feasible within a contemporary care pathway and was associated with a consistent pattern of clinical improvement over 3 months. Among survivors, symptoms improved rapidly, hypotension became less frequent, mean LVEF increased, and renal indices improved, while no adverse effects prompted drug withdrawal. Taken together, these findings support the practical observation that vericiguat can be introduced early in selected post-infarction patients despite substantial hemodynamic vulnerability at presentation.

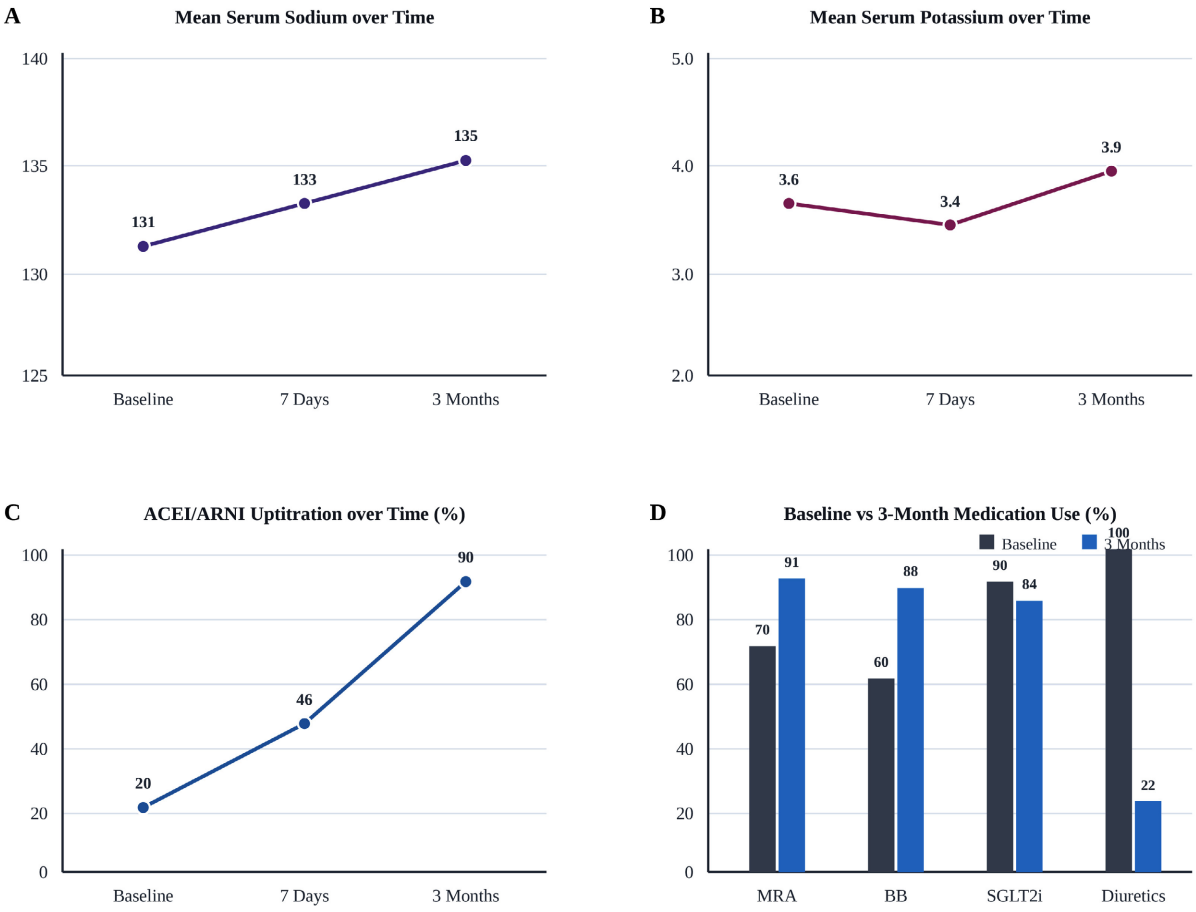

Figure 3. Laboratory and Treatment Trajectories. Panel A shows mean serum sodium at baseline, 7days, and 3 months; Panel B shows mean serum potassium across the same time points. Panel C depicts the increase in ACEI/ARNI use across follow-up. Panel D compares medication use at baseline and 3 months for MRA, beta-blockers (BB), SGLT2 inhibitors, and diuretics; 7-day values for these agents were not reported in the source dataset and are therefore not displayed.

The clinical context of this study differs importantly from that of the VICTORIA trial, which enrolled patients with chronic HFrEF and recent worsening heart failure rather than de novo post-AMI decompensation [6]. Our cohort therefore addresses a narrower and more unstable population, one in whom initiation of disease-modifying therapy is often limited by congestion, renal dysfunction, and blood-pressure lability [1]-[3]. The observed decline in hypotension, together with stable sodium and potassium levels, is clinically reassuring, but should not

be interpreted as proof of a specific causal hemodynamic effect of vericiguat. Rather, these data suggest compatibility of early vericiguat exposure with short-term stabilization in a setting where evidence remains sparse. Current guidelines support vericiguat for selected patients with high-risk HFrEF despite GDMT [4], but do not establish its role in de novo post-AMI heart failure.

Interpretation must also account for the broader recovery pathway. Uptitration of foundational therapy was marked, with ACEI/ARNI, MRA, and beta-blocker use increasing over follow-up, while dependence on diuretics fell sharply. Universal PCI among the analytic survivors and expected myocardial recovery after infarction almost certainly contributed to improvements in symptoms, ventricular function, and renal perfusion [3] [4]. Accordingly, this manuscript describes outcomes observed during treatment with vericiguat plus GDMT and revascularization, not the isolated effect of vericiguat itself.

The mortality burden in the treated cohort and the exclusion of 5 deaths from paired follow-up analyses emphasize the severity of illness and the likelihood of survivor bias. Even so, the internally consistent direction of change across functional class, LVEF, eGFR, blood-pressure tolerance, and medication use provides a rationale for prospective study. A definitive assessment will require controlled trials with prespecified end points, standardized titration, and full accounting of early deaths and intolerance [4] [6].

5. Limitations

The observations reported here are subject to significant limitations. The study was conducted at a single center, utilized a retrospective design, and lacked a randomized control arm, precluding definitive conclusions regarding the specific efficacy of vericiguat independent of GDMT and PCI. Most importantly, the exclusion of the 5 patients who died from the primary longitudinal comparative analysis introduces clear survivor bias. This likely overestimates the degree of clinical improvement in the remaining cohort. Consequently, these findings must be interpreted solely as hypothesis-generating associations rather than proof of therapeutic efficacy.

6. Conclusions

Early initiation of vericiguat alongside standard GDMT for de novo ADHF following AMI was well-tolerated in this pilot cohort and was associated with short-term clinical stabilization and hemodynamic improvement. These preliminary findings highlight the feasibility of early vericiguat deployment in high-risk, acute post-infarction settings, but mandate larger, randomized, placebo-controlled trials to robustly evaluate safety, efficacy, and outcome benefits.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Abbreviations

ACEI, angiotensin-converting enzyme inhibitor;
ADHF, acute decompensated heart failure;
AMI, acute myocardial infarction;
ARNI, angiotensin receptor-neprilysin inhibitor;
GDMT, guideline-directed medical therapy;
HFmrEF, heart failure with mildly reduced ejection fraction;
HFrEF, heart failure with reduced ejection fraction;
LVEF, left ventricular ejection fraction;
MRA, mineralocorticoid receptor antagonist;
NT-proBNP, N-terminal pro-B-type natriuretic peptide;
NYHA, New York Heart Association;
PCI, Percutaneous Coronary Intervention;
SGLT2, sodium-glucose cotransporter-2.