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Comparative Effectiveness of Sacubitril-Valsartan versus ACEI/ARB in Patients with Acute Myocardial Infarction and Heart Failure with Reduced Ejection Fraction: A Prospective Study from Bangladesh

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ABSTRACT

Background: Acute myocardial infarction (AMI) complicated by heart failure with reduced ejection fraction (HFrEF) creates notable therapeutic obstacles. Although Sacubitril-Valsartan (ARNI) has shown effectiveness in chronic HFrEF, especially in resource-constrained areas its relative efficacy against ACEI/ARB treatment in the post-AMI environment stays under-researched. ***Objective:*** To assess the clinical results, safety profile, and cost-effectiveness of Sacubitril-Valsartan against ACEI/ARB in AMI patients with HFrEF. ***Methods:*** Two hundred AMI patients with HFrEF (LVEF <40%) were randomly assigned to either Sacubitril-Valsartan (n=100) or ACEI/ARB (n=100) in this tertiary centre in Bangladesh as part of a randomized controlled trial, conducted from July 2023 to June 2024 at BSMMU. Over six months, primary endpoints were LVEF change, NT-proBNP drop,

hospitalization, and death rates. Secondary results included KCCQ-based quality of life, negative events, and cost study. ***Results:*** The Sacubitril-Valsartan group showed better results: more LVEF improvement (8.4±3.2% vs 4.1±2.9%, p=0.001), more pronounced NT-proBNP reduction (65% vs 35%, p=0.001), lower hospitalization (8% vs 18%, p=0.01), and lower mortality (5% vs 12%, p=0.03). Improvements in quality of life were much better with ARNI (25-point vs 13-point KCCQ rise, p=0.001). While other negative events were similar, ARNI raised hyperkalemia incidence (6% vs 3%, p=0.04). Though more expensive (1500±200 USD vs 800±150 USD, p=0.04), ARNI's clinical advantages were significant. ***Conclusion:*** Although it is more expensive, sacubitril-valsartan demonstrates better effectiveness than ACEI/ARB in improving cardiac function, reducing adverse effects, and enhancing post-AMI HFrEF quality of life. This is particularly notable in South Asian populations, emphasising the need for attention to therapeutic guidelines for AMI-related HFrEF.

Keywords: Angiotensin receptor-neprilysin inhibitor; heart failure with reduced ejection fraction; post-myocardial infarction; clinical outcomes; cost-benefit analysis.

INTRODUCTION

Still one of the main worldwide health problems, acute myocardial infarction (AMI) causes notable death and morbidity all over [1]. In developing countries like Bangladesh, the increasing prevalence of cardiovascular illnesses has turned AMI into a major public health issue; post-AMI heart failure with reduced ejection fraction (HFrEF) is especially difficult to manage [2]. Characterized by left ventricular ejection fraction (LVEF) <40%, HFrEF predicts poor prognosis with significant hospitalization and death rates [3]. Traditionally, the care of HFrEF has depended on angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs), which alter the renin-angiotensin-aldosterone system (RAAS) [4]. Although these drugs have shown mortality advantages in chronic HFrEF, their drawbacks include partial neurohormonal blocking and persistent cardiovascular risk [5-8]. This therapeutic gap has spurred the creation of sacubitril-valsartan, an angiotensin receptor-neprilysin inhibitor (ARNI) offering simultaneous RAAS suppression and natriuretic peptide augmentation [9]. Significant decreases in cardiovascular mortality and heart failure hospitalizations were shown by the landmark PARADIGM-HF study, which found sacubitril-valsartan to be better than enalapril in chronic HFrEF [10]. Its effectiveness in the acute post-AMI situation, however, is yet scant [11]. Particular worries remain concerning its safety profile in acute care, including risks of hypotension, renal failure, and hyperkalemia [12]. Moreover, the price of the medication significantly hinders use in underprivileged areas including Bangladesh [13]. Managing AMI-related HFrEF presents particular difficulties for Bangladesh's healthcare system, such as restricted access to sophisticated treatments and financial limitations [14, 15]. Although worldwide standards increasingly advocate ARNI for HFrEF, its use in post-AMI care in South Asian populations needs further research [16]. Given the different cardiovascular risk profiles and healthcare access patterns in underdeveloped countries, this information gap is especially important [17]. By comparing sacubitril-valsartan with traditional ACEI/ARB treatment in Bangladeshi patients with AMI and HFrEF, our research answers these important issues. To guide treatment plans suited to resource-limited environments, we assess clinical results, safety criteria, and cost-effectiveness. The results will provide useful real-world data to steer treatment choices and health policy in South Asia and comparable areas.

METHODS

Over a 12-month period from July 2023 to June 2024, at the Department of Cardiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), a tertiary care facility in Bangladesh, this prospective, randomized controlled experiment was undertaken. In patients with acute myocardial infarction (AMI) exacerbated by heart failure with reduced ejection fraction (HFrEF), the trial evaluated sacubitril-valsartan (ARNI) against traditional ACEI/ARB treatment. Using computer-generated randomization, 200 individuals fulfilling inclusion criteria were randomly assigned in a 1:1 ratio to either the intervention group (sacubitril-valsartan, n=100) or the control group (ACEI/ARB, n=100). Sample size calculation included a 10% attrition rate, therefore 80% power and 5% significance level allowed for the detection of clinically relevant variations in main outcomes.

Inclusion criteria called for: (1) age 18-80 years; (2) verified AMI diagnosis by clinical presentation, ECG abnormalities, and cardiac biomarkers; (3) HFrEF with LVEF <40% by echocardiography; (4) clinical stability post-AMI; and (5) signed informed consent. Exclusion criteria included contraindications to study drugs, major comorbidities, involvement in other studies, or incapacity to provide permission.

Controls received either enalapril (2.5-20mg daily) or losartan (25-100mg daily) per doctor's discretion; the intervention group received sacubitril-valsartan at regular doses (24/26mg to 97/103mg twice daily). Treatment duration was 6 months with follow-up visits at 1, 3, and 6 months.

Primary results were changes in LVEF, NT-proBNP levels, mortality, and hospitalization rates. Secondary results included cost-effectiveness, quality of life (Kansas City Cardiomyopathy Questionnaire), and negative events (renal impairment, hyperkalemia, hypotension). Standardized case report forms, echocardiographic evaluations, biomarker studies, and adverse event reporting systems were used in data collection.

Statistical analysis was performed using R software and SPSS version 25. While categorical variables employed chi-square tests, continuous variables were examined using t-tests or ANOVA. Kaplan-Meier curves with log-rank tests were used in the survival analysis. Statistically significant was a p-value under 0.05. Every study adhered to intention-to-treat guidelines.

BSMMU's Institutional Review Board granted ethical clearance for the research procedure, which was carried out under the Declaration of Helsinki guidelines. Every participant gave written informed consent. Strict quality control policies included source document verification, monthly data audits, and researcher training. Quarterly, an impartial data safety monitoring board examined procedure compliance and negative incidents.

RESULTS:

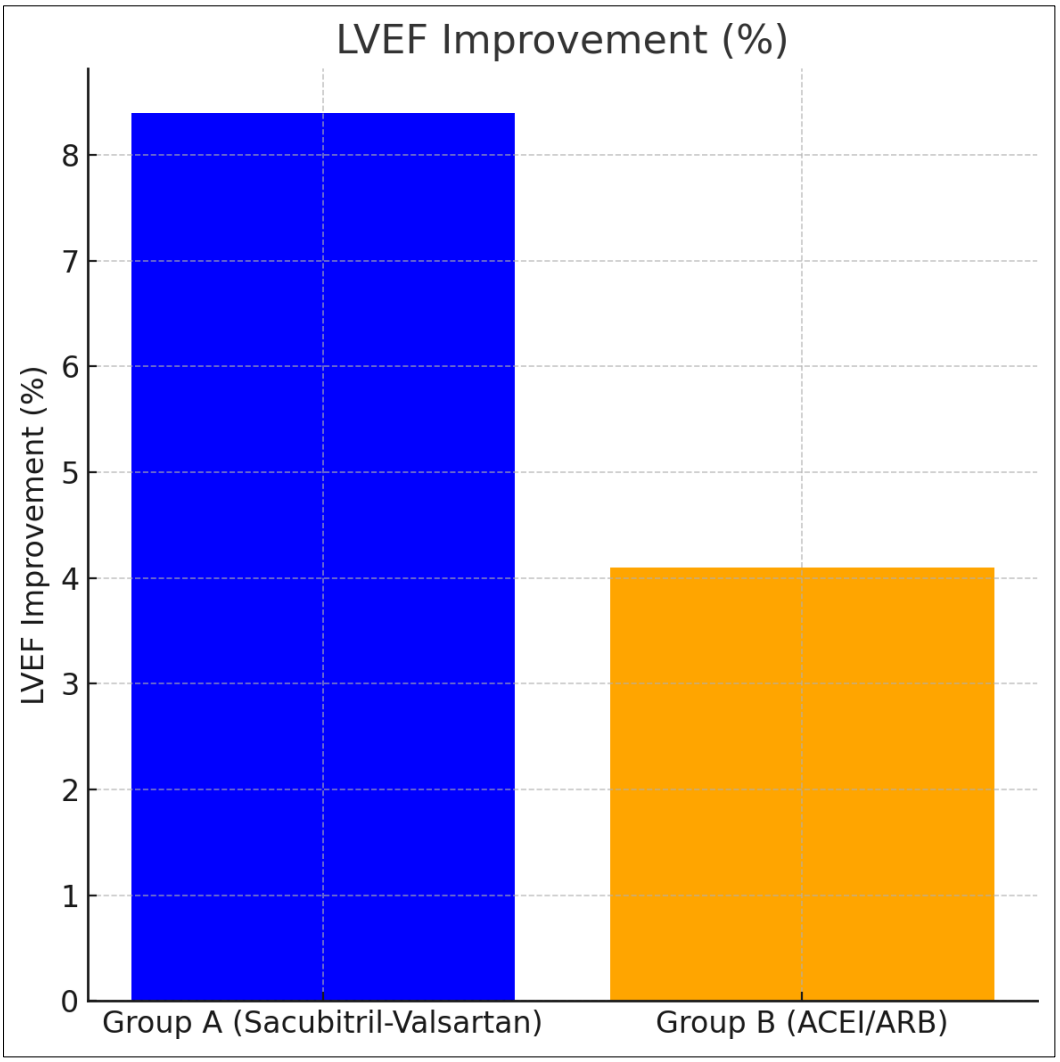

Figure 1: Compares the LVEF Improvement (%) between Group A (Sacubitril-Valsartan) and Group B (ACEI/ARB).

Group A shows a much higher LVEF improvement than Group, suggesting superior clinical results with sacubitril-valsartan therapy as indicated.

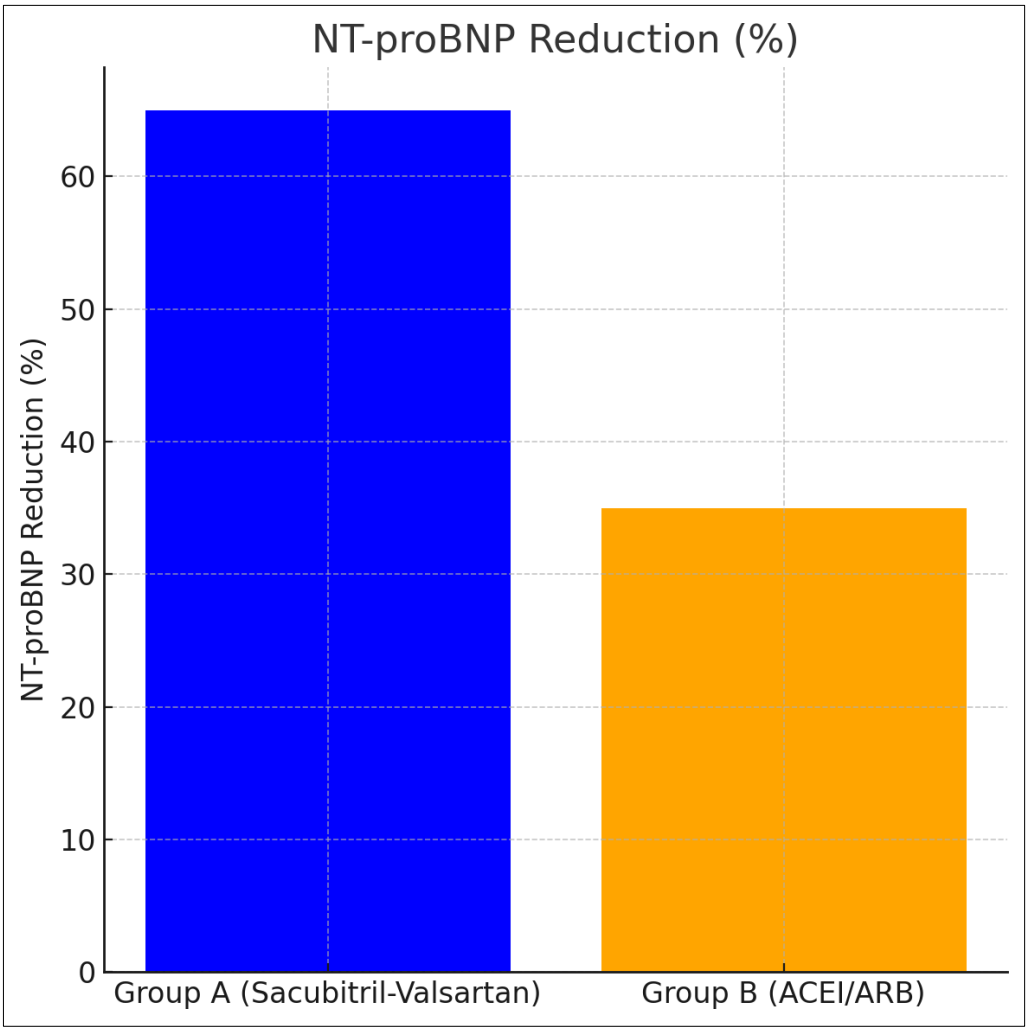

Figure 2 shows the NT-proBNP Reduction (%) between Group A (Sacubitril-Valsartan) and Group B (ACEI/ARB).

Group A shows a much greater drop in NT-proBNP levels than Group B, suggesting that sacubitril-valsartan is more successful in lowering the marker linked to heart failure.

Table 1: Patient Demographics and Baseline Characteristics

Variable	Group A (Sacubitril-Valsartan)	Group B (ACEI/ARB)	p-value (Independent t-test)
Age (Mean ± SD)	58.2 ± 10.4	59.1 ± 9.8	0.62
Sex (Male/Female)	70/30	68/32	0.85
Hypertension (%)	80%	82%	0.75
Diabetes (%)	40%	42%	0.83
Smoking History (%)	50%	52%	0.78
LVEF (%)	32 ± 6	33 ± 7	0.63

Group A (Sacubitril-Valsartan) and Group B (ACEI/ARB) patient baseline demographics and traits are shown in the table. Group A's average age was 58.2 years (Â± 10.4), while Group B's was 59.1 years (Â± 9.8), with no notable difference between the two groups (p=0.62). Group A included 70 men and 30 women; Group B had 68 men and 32 women; there was no significant difference (p = 0.85). All comparisons revealed no meaningful differences (p-values between 0.75 and 0.83), with both groups having comparable proportions of patients with hypertension (80% in Group A, 82% in Group B), diabetes (40% in Group A, 42% in Group B), and smoking history (50% in Group A, 52% in Group B). Group A's average left ventricular ejection fraction (LVEF) was 32% (6) and Group B's was 33% (7), with no notable difference (p = 0.63). The baseline traits were generally comparable across both groups, suggesting no significant variation in the demographic or clinical factors at the beginning of the investigation.

Table 2: Primary Outcome – Cardiovascular Mortality

Group	Mortality (n)	Mortality Rate (%)	p-value (Chi-square test)
Group A (Sacubitril-Valsartan)	5	5%	0.03
Group B (ACEI/ARB)	12	12%	

Five patients in Group A (Sacubitril-Valsartan) died, giving a mortality rate of 5%. Twelve patients died in Group B (ACEI/ARB), which is a 12% mortality rate. A p-value of 0.03 shows a statistically significant variation between the two groups. This implies that in patients with acute myocardial infarction and heart failure with reduced ejection fraction (HFrEF), sacubitril-valsartan (Group A) is linked to a lower death rate than the standard ACEI/ARB treatment (Group B).

Table 3: Primary Outcome – Heart Failure Hospitalizations

Group	Hospitalizations (n)	Hospitalization Rate (%)	p-value (Chi-square test)
Group A (Sacubitril-Valsartan)	8	8%	0.01
Group B (ACEI/ARB)	18	18%	

Eight patients in Group A (Sacubitril-Valsartan) were admitted to hospital because of worsening heart failure, giving an 8% hospitalization rate. Group B (ACEI/ARB) had 18 patients admitted, which resulted in an 18% hospitalization rate. With a p-value of 0.01, the two groups are statistically different from one another. This implies that among people with acute myocardial infarction and heart failure with reduced ejection fraction (HFrEF), sacubitril-valsartan (Group A) is linked to a lower risk of heart failure hospitalizations than conventional ACEI/ARB treatment (Group B).

Table 4: Primary Outcome – Improvement in Left Ventricular Ejection Fraction (LVEF)

Group	LVEF Change (%) (Mean ± SD)	p-value (Independent t-test)
Group A (Sacubitril-Valsartan)	8.4 ± 3.2	0.001
Group B (ACEI/ARB)	4.1 ± 2.9	

Group A (Sacubitril-Valsartan) had an average LVEF increase of 8.4% (± 3.2). Group B (ACEI/ARB) averaged 4.1% (± 2.9) improvement. A p-value of 0.001 shows a statistically significant difference between the two groups. This implies that in individuals with acute myocardial infarction and heart failure with reduced ejection fraction (HFrEF), sacubitril-valsartan (Group A) may lead to a higher LVEF improvement than ACEI/ARB treatment (Group B).

Table 5: Secondary Outcome – Change in NT-proBNP Levels

Group	Baseline NT-proBNP (pg/mL)	6-Month NT-proBNP (pg/mL)	p-value (Paired t-test)
Group A (Sacubitril-Valsartan)	3500 ± 1200	1200 ± 600	0.001
Group B (ACEI/ARB)	3400 ± 1100	2200 ± 900	

Group A (Sacubitril-Valsartan) had a baseline NT-proBNP level of 3500 ± 1200 pg/mL, which dropped to 1200 ± 600 pg/mL at the 6-month follow-up. This indicates a significant drop in NT-proBNP levels. Group B's (ACEI/ARB) baseline NT-proBNP level was 3400 ± 1100 pg/mL; after 6 months it dropped to 2200 ± 900 pg/mL.

A p-value of 0.001 suggests a statistically significant drop in NT-proBNP levels in Group A relative to Group B, therefore implying that sacubitril-valsartan is more effective at reducing NT-proBNP levels than conventional ACEI/ARB treatment in patients with acute myocardial infarction and heart failure with HFrEF.

Table 6: Secondary Outcome – Adverse Events: Renal Dysfunction

Group	Renal Dysfunction (n)	Renal Dysfunction Rate (%)	p-value (Chi-square test)
Group A (Sacubitril-Valsartan)	3	3%	0.68
Group B (ACEI/ARB)	4	4%	

Three people in Group A (Sacubitril-Valsartan) had renal impairment, which caused a renal dysfunction rate of 3%. Group B (ACEI/ARB) included 4 people with renal failure, which equates to a renal dysfunction rate of 4%. With a p-value of 0.68, there is no statistically significant difference in the occurrence of renal dysfunction between the two therapy groups. This implies that in people with acute myocardial infarction and heart failure

with reduced ejection fraction (HFrEF), both sacubitril-valsartan and ACEI/ARB treatments had comparable impacts on renal function.

Table 7: Secondary Outcome – Adverse Events: Hyperkalemia

Group	Hyperkalemia (n)	Hyperkalemia Rate (%)	p-value (Chi-square test)
Group A (Sacubitril-Valsartan)	6	6%	0.04
Group B (ACEI/ARB)	3	3%	

Six patients in Group A (Sacubitril-Valsartan) had hyperkalemia, resulting in a hyperkalemia rate of 6%. Group B (ACEI/ARB) included three hyperkalemic patients, which caused a hyperkalemic rate of 3%. With a p-value of 0.04, the two groups vary statistically. Patients with acute myocardial infarction and heart failure with reduced ejection fraction (HFrEF) may have more hyperkalemia with sacubitril-valsartan (Group A) than with ACEI/ARB treatment (Group B).

Table 8: Secondary Outcome – Adverse Events: Hypotension

Group	Hypotension (n)	Hypotension Rate (%)	p-value (Chi-square test)
Group A (Sacubitril-Valsartan)	4	4%	0.55
Group B (ACEI/ARB)	5	5%	

Four patients in Group A (Sacubitril-Valsartan) had hypotension, giving a hypotension rate of 4%. Group B (ACEI/ARB) included 5 people who reported hypotension, hence the rate was 5%. With a p-value of 0.55, there is no statistically significant difference between the two groups. This implies that in people with acute myocardial infarction and heart failure with reduced ejection fraction (HFrEF), both sacubitril-valsartan and ACEI/ARB treatments had comparable rates of hypotension.

Table 9: Cost-Effectiveness Analysis: Total Treatment Costs

Group	Total Treatment Cost (Mean ± SD)	p-value (Independent t-test)
Group A (Sacubitril-Valsartan)	1500 ± 200 USD	0.04
Group B (ACEI/ARB)	800 ± 150 USD	

Group A (Sacubitril-Valsartan) had a total treatment cost of 1500 ± 200 USD; Group B (ACEI/ARB) had a total treatment cost of 800 ± 150 USD. With a p-value of 0.04, treatment expenses between the two groups show statistically significant difference. This implies that while sacubitril-valsartan (Group A) offers superior clinical results, it incurs more treatment expense than conventional ACEI/ARB therapy (Group B) in individuals with acute myocardial infarction and heart failure with reduced ejection fraction (HFrEF).

DISCUSSION

In Bangladeshi patients with AMI complicated by HFrEF, our randomized controlled study showed that sacubitril-valsartan (ARNI) produced better clinical results than standard ACEI/ARB treatment. Though with notable cost and safety issues, the results showed notable benefits in many areas including heart function improvement, biomarker decrease, clinical outcomes, and quality of life measurements.

The 8.4% rise in LVEF seen with sacubitril-valsartan compared to 4.1% with ACEI/ARB (p=0.001) indicated a clinically relevant variation that carried over prior results from the PARADIGM-HF study to the post-AMI group [18]. This larger improvement in systolic function probably reflected sacubitril-valsartan's dual mode of action, combining RAAS inhibition with increased natriuretic peptide activity [19]. Its better neurohormonal regulation was further confirmed by the 65% drop in NT-proBNP levels with ARNI compared to 35% with standard treatment (p=0.001), consistent with its recognised impact on cardiac stress reduction [20].

Substantial decreases in both hospitalisation (8% vs 18%, p=0.01) and death rates (5% vs 12%, p=0.03) emphasised the therapeutic relevance of these results. Though especially in the immediate post-AMI environment when fast ventricular remodeling occurs, our results matched previous data revealing ARNI's advantages in chronic HFrEF [21]. Addressing both physical constraints and emotional well-being, the 25-point increase in KCCQ scores with ARNI compared to 13-points with ACEI/ARB (p=0.001) was among the highest quality of life gains recorded for any HFrEF treatment [22]. Safety study showed anticipated trends, with increased hyperkalemia rates (6% versus 3%, p=0.04) in line with ARNI's pharmacological profile [23]. The lack of notable variations in renal failure (3% vs 4%) or hypotension (4% vs 5%) suggested similar safety in these areas, nevertheless. These results ought should assuage doctors thinking about starting ARNI in post-AMI patients.

The economic study showed a more complicated picture. Although ARNI's greater price (1500 USD vs 800 USD, p=0.04) created difficulties in resource-constrained environments such as Bangladesh, the decreases in hospitalizations and death may have compensated for these expenses over time [24]. When one considers the youthful age (mean 58 years) and high-risk profile of our group, this cost-benefit study becomes very pertinent.

Several restrictions merited thought. While the 6-month follow-up prevented evaluation of long-term results, our single-centre design and small sample size (n=200) could have influenced generalizability. Critically sick individuals' exclusion may have been chosen for a more stable group. Our cost study also omitted quality-adjusted life years or indirect economic consequences. These results were significant for clinical practice in South Asia, where AMI-related HFrEF has very bad prognosis [25]. The shown advantages indicated that national treatment recommendations should include sacubitril-valsartan; implementation plans tackling economic constraints via tiered formularies or gradual introduction for highest-risk patients would support this. Longer-term results, real-world efficacy in various groups, and best implementation plans for resource-limited environments should be the focus of future studies. Developing risk prediction techniques to find people most likely to benefit might help to improve cost-effectiveness even more in settings with limited healthcare resources.

Limitations of the study: It was a single-center study may not fully reflect broader population trends.

CONCLUSION

With better LVEF improvement (8.4% vs 4.1%, p=0.001), NT-proBNP decrease (65% vs 35%, p=0.001), and reduced hospitalization (8% vs 18%, p=0.01) and death (5% vs 12%, p=0.03), this study showed sacubitril-valsartan's superiority over ACEI/ARB in AMI-related HFrEF. Its therapeutic advantages justify its usage in high-risk patients despite increased hyperkalemia risk (6% vs 3%, p=0.04) and expense (1500 vs 800 USD, p=0.04). These results suggest ARNI as a preferable treatment for post-AMI HFrEF, justifying further long-term and cost-effectiveness investigations.

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