

## Original Article

# Colchicine for Preserving Left Ventricular Systolic Function in Patients With STEMI Following Successful Primary PCI: A Speckle-Tracking Echocardiography Study

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### ABSTRACT

**Background:** Colchicine is a safe and well-tolerated medication in patients with cardiovascular disease. Speckle-tracking echocardiography (STE) with global longitudinal strain average is a validated method for evaluating left ventricular (LV) function. Utilizing 2D STE, this study aimed to investigate the safety and efficacy of colchicine administration on LV systolic function in anterior ST-segment elevation myocardial infarction (STEMI) patients following a successful primary percutaneous coronary intervention (PPCI).

**Methods:** This randomized clinical trial involved 200 anterior STEMI patients who underwent successful PPCI, allocated to 2 groups: Group I (control group), receiving guideline-directed medical therapy (GDMT), and Group II (colchicine group), receiving both GDMT and colchicine (loading and maintenance dose) for 6 months. Assessment of LV systolic function was performed using Simpson's method, along with 2D STE and global longitudinal strain GLS averages. This evaluation was conducted for all patients during their hospital stay and followed up 6 months later.

**Results:** Assessment of LV systolic function, measured as ejection fraction (EF [%]), calculated using Simpson's method, indicated a significant improvement in the colchicine group compared to the control group at the 6-month follow-up (EF = 41.38% ± 3.98 in the colchicine group vs 39.38% ± 7.74 in the control group;  $P = 0.011$ ). Additionally, there was a highly statistically significant improvement in LV GLS average ( $-13.28 \pm 2.13$  in the colchicine group vs  $-11.64 \pm 2.73$  in the control group;  $P = 0.001$ ). No significant difference was observed in the rate of acute and chronic complications during the follow-up between the control and colchicine groups.

**Conclusions:** Colchicine administration in anterior STEMI patients following a successful PPCI was found to significantly improve LV systolic function without an increase in the incidence of complications. (*Iranian Heart Journal 2024; 25(4): 84-95*)

**KEYWORDS:** Anterior ST-segment elevation myocardial infarction, Colchicine, global longitudinal strain, Speckle-tracking echocardiography, Primary percutaneous coronary intervention

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Acute myocardial infarction (AMI) is the most severe manifestation of coronary artery disease.<sup>1</sup> Percutaneous coronary intervention (PPCI) is the preferred treatment strategy for patients suffering from ST-elevation myocardial infarction (STEMI).<sup>2</sup> Following acute ischemia and AMI, endogenous inflammation ensues, resulting in myocardial necrosis and subsequent cardiac injury, leading to ventricular dilatation, dysfunction, and remodeling.<sup>3</sup> Persistent elevation of inflammatory mediators exacerbates cardiac dysfunction, induces further cardiomyocyte loss, and triggers myocardial apoptosis.<sup>4</sup> The inflammatory process serves as the key mechanism underlying the detrimental effects associated with ischemia/reperfusion injuries in patients experiencing STEMI. Existing research has not conclusively established the efficacy of anti-inflammatory interventions in ameliorating cardiac dysfunction, heart failure, and survival rates post-MI. Multiple studies investigating the use of cyclosporine, non-steroidal anti-inflammatory drugs, or glucocorticosteroids have failed to demonstrate significant advantages in the context of MI.<sup>5</sup> Colchicine, a potent anti-inflammatory agent with a unique mechanism of action, has been demonstrated to be a safe treatment option for patients affected by cardiovascular disease.<sup>6</sup> Colchicine is an affordable and efficacious orally administered anti-inflammatory medication. Its therapeutic action is attributed to the inhibition of microtubule assembly, and it has been suggested to modulate the inflammasome, inflammatory chemokines, and cellular adhesion molecules, thereby exerting its anti-inflammatory effects.<sup>7</sup> Recent evidence has indicated that colchicine, when administered daily at a dosage of 0.5 mg, can leverage its anti-inflammatory effects to significantly improve cardiovascular outcomes in patients suffering from STEMI.<sup>8</sup>

Echocardiography-based investigations have provided compelling evidence that myocardial strain analysis is an exceptionally sensitive diagnostic tool capable of predicting clinical outcomes across various cardiac pathologies.<sup>9</sup> Speckle-tracking echocardiography (STE) represents a convenient and accessible modality that enables more comprehensive evaluation of myocardial strain patterns, augmenting traditional echocardiogram parameters. STE has been shown to offer greater precision than tissue Doppler imaging (TDI), partially attributable to TDI's susceptibility to beam angle-related artifacts.<sup>10</sup> Employing Simpson's method and 2D STE for analysis, this study aimed to explore the impact of colchicine administration on left ventricular (LV) systolic function in anterior STEMI patients undergoing a successful PPCI.

## METHODS

This case-control, prospective interventional study was conducted between August 2020 and May 2022 at Ain Shams University hospitals. The study enrolled anterior STEMI patients who had undergone a successful PPCI and met the predefined inclusion criteria. The primary objective was to assess the effects of colchicine administration on LV systolic function in these patients. All participating patients provided their informed written consent before being enrolled in the study. The research protocol was reviewed and approved by the Research Ethics Committee of Ain Shams University's Faculty of Medicine (approval number: FAMUS MD 160/2020). The enrolled patients were divided into 2 distinct groups for the purpose of this study: Group I: This group comprised 100 patients who received standard guideline-directed medical therapy (GDMT) only. Group II: This group consisted of 100 patients who were administered a 1 mg loading dose of colchicine before PPCI and subsequently

treated with a daily dose of 0.5 mg colchicine for 6 months, in addition to standard GDMT.

The study enrolled patients exhibiting ECG criteria indicative of anterior STEMI<sup>11</sup> and demonstrating successful PPCI based on angiographic evaluation (thrombolysis in myocardial infarction [TIMI] flow grade III and myocardial blush grade [MBG] II–III).

<sup>11</sup> To meet the inclusion criteria for this study, participants needed to present within a 12-hour time frame from the onset of their maximum chest pain. Participants were excluded from the study based on the following criteria:

1. A history of previous AMI
2. Previous PCI or coronary artery bypass graft surgery
3. The presence of cardiogenic shock
4. Significant concomitant coronary artery lesions with more than 50% stenosis in the right coronary and/or left circumflex arteries
5. Heavy thrombus burden lesions in coronary angiography, where medical therapy was advised over interventional treatment
6. Poor echogenicity leading to inadequate visualization of the endocardium
7. Severe valvular heart disease that could impact LV systolic function
8. Inability to tolerate colchicine due to severe side effects
9. Significant renal or hepatic impairment

A detailed history was taken from all patients, with an emphasis on pain-to-door timing and cardiovascular disease risk factors. Patients underwent clinical examinations and 12-lead surface ECG on admission to diagnose anterior STEMI.<sup>12</sup> Routine laboratory tests, including serum creatinine, hemoglobin, HbA1c, and low-density lipoprotein (LDL) levels, were performed. Additionally, data regarding coronary angiography and PPCI, including culprit vessel lesion, thrombus burden, TIMI flow grades post-PCI, MBG post-PCI, and post-PCI complications, were

collected. Transthoracic echocardiography, including standard transthoracic 2D echocardiographic examinations, using a machine-integrated ECG recording and a Vivid E9 machine equipped with an M4S matrix sector array probe operating at a frequency of 2.5 MHz (General Electric Vingmed Ultrasound, Horten, Norway), was performed within 48 hours after PPCI. Six months afterward, patients underwent follow-up echocardiography, including parasternal and left lateral position examinations. To determine LVEF, a biplane-modified Simpson's method was employed utilizing the apical 4- and 2-chamber views, with a preference for an LV-focused view. This technique involved the identification of images with a well-defined endocardial border to accurately delineate the interface between the compacted myocardium and the cavity and the tracing of the endocardial-blood pool interface at 2 critical points in the cardiac cycle (end-diastole and end-systole) using the apical 4- and 2-chamber views.

Via the biplane Simpson's method,<sup>13</sup> LV end-diastolic volume (EDV) and LV end-systolic volume (ESV) were calculated. The wall motion score index (WMSI) was determined by dividing the LV into 16 segments. A semi-quantitative scoring system was used to determine the segment scores: 1: normal, 2: hyperkinesia, 3: akinesia, and 4: dyskinesia. Once the individual segment scores were assigned using the semi-quantitative scoring system, WMSI was calculated. This was achieved by summing all segment scores and dividing the total by the number of segments assessed, as per the established protocol.<sup>14</sup> In addition, the global longitudinal strain (GLS) value was measured using automated function imaging, a technique that employs 2D STE to evaluate the average peak systolic function of the LV. The GLS value, derived from the overall longitudinal strain pattern, serves as a comprehensive representation of the

individual segments of the LV. The calculation of longitudinal strain (%) is based on the following formula:

$$\text{longitudinal strain (\%)} = [(L_{\text{end-systole}} - L_{\text{end-diastole}}) / L_{\text{end-diastole}}] \times 100\%$$

Here, L represents the length of the region of interest at specific points in the cardiac cycle.<sup>15</sup>

The peak systolic longitudinal strain for each LV segment was determined using an automated algorithm based on a 17-segment model. The results were presented in a visually intuitive “bull's eye” plot, which provided a clear representation of the peak systolic strain values across all segments. Moreover, the average peak systolic GLS values were displayed for each view, as well as the overall average peak systolic GLS value for the entire LV. Longitudinal strain values are typically expressed as negative values, with more negative values indicating a lesser degree of LV systolic function impairment. In the present study, images were acquired at a mean frame rate of 70 frames per second, with a range of 40 frames per second. The normal reference value for GLS has been established as  $-19.7 \pm 3\%$ <sup>16</sup> (Figure 1).

In accordance with the established hospital protocol and the guidelines set forth by the European Society of Cardiology (ESC),<sup>17</sup> patients were prescribed dual antiplatelet therapy. Patients were initiated on oral  $\beta$ -blockers, angiotensin receptor blockers, and angiotensin-converting enzyme inhibitors within the first 24 hours, provided there were no contraindications. These medications were up-titrated to the highest tolerable doses for each patient. In cases where EF was  $\leq 40\%$  and patients were already receiving  $\beta$ -blockers and angiotensin-converting enzyme inhibitors, an aldosterone antagonist was prescribed, except in situations where it was contraindicated. Additionally, sodium-glucose cotransporter 2 inhibitors were used. All patients also received high-intensity

statin therapy as part of their overall treatment regime.

The primary endpoint of this study focused on assessing LV systolic function, as represented by the GLS pattern, during the patient's hospital stay and at a 6-month follow-up. The secondary endpoint of the study was the occurrence of major adverse cardiac events (MACE) within the 6-month follow-up period.

### Statistical Analysis

The data collection process involved gathering, coding, editing, and importing the information into the IBM SPSS software, version 20 of the Statistical Package for Social Science. The presentation format for qualitative data included numbers and percentages, while quantitative data with parametric distribution were represented using mean, standard deviation, and range values.

To compare qualitative data between the 2 study groups, the  $\chi^2$  test was employed. For quantitative data with a parametric distribution, the independent T-test was utilized to compare the 2 groups. A 5% margin of error and a 95% confidence interval (CI) were established as the statistical thresholds for determining significance.

## RESULTS

The statistical analysis of demographic data and cardiovascular risk factors between the 2 study groups revealed no significant differences, except for smoking and hypertension. A higher incidence of smokers was observed in the colchicine group, while the control group showed a higher incidence of hypertensive patients. These findings are summarized in Table 1. Table 1 indicates that there was no statistically significant difference observed between the control group and the colchicine group concerning the baseline laboratory profile.

As presented in Table 2, there were no statistically significant differences identified

between the study groups concerning the anterior STEMI criteria in ECG, Killip classification, pain-to-door time, and door-to-balloon time. The median pain-to-door time was 5 hours for both groups, while the median door-to-balloon time was 18 minutes in each group. As demonstrated in Table 3, there were no statistically significant differences noted between the 2 study groups regarding the culprit vessel, except for 1 patient with left main disease in the colchicine group. Additionally, no significant disparities were observed concerning the level of left anterior descending artery occlusion, TIMI flow grades, thrombus burden, and MBG before the procedure. The groups also showed no significant differences in pre-stenting balloon dilatation, thrombus aspiration, and the number of stents used during the intervention. As indicated in Table 4, no statistically significant differences were found between the study groups vis-à-vis acute and chronic

complications during the hospital stay and at the 6-month follow-up.

According to Table 5, there were no statistically significant differences between the colchicine and control groups concerning baseline echocardiographic parameters. This includes LV systolic function assessment using Simpson's technique ( $P = 0.101$ ) and M-mode method for EF (%), as well as average systolic GLS of the LV estimated by STE ( $P = 0.130$ ). Additionally, no significant disparities were noted in WMSI within 48 hours of hospital admission following PPCI.

As demonstrated in Table 5, the LV systolic function assessment using Simpson's technique for EF (%) showed a statistically significant improvement in the colchicine group during the 6-month follow-up period ( $P = 0.011$ ). Furthermore, there was a highly statistically significant improvement in the average GLS by STE in the colchicine group over the same period.

**Table 1:** Demographic Characteristics, Baseline Laboratory Profile, and Risk Factors of the Study Groups

		Control group	Colchicine group	Test value	P value	Sig.
		No.= 100	No.= 100			
Age, y	Mean±SD	54.23 ± 7.66	56.30 ± 10.50	-1.593*	0.113	NS
	Range	39 – 69	23 – 83			
Sex	Female	29 (29.0%)	18 (18.0%)	3.365*	0.067	NS
	Male	71 (71.0%)	82 (82.0%)			
BMI, kg/m <sup>2</sup>	Mean±SD	32.10 ± 4.62	30.83 ± 4.72	1.922*	0.056	NS
	Range	23 – 41	21 – 40			
Smoking	Smoker	57 (57.0%)	61 (61.0%)	10.082*	0.006	HS
	Ex-smoker	0 (0.0%)	8 (8.0%)			
	Non-smoker	43 (43.0%)	31 (31.0%)			
HTN	No	30 (30.0%)	56 (56.0%)	13.790*	0.000	HS
	Yes	70 (70.0%)	44 (44.0%)			
DM	No	43 (43.0%)	56 (56.0%)	3.380*	0.066	NS
	Yes	57 (57.0%)	44 (44.0%)			
Family history of premature coronary artery disease	No	91 (91.0%)	90 (90.0%)	0.058*	0.809	NS
	Yes	9 (9.0%)	10 (10.0%)			
Dyslipidemia	No	0 (0.0%)	0 (0.0%)	–	–	–
	Yes	100 (100.0%)	100 (100.0%)			
Hb, g/dL	Mean±SD	13.86 ± 1.68	13.50 ± 1.92	1.440	0.151	NS
	Range	10.5 – 18	9.7 – 18.5			
LDL, mg/dL	Mean±SD	159.40 ± 28.58	154.92 ± 36.33	0.970	0.333	NS
	Range	110 – 220	11.5 – 263			
HbA1C, %	Mean±SD	7.08 ± 2.05	6.87 ± 2.19	0.708	0.480	NS
	Range	4 – 13	4 – 13			
Creatinine, mg/dL	Mean±SD	1.02 ± 0.29	1.01 ± 0.33	0.215	0.830	NS
	Range	0.07 – 1.6	0.4 – 2.5			

$P > 0.05$ : nonsignificant (NS),  $P < 0.05$ : significant (S),  $P < 0.01$ : highly significant (HS)

\*:  $\chi^2$  test; •: independent T-test

HTN: hypertension, DM: diabetes mellitus, BMI: body mass index, Hb: hemoglobin, LDL: low-density lipoprotein, HBA1c: glycosylated hemoglobin

**Table 2:** Anterior STEMI Criteria in ECG, Killip Classification, PTD Time, and DTB Time

		Control Group	Colchicine Group	Test value	P value	Sig.
		No.= 100	No.= 100			
Anterior STEMI criteria In ECG	Anterolateral	19 (19.0%)	24 (24.0%)	2.275*	0.517	NS
	Anteroseptal	20 (20.0%)	23 (23.0%)			
	Anterior	41 (41.0%)	31 (31.0%)			
	Extensive anterior	20 (20.0%)	22 (22.0%)			
Killip Classification	I	97 (97.0%)	96 (96.0%)	2.205*	0.332	NS
	II	3 (3.0%)	2 (2.0%)			
	III	0 (0.0%)	2 (2.0%)			
PTD time, h	Median (IQR)	5 (4 – 8)	5 (3 – 10)	-0.371‡	0.711	NS
	Range	1 – 12	1 – 12			
DTB time, min	Mean±SD	18.60 ± 7.66	18.25 ± 7.36	0.329•	0.742	NS
	Range	10 – 40	10 – 40			

$P > 0.05$ : nonsignificant (NS),  $P < 0.05$ : significant (S),  $P < 0.01$ : highly significant (HS)

‡: Mann-Whitney test

STEMI: ST-segment elevation myocardial infarction, PTD: pain-to-door time, DTB: door-to-balloon time

**Table 3:** Comparisons of the Study Groups Regarding Angiographic Data

		Control Group	Colchicine Group	Test value	P value	Sig.
		No.= 100	No.= 100			
Culprit vessel	LAD	100 (100.0%)	99 (99.0%)	1.005*	0.316	NS
	LM-LAD	0 (0.0%)	1 (1.0%)			
Site of total occlusion	Mid	39 (39.0%)	32 (32.0%)	1.406*	0.495	NS
	Proximal	58 (58.0%)	66 (66.0%)			
	Distal	3 (3.0%)	2 (2.0%)			
Thrombus burden	II	0 (0.0%)	1 (1.0%)	1.571*	0.666	NS
	III	8 (8.0%)	11 (11.0%)			
	IV	33 (33.0%)	31 (31.0%)			
	V	59 (59.0%)	57 (57.0%)			
TIMI flow pre-PPCI	TIMI 0	79 (79.0%)	71 (71.0%)	1.707*	0.191	NS
	TIMI 1	21 (21.0%)	29 (29.0%)			
MBG pre-PPCI	MBG 0	79 (79.0%)	73 (73.0%)	0.987*	0.321	NS
	MBG I	21 (21.0%)	27 (27.0%)			
Thrombus aspiration used	No	97 (97.0%)	99 (99.0%)	1.020*	0.312	NS
	Yes	3 (3.0%)	1 (1.0%)			
Balloon pre-dilatation	No	39 (39.0%)	40 (40.0%)	0.021*	0.885	NS
	Yes	61 (61.0%)	60 (60.0%)			
Number of stents used	0	0 (0.0%)	2 (2.0%)	4.561*	0.207	NS
	1	84 (84.0%)	77 (77.0%)			
	2	16 (16.0%)	19 (19.0%)			
	3	0 (0.0%)	2 (2.0%)			

$P > 0.05$ : nonsignificant (NS),  $P < 0.05$ : significant (S),  $P < 0.01$ : highly significant (HS)

\*:  $\chi^2$  test; •: independent T-test; ‡: Mann-Whitney test

PPCI: primary percutaneous coronary intervention, LAD: left anterior descending coronary artery, LM: left main coronary artery, TIMI: Thrombolysis in myocardial infarction, MBG: myocardial blush grade

**Table 4:** Comparisons Between the Control and Colchicine Groups Regarding Acute and Chronic Complications During a 6-Month Follow-Up

Complications	Control Group	Colchicine Group	Test value*	P value	Sig.
Free wall rupture or ventricular septal rupture	0 (0.0%)	0 (0.0%)	NA	NA	NA
Acute stent thrombosis	0 (0.0%)	0 (0.0%)	NA	NA	NA
LV thrombus	2 (2.0%)	3 (3.0%)	NA	NA	NS
VT / VF	0 (0.0%)	3 (3.0%)	3.046	0.081	NS
AF	3 (3.0%)	2 (2.0%)	F	0.651	NS
Major bleeding	0 (0.0%)	0 (0.0%)	NA	NA	NA
Acute limb ischemia	0 (0.0%)	0 (0.0%)	NA	NA	NA
CIN	10 (10.0%)	7 (7.0%)	0.579	0.447	NS
Cardiovascular death and resuscitated cardiac arrest	0 (0.0%)	0 (0.0%)	NA	NA	NA
Cerebrovascular stroke	0 (0.0%)	0 (0.0%)	NA	NA	NA
Post MI angina CCS III/IV	0 (0.0%)	0 (0.0%)	NA	NA	NA
Re-infarction or MI	0 (0.0%)	0 (0.0%)	NA	NA	NA

F: Fisher's exact test; NA: not applicable

$P > 0.05$ : nonsignificant (NS),  $P < 0.05$ : significant (S),  $P < 0.01$ : highly significant (HS)

\*:  $\chi^2$  test

VT: ventricle, AF: atrial fibrillation, VF, ventricular fibrillation, LV: left ventricle, HF: heart failure, CIN: contrast-induced nephropathy, MI: myocardial infarction, CCS: Canadian Cardiovascular Society

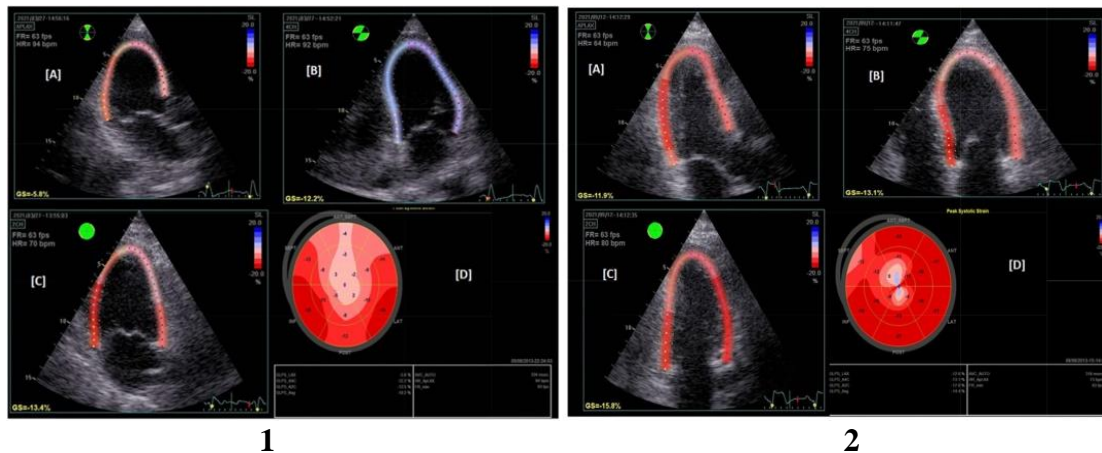
**Table 5:** Echocardiographic Assessments Within 48 Hours of Hospital Admission and After 6 Months

		Control Group No. = 100	Colchicine Group No. = 100	Test value	P value	Sig.
<b>Within 48 Hours of Hospital Admission</b>						
EF, % (Simpson's method)	Mean $\pm$ SD	34.90 $\pm$ 5.94	35.37 $\pm$ 5.54	-0.578•	0.564	NS
	Range	24.44 – 44.8	24.53 – 42.74			
LVEDV, mL	Mean $\pm$ SD	106.55 $\pm$ 7.70	108.30 $\pm$ 6.69	-1.716•	0.088	NS
	Range	90 – 125	96 – 118			
LVESV, mL	Mean $\pm$ SD	68.85 $\pm$ 4.00	69.70 $\pm$ 3.61	-1.578•	0.116	NS
	Range	62 – 77	65 – 80			
Average GLS, %	Mean $\pm$ SD	-9.30 $\pm$ 2.56	-9.87 $\pm$ 2.70	-1.520•	0.130	NS
	Range	-14.2 – -5	-16.5 – -5.5			
Wall motion score index	Mean $\pm$ SD	1.41 $\pm$ 0.17	1.41 $\pm$ 0.19	0.145•	0.885	NS
	Range	1.1 – 1.75	1 – 1.8			
<b>After 6 Months</b>						
EF at follow-up, % (Simpson's method)	Mean $\pm$ SD	39.38 $\pm$ 7.74	41.38 $\pm$ 3.98	-2.292•	0.023	S
	Range	25.26 – 55.1	32.32 – 47.58			
LVEDV, mL	Mean $\pm$ SD	114.10 $\pm$ 10.56	116.55 $\pm$ 9.59	-1.718•	0.087	NS
	Range	95 – 147	99 – 132			
LVESV, mL	Mean $\pm$ SD	68.50 $\pm$ 4.79	68.10 $\pm$ 4.70	0.596•	0.552	NS
	Range	60 – 78	60 – 80			
Average GLS at follow-up, %	Mean $\pm$ SD	-11.64 $\pm$ 2.73	-13.28 $\pm$ 2.13	-4.749•	0.001	HS
	Range	-17 – -5.6	-18 – -7.6			
Wall motion score index at follow-up	Mean $\pm$ SD	1.35 $\pm$ 0.16	1.34 $\pm$ 0.19	0.251•	0.802	NS
	Range	1 – 1.7	1 – 1.7			

$P > 0.05$ : nonsignificant (NS),  $P < 0.05$ : significant (S),  $P < 0.01$ : highly significant (HS)

•: independent T-test; †: Mann-Whitney test

EF: ejection fraction, GLS: global longitudinal strain, LVEDD: left ventricular end-diastolic diameter, LVESD: left ventricular end-systolic diameter, LVEDV: left ventricular end-diastolic volume, LVESV: left ventricular end-systolic volume



**Figure 1:** The images present case number 36 of the colchicine group.

- 1) Baseline global longitudinal strain (GLS) in patients from the colchicine group:
  - [A] GLS  $-5.8\%$  in the apical long-axis view; [B] GLS  $-12.2\%$  in the apical 4-chamber view. [C] GLS  $-13.4\%$  in the apical 2-chamber view; [D] a bull's eye view showing an average peak systolic GLS pattern of  $-10.2\%$
- 2) GLS in a patient from the colchicine group at the 6-month follow-up:
  - [A] GLS  $-11.9\%$  in the long-axis view; [B] GLS  $-13.1\%$  in the 4-chamber view. [C] GLS  $-15.8\%$  in the 2-chamber view; [D] a bull's eye view showing an average peak systolic GLS pattern of  $-14.4\%$

## DISCUSSION

In the present study, the baseline echocardiographic assessment conducted within 48 hours of hospital admission revealed reduced LVEF as calculated by Simpson's method. Interestingly, no statistically significant difference was observed between the 2 study groups in terms of LVEF at this early time point. This finding can likely be attributed to the phenomenon of early myocardial stunning following a successful PPCI.

Myocardial stunning, a phenomenon characterized by temporary and reversible myocardial contractile dysfunction, is typically observed following acute ischemia when blood supply is promptly restored through reperfusion. Notably, even a brief period of total coronary artery blockage lasting between 5 and 15 minutes can result in LV wall motion abnormalities that may persist for several days, despite successful reperfusion. The underlying pathophysiology of myocardial stunning is primarily explained by 2 main theories: a reduction in the sensitivity of contractile filaments to calcium and the generation of

free radicals derived from oxygen during reperfusion.<sup>18</sup>

During the follow-up period, the assessment of LVEF using Simpson's method revealed a significant improvement in LV systolic function in the colchicine group compared with the control group. Remarkably, this study also demonstrated a statistically significant improvement in LV systolic function using speckle-tracking longitudinal strain patterns in the colchicine group in comparison with the control group. To our knowledge, this is the first study to evaluate the impact of colchicine administration on longitudinal strain patterns in patients with anterior STEMI. A reduction in adverse LV remodeling, a component of the myocardium's healing process following an MI, may have contributed to the improvement in LV systolic function.<sup>19</sup>

Inflammation plays a significant role in exacerbating adverse LV remodeling, which can ultimately lead to heart failure. The findings of this study align with those of Mastrocola et al,<sup>20</sup> who investigated the effects of colchicine administered immediately after acute coronary syndrome. Preliminary in vivo data from their study demonstrated that pharmacological inhibition

of the NLRP3 inflammasome with colchicine could attenuate MI reperfusion injury and limit infarct size in mouse models.

A pilot study involving 151 participants, with 60 individuals included in the magnetic resonance imaging sub-study, demonstrated that colchicine administration might result in reduced levels of cardiac biomarkers and late gadolinium enhancement-defined infarct size when given to patients with STEMI within 12 hours of symptom onset. Notably, this reduction in infarct size was observed when there was a 50% decrease in the size of the infarct, as measured by the area under the curve of creatinine kinase myocardial brain fraction.<sup>21</sup>

The Colchicine for Left Ventricular Infarct Size Reduction in Acute Myocardial Infarction (COVERT-MI) study (192 patients) investigated the effects of colchicine on the initial inflammatory response to reperfusion injury in acute coronary syndrome. **II** A high-dose of colchicine (2 mg loading dose, followed by 0.5 mg twice daily) or placebo was administered for a short-term period (5 d) to patients admitted for PCI following a first episode of STEMI. As opposed to our results, no differences were found between the groups in the primary outcome of myocardial injury (at 6, 24, and 48 hours of follow-up), biomarkers of inflammation (including C-reactive protein), or gadolinium-enhanced infarct size on magnetic resonance imaging ( $P = 0.87$ ). At 3 months of follow-up, there were no variations in the longer-term secondary outcomes of LV remodeling and infarct size.

The discrepancy between the results of this current study and the COVERT-MI study can potentially be explained by differences in the target study populations and the duration of colchicine administration. In the COVERT-MI study, the researchers enrolled a broader range of STEMI patients, whereas this present study focused specifically on anterior STEMI patients. Anterior STEMI patients are known to have a higher risk of adverse LV

remodeling and worse outcomes, which could potentially make them more responsive to the cardioprotective effects of colchicine. Another factor to consider is the difference in the duration of colchicine administration. In the COVERT-MI study, colchicine was given for a shorter period of 5 days, whereas in this current study, colchicine was administered for a more extended period of 6 months. In assessing the composite of acute complications during hospitalization for MI, no statistically significant difference was found between the 2 studied groups concerning mechanical complications, LV thrombus formation, major arrhythmias (ventricular tachycardia/ventricular fibrillation), major bleeding events, acute limb ischemia, and contrast-induced nephropathy. In this study, there was no significant difference in the number of patients with LV thrombus between the 2 groups. This finding contrasts with the results of the COVERT-MI study, which showed a higher incidence of LV thrombus in the colchicine group than in the placebo group at 5 days, although this difference was not observed at 3 months. This discrepancy in findings may be due to the different imaging modalities used to detect LV thrombus in the 2 studies. The COVERT-MI study employed cardiac magnetic resonance imaging, known to be more accurate in detecting LV thrombus than echocardiography, the method used in this current study.

In this study, the control group demonstrated a higher incidence of contrast-induced nephropathy, characterized by renal function impairment with an absolute increase  $\geq 0.5$  mg/dL or a relative increase  $\geq 25\%$  in baseline serum creatinine levels within 48 hours. This finding may be attributable to colchicine's anti-inflammatory properties and its potential role in reducing reactive oxygen species production, which has been suggested as a protective mechanism against contrast-induced nephropathy.<sup>22</sup> In this study, a higher

incidence of atrial fibrillation was observed in the control group than in the colchicine group, although the difference did not reach statistical significance. The findings of the current study align with those of a meta-analysis by Imazio et al,<sup>23</sup> which evaluated the role of colchicine in preventing postoperative atrial fibrillation in 912 patients across multiple double-blind randomized controlled trials. The meta-analysis found that perioperative colchicine administration led to a 35% reduction in the incidence of atrial fibrillation (relative risk, 0.65; 95% CI, 0.46 to 0.91) during a follow-up period of 1 to 6 months. The cardioprotective effects of colchicine in reducing the incidence of atrial fibrillation may be attributed to its potential role in reversing cardiac remodeling of the LV, similar to the proposed mechanism for LV reverse remodeling.

Further evidence supporting the potential benefits of colchicine in coronary artery disease can be found in a 2020 meta-analysis that pooled data from several large randomized controlled trials, including the Colchicine Cardiovascular Outcomes Trial (COLCOT) and the Low-Dose Colchicine (LoDoCo) trials. The meta-analysis demonstrated that, compared with placebo, colchicine was associated with significant reductions of 32% in the composite outcome of cardiovascular mortality, MI, ischemic stroke, and urgent coronary revascularization, as well as 38% for MI, 62% for stroke, and 44% for urgent coronary revascularization. In the meta-analysis, no significant differences were observed in mortality endpoints or various adverse events, such as hospitalization for gastrointestinal events, infection, or pneumonia, when comparing colchicine-treated patients to those receiving placebo. Nonetheless, a numerically nonsignificant increase in non-cardiovascular death was noted in the colchicine group (relative risk, 1.38; 95% CI, 0.99 to 1.93).

In the current study, colchicine administration was found to be safe when compared with the

control group, as there were no statistically significant differences observed in terms of MACE, cerebrovascular stroke, post-MI angina, and re-infarction. The findings of the current study differ from those of the COLCOT trial, which demonstrated that long-term colchicine administration at a dose of 0.5 mg daily, initiated within 30 days following an MI, was associated with a significantly lower risk of ischemic cardiovascular events than placebo. One potential explanation for the discrepancy between these findings may be the differences in sample size and patient demographics between the 2 studies. The COLCOT trial included a much larger patient population (n=4,754) than the present study (n=200).

In the present study, there was no statistically significant difference between the 2 studied groups regarding EF (%) by Simpson's method. On the other hand, there was a statistically significant improvement in GLS by STE in the colchicine group when compared with the control group. This finding may be attributed to the accuracy of GLS in the assessment of LVEF by comparison with Simpson's method. Furthermore, echocardiography is associated with a high level of interobserver variability.<sup>25</sup>

## CONCLUSIONS

The current study demonstrated that administering colchicine to anterior STEMI patients with a successful PPCI was both safe and effective. After a 6-month follow-up, colchicine improved LV systolic function, as measured by average longitudinal GLS using STE and Simpson's method. Additionally, at the 6-month follow-up, both studied groups showed comparable rates of mortality and morbidity, along with a nonsignificant decrease in the incidence of contrast-induced nephropathy and atrial fibrillation in the colchicine group.

## Limitations

This single-center study had a brief follow-up period and a small sample size.

## Declarations

**Ethical Approval and Consent to Participate:** The study design was reviewed and approved by the Ethical Committee of Ain Shams University (FMASU M D 160/2020), adhering to the principles outlined in the Declaration of Helsinki, last updated in 2008. Informed written consent was obtained from all participants before their involvement in the study.

**Consent for Publication:** Not applicable.

**Availability of Data and Materials:** The data sets generated and analyzed during the current study can be obtained from the corresponding author upon reasonable request.

**Conflict of Interest:** The authors declare that they have no competing interests.

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## Authors' contributions:

MM generated the idea of the research and was a major contributor to data collection, and analysis of echocardiography and ECG in addition to writing the manuscript.

AAS revised the data set and participated in data analysis.

HG revised the data set and participated in data analysis.

HK participated in the revision and analysis of patient data, statistical analysis, and writing the manuscript.

All the authors read and approved the final manuscript.

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