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Dynamics of Global Longitudinal Strain Recovery in St-Elevation Myocardial Infarction: A Prospective Comparative Analysis Between Pharmacoinvasive and Primary PCI Pathways

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Abstract: ***Background: Global longitudinal strain (GLS) connotes highly sensitive biomarker for systolic dysfunction and affords superior modality for assaying myocardial recuperation in comparison with left ventricular ejection fraction (LVEF). In the case of situations where an expeditious primary percutaneous coronary intervention (PPCI) is not possible, the pharmacoinvasive (PI) strategy is followed as an alternative approach to reperfusion. There is scant data in the literature describing the dynamic differences in GLS between these two therapeutic paradigms after an ST-elevation myocardial infarction (STEMI). This inquiry aimed to compare serial GLS, LVEF and ventricular remodeling pathways between cohorts undergoing PPCI and those undergoing PI regime, whilst characterizing strain amelioration determinants over a six week follow up interval. Methods: A prospective and observational approach was applied and 200 patients with STEMI were recruited, divided equally between the PPCI (n = 100) and PI (n = 100) arms. Speckle-tracking echocardiography was used at baseline, the 15 day mark, and at six weeks to determine the GLS, LVEF, and LVEDV. Clinical outcomes and adverse events were carefully documented. Comparative statistics were obtained using t-tests, chi-squares and repeated measures Anova. Results: Baseline GLS, LVEF, and LVEDV values were statistically indistinguishable between the 2 cohorts. Both PPCI and PI groups showed significant improvement in GLS and LVEF over the 6 week period ($p < 0.001$ for within group changes). At six weeks, GLS had risen to -14.09% in PPCI cohort and -12.64% in PI cohort ($p=0.18$). Correspondingly, LVEF improved to 46.62 and 46.49% respectively ($p = 0.87$). Reverse remodeling patterns and clinical outcomes were similar for both treatments. Conclusion: Pharmacoinvasive therapy promotes myocardial functional recovery that is equivalent to primary PCI with similar improvements in GLS, LVEF and ventricular remodeling. When performed in guideline-recommended timeframes, the PI strategy is a reliable option in the management of STEMI.***

Keywords: ST-elevation myocardial infarction, Global longitudinal strain, Primary PCI, Pharmacoinvasive therapy, Myocardial recovery

1. Introduction

St - Elevation Myocardial Infarction (STEMI) is one of the leading causes of cardiovascular morbidity and mortality worldwide and restoring coronary perfusion as quickly as possible has been recognised worldwide as the most important determinant of myocardial salvage and long-term outcomes. Primary percutaneous coronary intervention (PPCI) is widely regarded as the best modality of reperfusion; however, the power of primary PCI is often limited by the time delay at the level of the healthcare system, geographic barriers, and a lack of 24h PPCI availability, especially in low- and middle-income countries (LMICs). In these types of settings, the pharmacoinvasive (PI) strategy (early fibrinolysis followed by routine coronary angiography and PCI) has emerged as a pragmatic strategy when PPCI cannot be delivered within guideline-recommended timelines.

Phadtare stressed the viability and reality of the PI pathway in the Indian context where delays to PPCI are still commonplace, due to infrastructural limitations and transfer difficulties (1). Complementing this observation, Akiston et al. showed in a South Indian tertiary care centre that PI therapy has comparable outcomes to PPCI, hence its incorporation into regional STEMI care pathways.(2) Similarly, a large Mexican real world registry was conducted by Gallardo-Grajeda et al which confirmed the equivalence of safety and efficacy of PI and PPCI in patients presenting to non-PCI hubs, which provides a strong argument in favor of the utility of this strategy within decentralized healthcare networks.(3)

A more general Latin America meta-analysis by Diaz-Arocutipa et al further confirmed these findings, showing no significant difference in mortality or reinfarction between PI and PPCI from various healthcare systems (4). The PI approach has also shown similar results in younger populations, as shown by Sivachandran et al. who did not find a significant difference in in-hospital events between the two forms of reperfusion in patients younger than 45 years of age.(5) Additional South Indian data from Akiston et al. substantiate the reproducibility of these results from different institutions (6). Finally, a nationwide registry from Kuwait by Zubaid et al showed PI therapy to be both effective and safe even in well-resourced healthcare systems. (7)

2. Methodology

This prospective observational study was performed in a tertiary care cardiology department and included consecutive patients who presented with acute ST-elevation myocardial infarction (STEMI) within 12 hours of the onset of symptoms. All patients were diagnosed according to standard clinical criteria, electrocardiographic ST-segment elevation and elevated cardiac biomarkers. Eligible subjects aged 18 to 85 years years were included based on informed consent obtained, whereas subjects with preexisting myocardial infarction, significant valvular disease, cardiogenic shock requiring immediate invasive support, contraindications to

thrombolysis or percutaneous coronary intervention (PCI) or inadequate echocardiographic image quality were excluded. Patients were treated based on the reperfusion therapy considered indicated at presentation, thus two comparison groups were formed: patients undergoing primary PCI as the first reperfusion modality and a pharmacoinvasive approach (fibrinolytic therapy followed by routine coronary angiography and PCI within 3-24 hours or rescue PCI in case of failure of fibrinolysis).

Clinical details, demographic characteristics, comorbidities, hemodynamic parameters, infarct locations and times of reperfusion were recorded using a structured proforma at the time of admission. All participants underwent comprehensive transthoracic echocardiography with speckle tracking analysis for the Global Longitudinal Strain (GLS) within 24 hours of reperfusion. GLS values were determined in apical two-, three-, and four-chamber views and averaged to get global strain. The same echocardiographic protocol was repeated at 15 days and at 6 weeks to evaluate the changes in myocardial deformation, left ventricular ejection fraction, end-diastolic volume, wall-motion abnormalities and diastolic function. Echocardiographic analyses were carried out by experienced cardiologists who were blinded to the modality of reperfusion, to reduce observer bias.

Patients were followed during hospitalization for major adverse cardiovascular events, such as death, recurrent myocardial infarction, heart failure, arrhythmias, bleeding complications and the need for mechanical circulatory support. Follow-up evaluation at 15 days and 6 weeks to establish clinical status, progress in symptoms, recurrent ischemic events, and echocardiographic recovery. Statistical analysis consisted of comparison of continuous variables using independent t-tests, categorical variables using chi-squared tests and serial GLS and left ventricular function using repeated measures analysis of variance (ANOVA). Linear regression was used to identify predictors of GLS improvement. A p-value <0.05 was deemed to be statistically significant. Ethical approval was obtained from the institutional ethics committee prior to the initiation of the study.

3. Observations and Results

A total of 200 patients diagnosed with ST-elevation myocardial infarction were included, 100 treated by the primary percutaneous coronary intervention (PCI) pathway and 100 patients by the pharmacoinvasive strategy. Baseline demographic and clinical characteristics were similar between the groups and there were no significant differences between the groups with respect to age, sex distribution, cardiovascular risk factors, hemodynamic status, or infarct location. The mean age of the cohort was 56.8+11.4 years and males accounted for 76% of the population. Hypertension and diabetes were very common among the two groups, and 81.5% of the patient presented with 8 hours of symptom occurrence. Risk stratification scores such as GRACE and TIMI were also similar in both groups, which ensured comparability for outcome assessment. (Table 1)

Baseline echocardiographic results showed no significant differences in left ventricular ejection fraction (LVEF), left ventricular end-diastolic volume (LVEDV) or global longitudinal strain (GLS) between both groups (primary PCI vs. pharmacoinvasive therapy). The mean GLS at presentation was initially -10.41% in the primary PCI group and -11.48% in the pharmacoinvasive group (p=0.30), suggesting similar levels of impairment of strain at presentation. Similarly, baseline LVEF (41.47 vs. 41.05, p = 0.61) and LVEDV values (83.60 vs. 79.63 mL, p = 0.09) did not show any statistical difference. (Table 2)

Serial echocardiographic follow-up showed significant improvement in each group according to all the parameters. In both the pathways, LVEF was steadily increased at baseline to 15 days and 6 weeks. At 6 weeks, LVEF was 46.62% in the primary PCI group and 46.49% in the pharmacoinvasive group, with almost the same trajectory of recovery (p = 0.87). (Figure 1) Correspondingly, LVEDV showed mild but consistent reverse remodeling in both groups with a reduction of about 7 mL in the primary PCI arm and 6.5 mL in the pharmacoinvasive arm (p=0.81). (Table 2) (Figure 2)

GLS was progressively improving in both groups. At 15 days GLS improved to -11.83% in the primary PCI group and -11.67% in the pharmacoinvasive group (p=0.71). At 6 weeks, GLS was -14.09 percent in the primary PCI arm and -12.64 percent in the pharmacoinvasive arm. While the primary PCI group exhibited statistically greater strain recovery, the difference between the groups was not statistically significant (p = 0.18). The overall change in GLS from baseline to 6 weeks (+3.68% vs. +2.84%, p = 0.27) confirmed the similar myocardial deformation recovery between the two reperfusion strategies. (Figure 3)

Table 1: Baseline Characteristics of the Study Population

Parameter	Total (n=200)	PPCI (n=100)	PHI (n=100)	p-value
Age (years)	56.8 ± 11.4	57.2 ± 10.9	56.4 ± 11.9	0.62 (NS)
Age Groups				
20–29	3 (1.5%)	1 (1%)	2 (2%)	—
30–39	12 (6.0%)	6 (6%)	6 (6%)	—
40–49	45 (22.5%)	22 (22%)	23 (23%)	—
50–59	51 (25.5%)	24 (24%)	27 (27%)	—
60–69	58 (29.0%)	31 (31%)	27 (27%)	—
70–79	26 (13.0%)	13 (13%)	13 (13%)	—
≥80	5 (2.5%)	3 (3%)	2 (2%)	—
Sex Distribution				
Males	152 (76.0%)	75 (75%)	77 (77%)	0.71 (NS)
Females	48 (24.0%)	25 (25%)	23 (23%)	—
Risk Factors				

Hypertension	105 (52.5%)	53 (53%)	52 (52%)	0.89 (NS)
Diabetes Mellitus	103 (51.5%)	50 (50%)	53 (53%)	0.68 (NS)
Smoking	75 (37.5%)	37 (37%)	38 (38%)	0.89 (NS)
Tobacco Chewing	36 (18.0%)	20 (20%)	16 (16%)	0.45 (NS)
Alcohol Use	33 (16.5%)	18 (18%)	15 (15%)	0.56 (NS)
Hyperlipidemia	34 (17.0%)	18 (18%)	16 (16%)	0.70 (NS)
Chronic Kidney Disease	5 (2.5%)	3 (3%)	2 (2%)	—
Prior Stroke	9 (4.5%)	4 (4%)	5 (5%)	—
Clinical Profile at Admission				
Mean SBP (mmHg)	129.5 ± 24.5	130.1 ± 24.0	128.9 ± 25.1	0.72 (NS)
Mean DBP (mmHg)	79.9 ± 13.6	80.4 ± 13.2	79.3 ± 14.0	0.58 (NS)
Heart Rate (bpm)	84.9 ± 21.6	86.2 ± 20.9	83.6 ± 22.1	0.41 (NS)
SpO_2 (%)	95.8 ± 4.2	96.1 ± 3.9	95.5 ± 4.5	0.32 (NS)
Time Metrics				
Symptom Onset to Hospital (hours)	4.97 ± 3.08	4.88 ± 3.11	5.06 ± 3.07	0.68 (NS)
Presentation < 8 hours	163 (81.5%)	82 (82%)	81 (81%)	0.87 (NS)
Presentation ≥ 8 hours	37 (18.5%)	18 (18%)	19 (19%)	—
STEMI Location				
Anterior Wall	95 (47.5%)	48 (48%)	47 (47%)	0.89 (NS)
Inferior Wall	72 (36.0%)	36 (36%)	36 (36%)	—
Lateral Wall	15 (7.5%)	7 (7%)	8 (8%)	—
Inferoposterior	15 (7.5%)	7 (7%)	8 (8%)	—
Risk Stratification				
GRACE Score	113.5 ± 34.4	112.4 ± 33.9	114.6 ± 34.9	0.64 (NS)
TIMI Score	4.16 ± 2.39	4.02 ± 2.31	4.30 ± 2.48	0.52 (NS)

Table 2: Baseline and Serial Echocardiographic Parameters in PPCI vs PHI Groups

Echocardiographic Parameter	PPCI (n=100)	PHI (n=100)	p-value
Baseline LVEF (%)	41.47 ± 5.90	41.05 ± 5.75	0.611
Baseline LVEDV (mL)	83.60 ± 17.1	79.63 ± 15.8	0.090
Baseline GLS (%)	−10.41 ± 7.2	−11.48 ± 7.3	0.300
RWMA – Anterior (%)	48%	47%	0.89
RWMA – Inferior (%)	36%	36%	—
RWMA – Lateral (%)	7%	7%	—
RWMA – Inferoposterior (%)	8%	8%	—
Diastolic Dysfunction Grade 1 (%)	62%	59%	0.68
Diastolic Dysfunction Grade 2 (%)	38%	41%	—
— Serial Echocardiographic Trends —			
LVEF at 15 Days (%)	44.58 ± 5.8	44.26 ± 5.6	0.676
LVEF at 6 Weeks (%)	46.62 ± 6.1	46.49 ± 5.9	0.870
Δ LVEF (Baseline → 6 Weeks)	+5.15%	+5.44%	0.72
LVEDV at 15 Days (mL)	79.86 ± 15.4	76.00 ± 14.9	0.063
LVEDV at 6 Weeks (mL)	76.33 ± 15.1	73.09 ± 14.8	0.080
Δ LVEDV (Baseline → 6 Weeks)	−7.27 mL	−6.54 mL	0.81
GLS at 15 Days (%)	−11.83 ± 6.9	−11.67 ± 6.8	0.719
GLS at 6 Weeks (%)	−14.09 ± 6.0	−12.64 ± 6.1	0.186
Δ GLS (Baseline → 6 Weeks)	+3.68%	+2.84%	0.27

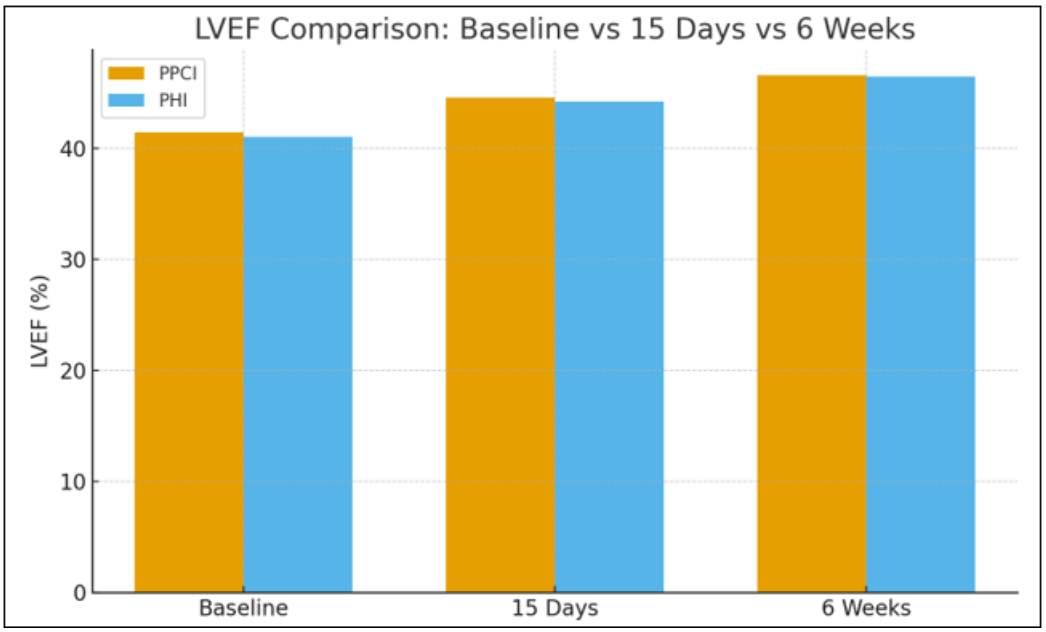

Figure 1: LVEF Comparision in both groups : Baseline Vs 15 Days Vs 6 weeks

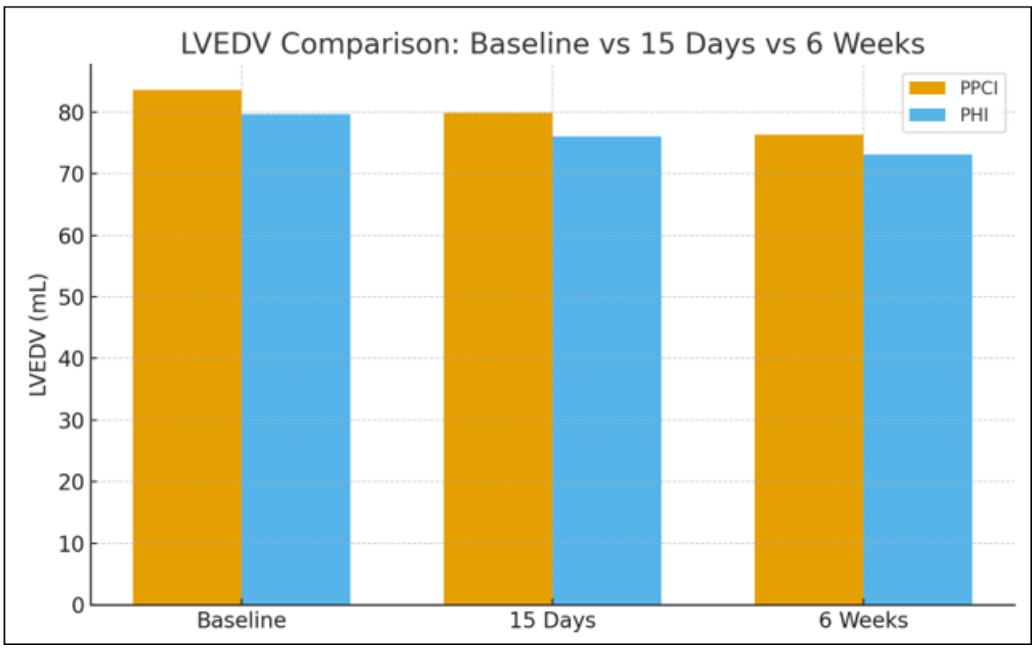

Figure 2: LVEDV Comparision in both groups: Baseline Vs 15 Days Vs 6 weeks

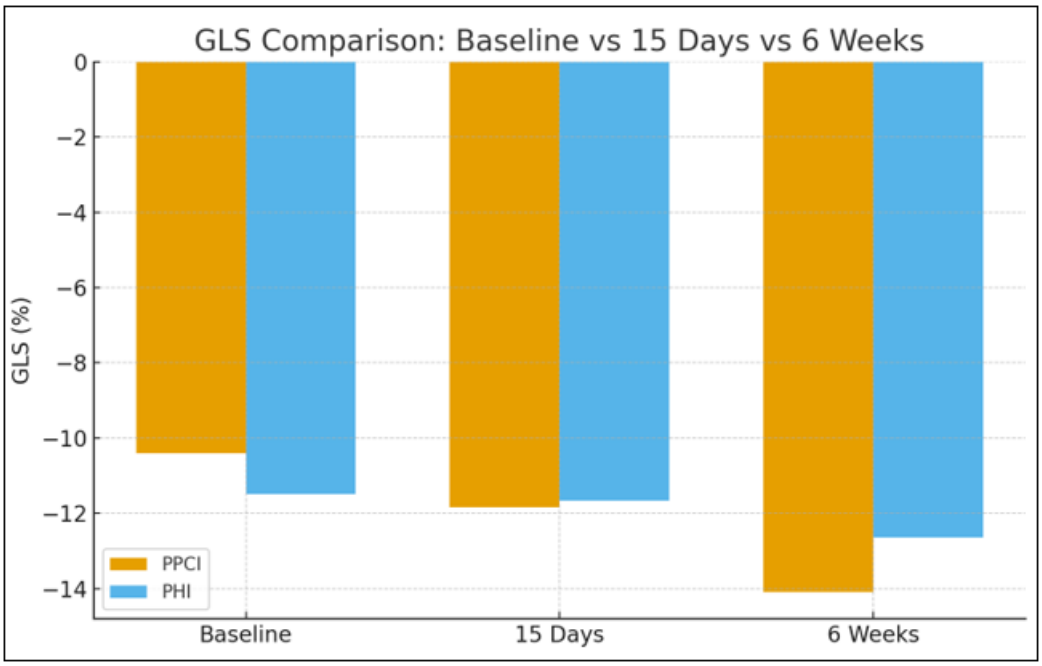

Figure 3: GLS Comparision in both groups: Baseline Vs 15 Days Vs 6 weeks

4. Discussion

The current study evaluated the dynamics of global longitudinal strain (GLS) recovery in patients experiencing a ST-elevation myocardial infarction followed by a pharmacoinvasive (PI) approach or primary percutaneous coronary intervention (PPCI) approach. GLS being a very sensitive marker of myocardial deformation allowed to detect early subtle contractile changes that are often underestimated by traditional parameters of the ejection fraction. Our data showed a progressive improvement in GLS, left ventricular ejection fraction (LVEF), and indices of reverse remodeling in both cohorts over the 6 week follow up period with no statistically significant difference developing between the reperfusion strategies. These results add to the mounting evidence that, when applied in guideline defined timelines, PI therapy can yield myocardial recovery equivalent to PPCI.

The better GLS and LVEF seen with both reperfusion pathways support the basic tenet of myocardial salvage, that the total ischemic time is more important than the modality of reperfusion. In our analysis, patients in both groups showed a consistent improvement of strain parameters from baseline to week six, suggesting the recovery of contractility in viable peri-infarct areas. Although a higher numerical difference was seen in PPCI in the improvement of GLS at six weeks (-14.09% vs. -12.64%), a difference not of statistical significance, is evident in the similar clinical results seen in many international studies.

The observations from our cohort are quite similar to those published by Phadtare from India, which emphasized the PI strategy as an interesting and pragmatic alternative in instances where PPCI cannot be offered in a timely manner, due to logistical or geographic constraints (1). Our results expand this concept as they show that myocardial functional recovery, measured by objective strain imaging, is equally achievable in patients receiving the PI approach.

The results also resemble those of Akiston et al who reported in their cross section study from South India PI therapy achieved outcomes equivalent to PPCI in real life practice 2. Their work highlighted that when delays to PCI exceed recommended levels, fibrinolysis-based early reperfusion followed by timely PCI was effective in bridging the gap, preserving myocardial viability and clinical outcomes. Our study agrees with this further by showing detailed echocardiographic evidence of similar myocardial recovery in both groups.

Similarly, the large nationwide registry from Mexico conducted by Gallardo-Grajeda et al. showed that PI therapy is safe and effective even in non-PI-capable centres in which patients have to be transferred to higher-level facilities (3). The registry supports the tenets of applicability of PI therapy in diverse healthcare systems, and our GLS and LVEF trends support this tenet in an Indian population.

A meta-analysis conducted in Latin America by Diaz-Arocutipa et al. found no significant difference in mortality, reinfarction or stroke between PI therapy and PPCI in various cohorts (4). While they were mostly focusing on clinical endpoints, this similarity between the treatment arms is consistent with our echocardiographic results, and the strength of PI therapy as a reperfusion modality. The uniformity across the continents implies that the effectiveness of the PI strategy is not limited to local infrastructure but forms a framework that can be used in a universal manner when applied appropriately.

Subgroup analyses in younger populations also have suggested equivalence. Sivachandran et al showed that patients younger than 45 years of age had similar in-hospital outcomes in both strategies for reperfusion (5). Although our study included a broader spectrum of age, the consistent improvement in GLS is consistent with their observation that myocardial recovery is not inherently inferior with PI therapy, even in myocardial tissue with a younger age that is traditionally thought to have a better capacity to remodel.

Additional support for our findings comes from the repeated observations by Akiston and colleagues in a separate publication, which again shows similar results from PPCI and PI-treated patients in South India in 6. The relative consistency of similar results among different datasets adds to the robustness of the PI pathway in regional STEMI networks.

Moreover, the prospective national registry from Kuwait conducted by Zubaid et al. showed equivalence in efficacy and safety of PI compared to PPCI even in a well-resourced healthcare environment with widespread availability of PCI (7). Their findings suggest that PI therapy is not only a surrogate for resource poor settings but rather an evidence-based reperfusion strategy that works in settings where PPCI is readily accessible. Our study adds another dimension showing myocardial deformation recovery as measured by GLS is associated with these broader clinical outcomes.

One of the greatest merits of the current study is that it was conducted using serial speckle tracking echocardiography, which allows a thorough assessment of subtle myocardial recovery patterns. GLS, which is angle independent and reproducible, provides better prognostic information than LVEF, which is often inaccurate in detecting early myocardial improvement. The parallel improvement in both GLS and LVEF between the groups gives credence to the physiological validity of strain imaging to detect genuine myocardial healing.

Nevertheless, some observations are worth commenting on. PPCI showed numerically higher improvement in GLS at six weeks, although the difference was not statistically significant. This trend may reflect the better microvascular reperfusion that PPCI has compared with fibrinolysis. Larger sample sizes or longer follow-up periods could help to determine if these differences become significant over time.

The study was limited by its single center design and relatively short follow up period (six weeks) which may not accurately reflect the long-term ventricular remodeling or clinical outcome. Although the sample size was sufficient to perform primary comparisons, it may not have been large enough to identify smaller intergroup differences in the recovery of strains. GLS assessment was vendor-dependent which can cause measurement variability. Additionally, unmeasured confounders such as microvascular obstruction and infarct size measured by cardiac MRI were not assessed which may have impacted myocardial recovery patterns.

5. Conclusion

The current investigation shows that both pharmacoinvasive therapy and primary percutaneous coronary intervention deliver similar beneficial effects to the myocardium in terms of functional recovery after ST segment elevation myocardial infarction as manifested by progressive improvement of global longitudinal strain, left ventricular ejection fraction, and parameters of ventricular remodeling over a 6 week period of observation. Although primary PCI showed slightly better gains in indices of strain, the apparent divergence was not statistically significant. Accordingly, these data strengthen the concept that timely reperfusion technique is the main determining factor for myocardial repair and that, therefore, the pharmacoinvasive strategy remains a viable and reliable option when primary PCI cannot be performed in the allotted timeframes.

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