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Role of Angiotensin Converting Enzyme Inhibitors and Angiotensin Receptor Blockers in Hypertensive Patients after Myocardial Infarction or Stroke

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ABSTRACT

Background: Hypertensive patients who have experienced myocardial infarction (MI) or ischemic stroke remain at high risk for recurrent cardiovascular events. Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) are key components of secondary prevention through inhibition of the renin–angiotensin system. However, comparative real-world evidence from Indian clinical practice is limited. **Methods:** This prospective observational study included 410 hypertensive patients discharged after MI or ischemic stroke from a tertiary care hospital. Participants received either ACEIs (n = 205) or ARBs (n = 205) and were followed for 12 months. The primary outcome was major adverse cardiovascular events (MACE), including cardiovascular death, recurrent MI, recurrent stroke, and hospitalization for heart failure. Secondary outcomes included changes in left ventricular ejection fraction (LVEF), renal function, blood pressure control, and drug tolerability. **Results:** Baseline characteristics were comparable between groups. MACE occurred in 16.6% of ACEI-treated patients and 22.9% of ARB-treated patients. After adjustment for clinical variables, ACEI therapy was associated with a significantly lower risk of adverse cardiovascular events, particularly in post-MI patients. Improvement in LVEF was greater with ACEIs ($p = 0.015$). Renal function and blood pressure control were similar. Cough was more frequent with ACEIs, whereas ARBs showed better tolerability. **Conclusion:** ACE inhibitors were associated with improved cardiovascular outcomes and ventricular recovery after MI. In post-stroke patients, ACEIs and ARBs showed comparable effectiveness. Individualized therapy based on clinical profile and tolerability remains essential.

Keywords: Hypertension, Angiotensin-converting enzyme inhibitors, Angiotensin receptor blockers, Major adverse cardiovascular events, Secondary prevention, Ventricular remodeling.

INTRODUCTION:

Hypertension is the most important modifiable risk factor for cardiovascular and cerebrovascular disease and plays a central role in the development of myocardial infarction and ischemic stroke.[1] Survivors of myocardial infarction or stroke with coexisting hypertension remain at persistently high risk of recurrent cardiovascular events, heart failure, renal dysfunction, and mortality despite advances in acute management and secondary prevention strategies.[2] Long term blood pressure control and attenuation of neurohormonal activation are therefore essential components of secondary prevention in these high-risk patients. Pharmacological inhibition of the renin–angiotensin system (RAS) has been shown to reduce cardiovascular morbidity and mortality by modulating vascular tone, myocardial remodeling, endothelial dysfunction, and renal hemodynamics.[3] Large outcome trials and meta-analyses have consistently demonstrated that effective antihypertensive therapy reduces the risk of stroke, myocardial infarction, heart failure, and cardiovascular death.[4] Angiotensin-converting enzyme inhibitors (ACEIs) have been extensively studied and are recommended as first-line agents in patients with hypertension and established cardiovascular disease. Randomized controlled trials in post-myocardial infarction populations have shown that ACEIs reduce mortality, prevent adverse left ventricular remodeling, and delay the progression to heart failure.[5] The cardiovascular benefits of ACEIs extend beyond blood pressure reduction and are mediated through suppression of angiotensin II formation and augmentation of bradykinin-dependent vasodilatory and endothelial protective effects.[6] Angiotensin receptor blockers (ARBs) provide an alternative approach to RAS inhibition by selectively blocking the angiotensin II type-1 receptor, thereby preventing angiotensin II mediated vasoconstriction, inflammation, and fibrosis without affecting bradykinin metabolism.[7] Unlike ACEIs, ARBs inhibit angiotensin II signaling irrespective of its pathway of generation, including non-ACE pathways such as chymase, which may remain active during chronic ACEI therapy, a phenomenon commonly referred to as “ACE escape”.[8] Comparative effectiveness studies evaluating ACEIs and ARBs have reported heterogeneous findings. Large real-world cohort studies and propensity-matched analyses have generally demonstrated no significant differences between ACEIs and ARBs with respect to overall mortality, myocardial infarction, and chronic kidney disease outcomes among hypertensive patients.[9] However, certain comparative analyses and meta-analyses have suggested a modest reduction in stroke risk associated

with ARB therapy compared with ACEIs, independent of blood pressure lowering.[10] Evidence from stroke-focused trials has further highlighted the importance of RAS blockade in both primary and secondary stroke prevention. Clinical trials have demonstrated that both ACEIs and ARBs reduce stroke risk beyond their antihypertensive effects, although the magnitude and timing of benefit may vary depending on patient characteristics and drug selection.[11] ARBs such as telmisartan have been postulated to offer additional cerebrovascular protection because of favorable pharmacokinetic properties and potential central nervous system penetration.[12] Despite extensive international literature, prospective real-world data comparing ACEIs and ARBs in hypertensive patients following myocardial infarction or ischemic stroke from Indian tertiary care settings remain limited. Most available studies are retrospective or lack systematic evaluation of combined cardiovascular, functional, and renal outcomes, limiting their applicability to routine clinical practice.[13] In this context, the present prospective observational study was undertaken to compare the clinical outcomes associated with ACE inhibitor and angiotensin receptor blocker therapy in hypertensive patients following myocardial infarction or ischemic stroke. By evaluating major adverse cardiovascular events, left ventricular ejection fraction, renal function, and blood pressure control over a structured one-year follow-up, this study aims to generate real-world evidence to inform optimal selection of RAS inhibitors in secondary cardiovascular and cerebrovascular prevention.

Aim of the Study

To compare the clinical outcomes associated with angiotensin-converting enzyme inhibitor therapy and angiotensin receptor blocker therapy in hypertensive patients following myocardial infarction or ischemic stroke.

Objectives of the Study

- To evaluate the incidence of major adverse cardiovascular events (MACE) in hypertensive patients receiving ACE inhibitors or ARBs following myocardial infarction or ischemic stroke.
- To compare changes in left ventricular ejection fraction among patients treated with ACE inhibitors and ARBs.
- To assess renal function outcomes in both treatment groups during follow-up.
- To evaluate blood pressure control achieved with ACE inhibitor versus ARB therapy over a one-year follow-up period.

Materials and Methods:

This was a prospective, observational cohort study conducted at RKDF Medical College Hospital and Research Centre (RKDFMCH & RC), a tertiary care teaching hospital in India. The study was carried out over a one-year period, with patients enrolled at the time of hospital discharge following myocardial infarction or ischemic stroke and followed prospectively for clinical outcomes. Adult patients with hypertension who were admitted with a diagnosis of myocardial infarction or ischemic stroke and discharged on either an angiotensin-converting enzyme inhibitor (ACEI) or an angiotensin receptor blocker (ARB) were screened for inclusion. A total of 410 patients were included in the final analysis, with 205 patients in the ACEI group and 205 patients in the ARB group.

Inclusion Criteria

- Age ≥18 years.
- Diagnosed hypertension.
- Confirmed diagnosis of myocardial infarction or ischemic stroke based on clinical. features, electrocardiographic findings, cardiac biomarkers, and/or neuroimaging as appropriate.
- Prescription of an ACE inhibitor or angiotensin receptor blocker at the time of hospital discharge.
- Ability to provide informed consent and comply with follow-up.

Exclusion Criteria

- Age <18 years.
- Non-prescription of ACEI or ARB at discharge.

- Documented contraindications to ACEIs or ARBs.
- Incomplete baseline data or anticipated inability to complete follow-up.
- Switching between ACEI and ARB therapy during the follow-up period.

Exposure Definition

Patients were categorized into two groups based on the renin–angiotensin system inhibitor prescribed at discharge:

- **ACEI group (n = 205):** Patients receiving angiotensin-converting enzyme inhibitors such as ramipril, enalapril, or lisinopril, at clinician-determined doses.
- **ARB group (n = 205):** Patients receiving angiotensin receptor blockers such as telmisartan, losartan, or valsartan, at clinician-determined doses.

Drug selection and dose titration were guided by treating physicians in accordance with standard clinical practice. Concomitant medications for secondary prevention, including antiplatelets, statins, beta-blockers, and diuretics, were prescribed as clinically indicated.

Follow-up and Data Collection

Participants were followed for a total duration of 12 months with a structured follow-up schedule at weeks 2, 4, 6, 8, 12, 16, 20, 24, 32, 40, 48, and 56. Follow-up assessments were conducted through outpatient department visits and supplemented by telephonic follow-up when required. At each visit, clinical status, blood pressure measurements, medication adherence, and adverse events were recorded.

Baseline demographic data, clinical characteristics, comorbidities, and relevant laboratory parameters were documented at enrollment. Echocardiographic assessment and renal function tests were performed at baseline and during follow-up as per institutional protocols.

Result:

1. Baseline Characteristics

A total of 410 patients were included in the study, with 205 patients each in the ACE inhibitor and ARB groups. Patients were stratified into post-myocardial infarction (MI) and post-stroke cohorts and followed for 56 weeks.

The baseline demographic and clinical characteristics were well balanced between the two treatment groups. The study population predominantly comprised middle-aged and elderly individuals, with a higher proportion of male patients across most age categories. The highest concentration of patients was observed in the 50–69-year age group.

Baseline systolic and diastolic blood pressure, left ventricular ejection fraction (LVEF), and serum creatinine values were comparable between the ACE inhibitor and ARB groups, indicating adequate baseline comparability and minimizing confounding in outcome assessment.

2. Primary Outcome: Major Adverse Cardiovascular Events (MACE)

During the one year follow-up, major adverse cardiovascular events occurred in 34 patients (16.6%) in the ACE inhibitor group and 47 patients (22.9%) in the ARB group. Overall, ACE inhibitor therapy was associated with a lower incidence of MACE compared with ARBs.

Among post myocardial infarction patients, MACE occurred in 22 patients (21.4%) receiving ACE inhibitors versus 33 patients (32.4%) receiving ARBs, with cumulative event curves demonstrating sustained separation over time. In post-stroke patients, MACE incidence was comparable between treatment groups (11.8% vs 13.6%).

On multivariable analysis adjusting for age, sex, index event, diabetes mellitus, and baseline left ventricular ejection fraction, ACE inhibitor use remained independently associated with a lower risk of MACE, while post-myocardial infarction status, diabetes, and lower baseline LVEF emerged as independent predictors of adverse cardiovascular outcomes.

Post-Myocardial Infarction Patients

In post-MI patients, the incidence of major adverse cardiovascular events (MACE) was significantly lower in the ACE inhibitor group compared with the ARB group ($p < 0.05$). The cumulative MACE curve demonstrated earlier and sustained separation between the two treatment arms over the 56-week follow-up period.

The absolute number of patients experiencing MACE was also lower in the ACE inhibitor group, supporting both relative and absolute risk reduction.

Post-Stroke Patients

In contrast, among post-stroke patients, the cumulative incidence and absolute number of MACE events were comparable between the ACE inhibitor and ARB groups, with no statistically significant difference ($p > 0.05$).

3. Secondary Outcomes

3.1 Left Ventricular Ejection Fraction (LVEF)

Post-Myocardial Infarction Patients

Post-MI patients treated with ACE inhibitors demonstrated a greater and more sustained improvement in LVEF over time compared with those receiving ARBs. The between-group difference in longitudinal LVEF improvement was statistically significant ($p = 0.015$).

A higher number of post-MI patients in the ACE inhibitor group achieved improvement in LVEF by Week 56 compared with the ARB group.

Post-Stroke Patients

In post-stroke patients, both ACE inhibitors and ARBs were associated with modest improvements in LVEF, with no statistically significant between-group difference ($p > 0.05$).

3.2 Renal Functions:

In both therapy groups, renal function remained steady over a 12-month follow-up. The mean serum creatinine decrease from baseline was modest and comparable between individuals using ACE inhibitors and those getting ARBs (-0.01 ± 0.06 mg/dL versus -0.01 ± 0.05 mg/dL; mean difference 0.00 mg/dL; 95% confidence interval [CI] -0.01 to 0.02; p = 0.94).

There were no statistically significant changes between groups in renal function at any follow-up time point. Both treatment methods showed similar renal safety profiles.

During early follow-up, a small proportion of patients in each group showed temporary increases in blood creatinine, which is consistent with the known hemodynamic consequences of renin-angiotensin system inhibition. However, these alterations were not progressive and did not cause clinically significant renal impairment or medication termination in the majority of individuals.

The incidence of hyperkalemia was low and similar between groups (2.9% in the ACE inhibitor group vs 2.4% in the ARB group; $p = 0.78$), further supporting the overall renal safety of both therapies in routine clinical practice.

3.3 Blood pressure control:

Over the one-year follow-up, both treatment groups achieved satisfactory and clinically meaningful blood pressure control, with no appreciable difference between ACE inhibitors and ARBs.

At 12 months, mean systolic blood pressure was 128.2 ± 8.6 mmHg in the ACE inhibitor group and 129.0 ± 8.9 mmHg in the ARB group, with a negligible between-group difference that was not statistically significant ($p = 0.48$). Diastolic blood pressure showed a similar pattern, averaging 78.3 ± 5.7 mmHg and 78.9 ± 5.9 mmHg in the respective groups ($p = 0.52$).

Both groups demonstrated a substantial reduction in blood pressure from baseline values, reflecting effective antihypertensive therapy. Importantly, the extent of blood pressure lowering was comparable across the two treatment strategies, suggesting equivalent efficacy in routine clinical practice.

A considerable proportion of patients in each group achieved target blood pressure levels in line with current guideline recommendations (<130/80 mmHg), underscoring the effectiveness of renin–angiotensin system blockade in this high-risk population.

Discussion

In this prospective observational study, angiotensin converting enzyme inhibitor therapy was associated with a lower incidence of major adverse cardiovascular events over one year compared with angiotensin receptor blocker therapy, with the effect predominantly observed among patients with prior myocardial infarction. After adjustment for age, sex, diabetes mellitus, index cardiovascular event, and baseline left ventricular ejection fraction, angiotensin-converting enzyme inhibitor use remained independently associated with reduced cardiovascular risk.

The benefit observed in post myocardial infarction patients is consistent with the established evidence base supporting angiotensin-converting enzyme inhibitors in secondary prevention. Landmark trials including Survival and Ventricular Enlargement (SAVE), Acute Infarction Ramipril Efficacy (AIRE), and Trandolapril Cardiac Evaluation (TRACE) demonstrated reductions in mortality and heart failure–related outcomes following myocardial infarction, particularly in patients with impaired ventricular function. In the present study, greater improvement in left ventricular ejection fraction among angiotensin converting enzyme inhibitor recipients provides mechanistic support for the observed clinical benefit, likely reflecting attenuation of adverse ventricular remodeling through sustained inhibition of the renin–angiotensin aldosterone system.

In contrast, among patients with prior ischemic stroke, major adverse cardiovascular event rates were comparable between treatment groups. This finding aligns with the Perindopril Protection Against Recurrent Stroke Study (PROGRESS), in which vascular risk reduction was largely attributed to blood pressure lowering rather than a differential class effect of renin–angiotensin system blockade. Consistently, both treatment groups in our cohort achieved similar reductions in systolic and diastolic blood pressure at one year.

Renal safety outcomes were reassuring, with stable serum creatinine levels over follow-up in both groups. Although mild early increases were observed in some patients receiving angiotensin-converting enzyme inhibitors, values stabilized by one year, consistent with the known hemodynamic effects of renin angiotensin system inhibition. Adverse events were infrequent overall; cough was more common with angiotensin-converting enzyme inhibitors, while angiotensin receptor blockers demonstrated slightly better tolerability. However, discontinuation rates were low in both groups.

Collectively, these findings support the preferential role of angiotensin converting enzyme inhibitors in patients with prior myocardial infarction while suggesting therapeutic equivalence between angiotensin converting enzyme inhibitors and angiotensin receptor blockers in patients with prior stroke when blood pressure control is adequately achieved.

Limitations

This study has several limitations. As an observational analysis, residual confounding cannot be entirely excluded despite multivariable adjustment. Treatment allocation was not randomized, and unmeasured variables such as medication adherence, socioeconomic factors, and comorbidity burden may have influenced outcomes. Event ascertainment relied on clinical documentation, which may lead to underreporting of non-fatal events. The follow-up duration was limited to one year, precluding assessment of long-term cardiovascular and renal outcomes. Finally, as a single-center cohort, external validity may be limited, and results should be interpreted in the context of the study population.

Conclusion

In this prospective cohort, angiotensin-converting enzyme inhibitor therapy was associated with a lower incidence of major adverse cardiovascular events at one year compared with angiotensin receptor blocker therapy, particularly among patients with prior myocardial infarction. Improvements in left ventricular ejection fraction likely contributed to this observed benefit. In patients with

prior ischemic stroke, cardiovascular outcomes were comparable between treatment groups, reflecting similar blood pressure control. Both therapies demonstrated acceptable renal safety and tolerability. These findings reinforce the established role of angiotensin-converting enzyme inhibitors in post myocardial infarction management and support individualized therapy selection in post stroke populations.

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Tables:

Table 1. Baseline Demographic and Clinical Characteristics of Study Participants

Characteristic	ACE Inhibitor Group (n = 205)	ARB Group (n = 205)
Age (years), mean ± SD	58.6 ± 10.4	59.1 ± 10.1
• Male	132 (64.4%)	128 (62.4%)
• Female	73 (35.6%)	77 (37.6%)
Index Event, n (%)		
• Post–Myocardial Infarction	103 (50.2%)	102 (49.8%)
• Post–Stroke	102 (49.8%)	103 (50.2%)
Baseline SBP (mmHg), mean ± SD	142.3 ± 11.8	141.9 ± 12.1
Baseline DBP (mmHg), mean ± SD	88.6 ± 7.4	88.1 ± 7.2
Baseline LVEF (%), mean ± SD	46.8 ± 6.9	47.1 ± 7.1
Baseline Serum Creatinine (mg/dL), mean ± SD	1.12 ± 0.24	1.11 ± 0.23
Diabetes Mellitus, n (%)	78 (38.0%)	82 (40.0%)
Dyslipidemia, n (%)	96 (46.8%)	101 (49.3%)
Smoking Status, n (%)		
• Current / Former Smoker	84 (41.0%)	87 (42.4%)
• Never Smoker	121 (59.0%)	118 (57.6%)
Concomitant Medications, n (%)		
• Beta-blockers	176 (85.9%)	173 (84.4%)
• Statins	189 (92.2%)	192 (93.7%)
• Antiplatelet agents	181 (88.3%)	184 (89.8%)

Table 2. Clinical Outcomes at One-Year Follow-up in ACE Inhibitor and ARB Groups

Outcome	ACE Inhibitor Group (n = 205)	ARB Group (n = 205)
Primary Outcome		
Major Adverse Cardiovascular Events (MACE), n (%)	34 (16.6%)	47 (22.9%)
Components of MACE, n (%)		
• Cardiovascular death	9 (4.4%)	14 (6.8%)
• Recurrent myocardial infarction	13 (6.3%)	18 (8.8%)
• Recurrent stroke	12 (5.9%)	15 (7.3%)
• Heart failure hospitalization	17 (8.3%)	24 (11.7%)
Secondary Outcomes		
Change in LVEF from baseline (%), mean	9.3	6.1
Change in serum creatinine from baseline (mg/dL), mean	-0.01	-0.01
Blood pressure at 1 year (mmHg), mean		
• Systolic BP	128.2	129.0
• Diastolic BP	78.3	78.9

Table 3. Multivariable Regression Analysis for Predictors of Major Adverse Cardiovascular Events

Variable	Adjusted Effect Estimate (aHR / aOR)	95% Confidence Interval	Interpretation
Treatment group			
• ACE inhibitor vs ARB	0.72	0.54 – 0.96	Lower risk of MACE
Age (per year increase)	1.03	1.01 – 1.05	Increased risk with age
Sex			
• Male vs Female	1.18	0.86 – 1.62	Not independently significant
Index event			
• Post-MI vs Post-Stroke	1.64	1.19 – 2.27	Higher risk after MI
Diabetes mellitus	1.42	1.05 – 1.93	Independent predictor
Baseline LVEF (per 5% increase)	0.81	0.70 – 0.93	Protective effect

aHR: adjusted hazard ratio (if time-to-event); aOR: adjusted odds ratio (if binary outcome).

Table 4. Drug-Related Adverse Events During Follow-up

Adverse Event	ACE Inhibitor Group (n = 205)	ARB Group (n = 205)
Cough, n (%)	18 (8.8%)	3 (1.5%)
Angioedema, n (%)	2 (1.0%)	0 (0.0%)
Hyperkalemia, n (%)	6 (2.9%)	5 (2.4%)
Symptomatic hypotension, n (%)	7 (3.4%)	6 (2.9%)
Drug discontinuation due to adverse events, n (%)	11 (5.4%)	4 (2.0%)

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Figures:

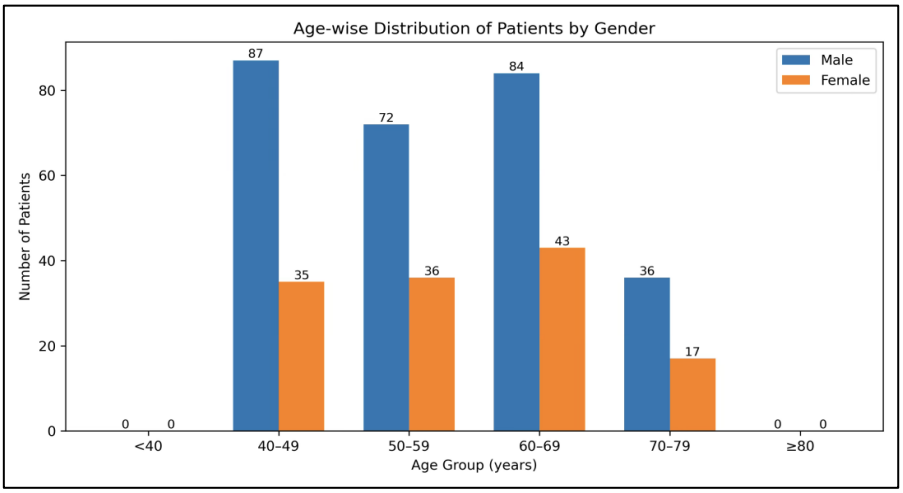

Figure 1: Age-wise Distribution of Patients by Gender

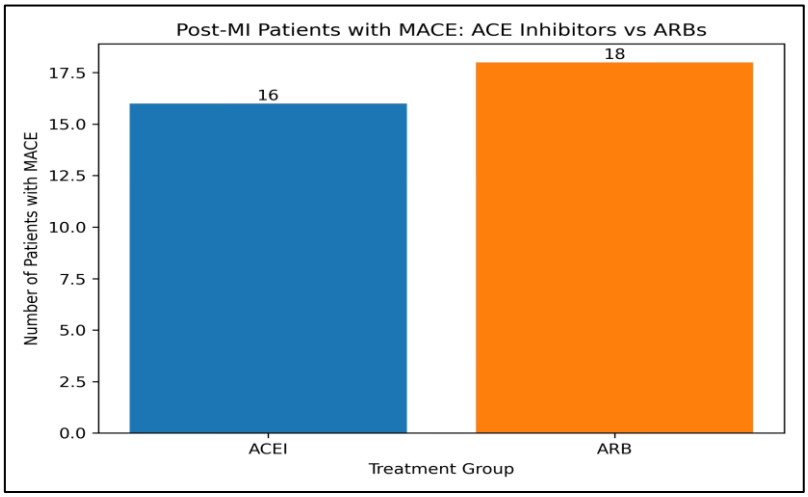

Figure 2: Post-MI Patients with MACE: ACE Inhibitors vs ARBS

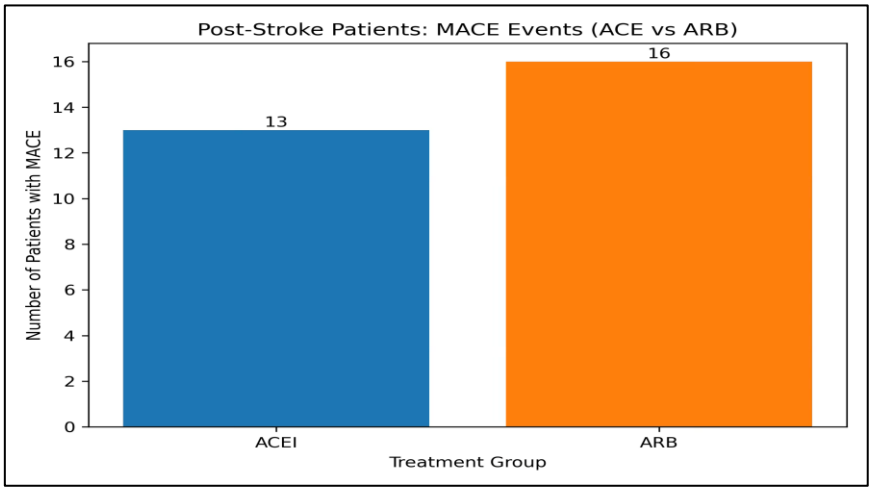

Figure 3: Post-Stroke Patients: MACE Events (ACE vs ARB)

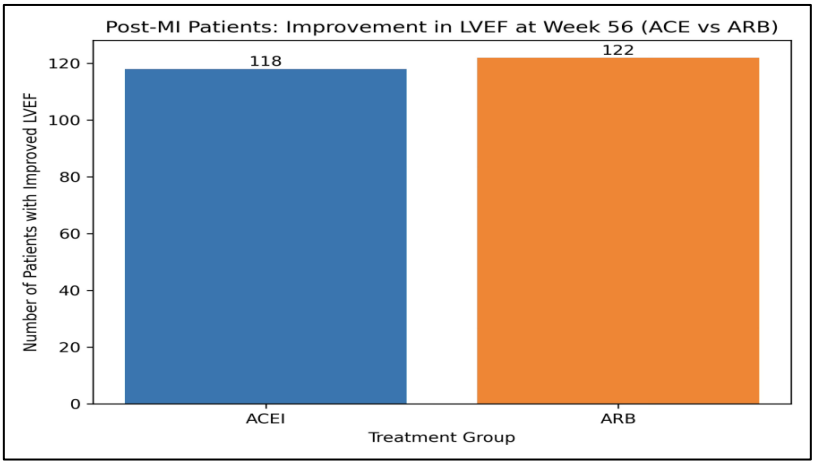

Figure 4.1: Change in LVEF Over Time in Post-Myocardial Infarction Patients

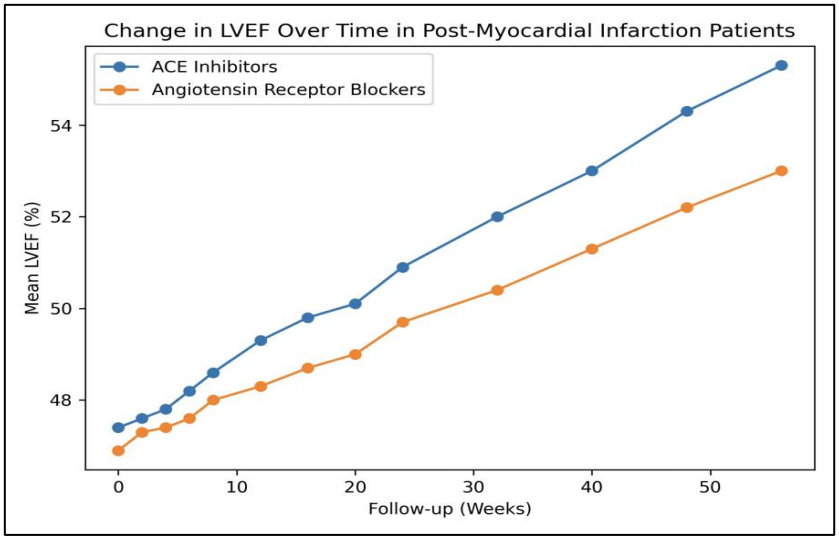

Figure 4.2: Change in LVEF Over Time in Post-Myocardial Infarction Patients

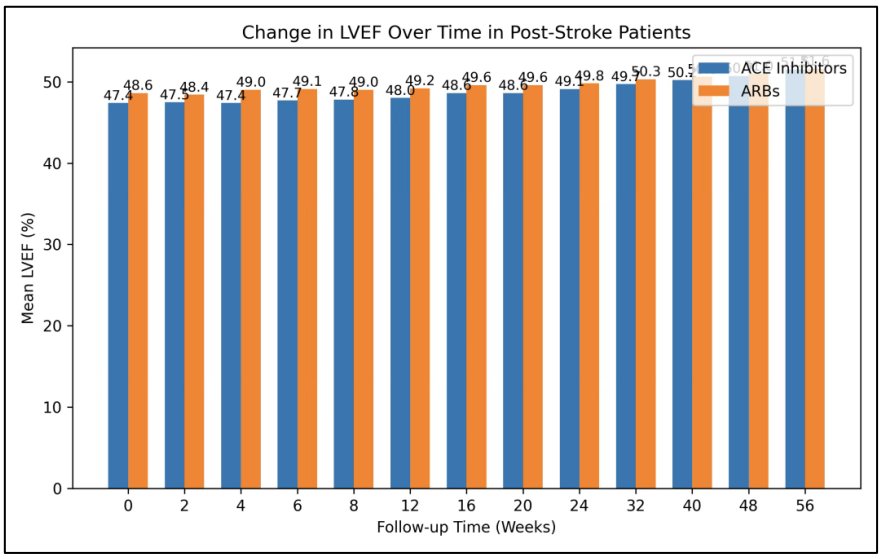

Figure 5.1: Change in LVEF Over Time in Post-Stroke Patients

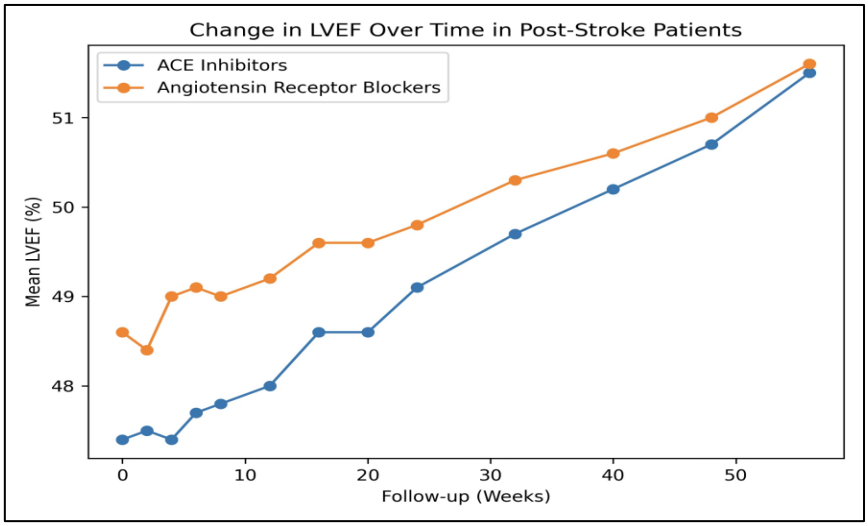

Figure 5.2: Change in LVEF Over Time in Post-Stroke Patients

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Conflict of Interest Statement: All authors have nothing else to disclose.

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