Improvements in Regional Left Ventricular Function Following Late Percutaneous Coronary Intervention for Anterior Myocardial Infarction

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ABSTRACT

BACKGROUND: Late revascularization following a myocardial infarction has questionable clinical benefit.

METHODS: We studied 13 patients with anterior wall myocardial infarction who underwent percutaneous coronary intervention within 2 weeks of the primary event, by quantitative analysis of 2-dimensional echocardiographic images. Endocardial segmentations of the left ventricular (LV) endocardium from the 4-chamber views were studied over time to establish cumulative wall displacements (CWDs) throughout the cardiac cycle.

RESULTS: Left ventricular end-systolic volume decreased to 42 ± 8 mL/body surface area (P = .034) and LV ejection fraction improved to 52% ± 7% (P = .04). Analysis of LV endocardial CWD demonstrated significant improvements in mid-systolic to late-systolic phases in the apical LV segments, from 3.5 ± 0.32 to 5.89 ± 0.43 mm (P = .019). Improvements in CWD were also observed in the late-diastolic phase of the cardiac cycle, from 1.50 ± 0.42 to 1.76 ± 0.52 mm (P = .04).

CONCLUSIONS: In our pilot patient cohort, following late establishment of infarct-related artery patency following an anterior wall myocardial infarction, regional improvements were noted in the LV apical segments during systole and late diastole.

KEYWORDS: Myocardial infarction, revascularization, infarct-related artery patency, percutaneous coronary intervention

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Introduction

The restoration of blood flow in an infarct-related artery (IRA) in the first 12 hours of infarct evolution is the cornerstone of treatment of acute myocardial infarction (MI).[1,2] It salvages the myocardium by decreasing infarct size, preventing infarct expansion, thereby preventing adverse ventricular remodelling and promoting electrical stability.[1,2] Late percutaneous coronary intervention (PCI) has also shown benefits in terms of improvements in left ventricular (LV) global function following patency of the IRA.[3] However, the largest trial on late revascularization, the OAT (Open Artery Trial), did not demonstrate clinical benefits following late revascularization following acute MI.[4] One of the drawbacks of this trial is the lack of imaging studies to quantify improvements in LV function. We hypothesized that following late revascularization, improvements in LV function may be significant and if so may translate into beneficial clinical outcomes in terms of morbidity from heart failure.

Improvements in global LV function quantified in terms of LV ejection fraction (LVEF) have been extensively studied following PCI for MI. Regional LV function following revascularization has not been adequately quantified. Regional LV function improvement has been noted after revascularization following an acute MI, in terms of improvements in regional wall motion. An improvement in regional LV dyssynchrony has not been quantified following revascularization. In this study, we test the hypothesis that regional LV function improvements are seen following late revascularization for patients with anterior wall MI. To quantify the regional LV function improvements, we used a new quantitative technique to establish the cumulative regional wall displacement in LV segments at baseline and after revascularization, starting with 2-dimensional (2D) echocardiographic imaging.

Methods

Clinical data

We studied 13 consecutive patients who presented with acute ST elevation MI (STEMI) to St. John's Medical College Hospital, between August 2013 and September 2014. Patients

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with anterior MI were included in the study. Patients above the age of 80 years, patients in cardiogenic shock, and those with mechanical complications following acute MI and with contraindications for PCI were excluded. Institutional Ethics Review Board approval was obtained for the study, and informed patient consent was taken for participation in the study.

Cardiac imaging

All patients underwent cardiac imaging on admission by 2D echocardiography using a GE Vingmed Ultrasound v7 imaging system. The LV end-diastolic volume (EDV), LV end-systolic volume (ESV), and LVEF were noted at admission and within 24 hours of PCI. All values were indexed to body surface area (BSA) in accordance with the ASE (American Society of Echocardiography) recommendations of chamber quantification.[5] The mitral inflow Doppler data were used to quantify LV diastolic function.[6]

The 4-chamber echocardiographic views were studied quantitatively over time after further processing for analysis of LV wall motion across several discrete phases of the cardiac cycle.

LV segmentation and function analysis

Automatic LV segmentation was conducted at each available image frame over a single cardiac cycle from video exports of 4-chamber echocardiographic views. The image-processing workflow entailed first endocardial segmentation of the LV from the 4-chamber echocardiographic view, using a region-partitioning active contour algorithm,[7] followed by smooth surface reconstruction of the resulting contours using an implicit Poisson surface fitting algorithm[8,9] to obtain smooth surface segmentations of the LV endocardium which were robust to speckle noise in the image data.

Next, cumulative LV endocardial wall displacement was analysed from the start of the cardiac cycle, as signalled by the start of LV contraction (ie, the R wave). Cumulative wall displacement (CWD) was analysed by an established regional distance metric between segmented contours extracted from consecutive frames of the echocardiography data. Cumulative wall displacement of the LV endocardium was quantified using a signed, regional Hausdorff distance[10–12] computed using an in-house plug-in for ParaView (Kitware, Inc.) at vertices of the LV segmentation, which inherently establishes point correspondences between each instantaneous LV segmentations with the LV segmentation in the first cardiac phase, assigning a vector as well as a colour based on the magnitude of regional displacement (signed positive for inward contractile motion relative to the first cardiac phase and negative for outward expansion) at each vertex defining the segmentation contours.

In previous studies by our group, phase-to-phase displacement was established by tracking segmentation vertices between pairs of temporally consecutive cardiac phases[12,13] as a means to identify a signature of LV function useful for classification of heart failure progress. However, in this study, CWD was a more viable option for robust tracking of the LV endocardial wall because it helped inherently to establish correspondences between the vertices of segmentations at each cardiac phase with the segmentation at the first phase of the cardiac cycle. In this manner, the displacement histories of each LV endocardial contour vertex was possible to be recorded over the entire cardiac cycle, with reference to a fixed LV centroid making the method more robust to small changes in the angulation of the echocardiographic probe during image acquisition. Colour maps of regional endocardial CWD were prepared at each instant of the cardiac cycle to provide a qualitative sense for the nature of regional wall motion.

The average and standard deviation in the endocardium-averaged CWD history were plotted as characteristic curves for each of our cohort patients. The CWD curves which resulted were sampled into 30 equally spaced cardiac phases, the same for each patient, for the purpose of comparison of the different patients as well as comparison of regional LV function before and after PCI or thrombolysis treatment. The cardiac cycle was possible to be resampled using only CWD characteristic curves into 30 phases (labelled from 0° to 360° in our figures, starting with the R wave) which were in turn categorized as per standardized period labels. Systole starts with phases 1 to 5 being termed isovolumetric contraction time and 5 to 17 as the ejection phase, followed by diastole which starts with phases 17 through 20 as isovolumetric relaxation time. Then, phases 20 to 25 define diastolic early-filling and 25 to 30 define the atrial or late-filling phases.

Statistical analysis

Unpaired Student t test was used to compare the differences between means and $P < .05$ was considered statistically significant. All statistical analyses were performed using SPSS v14 (SPSS Inc., Chicago, IL, USA). All continuous variables are expressed as mean ± SD.

Results

Clinical outcomes

There were 13 patients presenting with anterior wall STEMI. The patients' age ranged from 41 to 76 years (mean age: 53.3 ± 15.7 years). There were 3 women and 10 men. There were 8 hypertensives and 7 diabetics. There was history of chronic smoking in 6 patients, whereas 2 had a strong family history of premature coronary artery disease. The mean body mass index was 22 ± 5 kg/m^2. The mean troponin I value was 5.2 ± 1.8 ng/dL. Percutaneous coronary intervention was done at

Table 1. Patient clinical characteristics at baseline.

PATIENT CHARACTERISTICS (N = 13)	
Age, y	53.3 ± 15.7
Females	3
Killip class	1.3 ± 0.9
Hypertension	8
Diabetes	7
Smoking	6
Family history of CAD	2
BMI, kg/m^2	22 vs 5
Time between primary event and PCI, d	0 ± 2.5

Abbreviations: BMI, body mass index; CAD: coronary artery disease; PCI: percutaneous coronary intervention.

10 ± 2.5 days following the primary event. In all patients, the primary event was an anterior wall STEMI. All patients were in Killip class 1.3 ± 0.9. All patients presented late to the hospital (ie, >28 ± 4.5 hours after MI) and therefore did not receive primary PCI (Table 1). All patients were on maximal tolerated doses of long-acting β-blockers, angiotensin-converting enzyme inhibitors, statins, dual antiplatelets, and low-molecular-weight heparin.

All patients demonstrated successful patency of the IRA with TIMI 3 flow grade. All patients had improvement in Killip class at discharge from hospital and no readmissions for angina, reinfarction, or heart failure. At 30 days following the primary event, there was no mortality or morbidity.

Cardiac imaging by 2D echocardiography

Left ventricular end-diastolic volume for our study cohort at baseline was 100 ± 13 mL/BSA. Left ventricular end-systolic volume at baseline was 55 ± 9 mL/BSA. Left ventricular ejection fraction at baseline was 41% ± 9%. There were 13 patients with LV diastolic dysfunction (LVDD) as defined by the mitral inflow Doppler pattern (LVDD grade 1.9 ± 0.4).

All 13 patients had regional wall motion abnormalities on 2D echocardiography in the anterior wall, septum, and apical areas. These areas corresponded to 20% ± 3% of the LV myocardium as assessed by segmental LV analysis. None of the patients had large scars in the infarct territory.

Following PCI, LV EDV reduced marginally to 96 ± 9 mL/BSA (P = .43). Left ventricular end-systolic volume decreased to 42 ± 8 mL/BSA (P = .034) and LVEF improved to 52% ± 7% (P = .04). Following PCI, there was a small insignificant improvement in LVDD from baseline to grade 1.2 ± 0.7 (P = .34) (Table 2).

Table 2. Comparison of 2-dimensional echocardiographic parameters at baseline and after PCI.

	PRE-PCI	POST-PCI	*P* VALUE
LV EDV	100 ± 13 mL	96 ± 9 mL	.43
LV ESV	55 ± 9 mL	42 ± 8 mL	.034
LVEF	41% ± 9%	52% ± 7%	.04
LVDD	1.9 ± 0.4	1.2 ± 0.7	.34

Abbreviations: LV EDV, left ventricular end-diastolic volume; LV ESV, left ventricular end-systolic volume; LVDD, left ventricular diastolic dysfunction; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention.

When LV endocardium-averaged CWD was plotted against time over the cardiac cycle, averaged across the study cohort (see Figure 1), it was apparent that the global LV cumulative displacement during systole demonstrated improvements as a result of PCI, although these improvements were statistically insignificant (ie, −0.61 ± 0.575 to −0.78 ± 1.27 mm/s, P = .88). When the timing to peak contraction was studied, there was a small but insignificant improvement from 13 ± 3.43 to 12 ± 2.8 ms (P = .24) suggesting an earlier onset of LV contraction following PCI. Mean regional/segmental CWD was studied in the lateral, apical, and septal regions of the LV (see Figure 2).

We additionally studied the cohort-averaged improvement in regional LV function after PCI. The lateral, apical, and septal LV wall regions were demarcated from the endocardium based on a division of the segmented contours at each time instant into equal thirds. In systole, significant improvements in regional average CWD (ie, 3.5 ± 0.32 mm to 5.89 ± 0.43 mm, P = .019) were noted during the ejection phase of systole in the apical region (ie, at time instants coded 9 and 10 in Figure 3) as well as in late-diastolic LV filling (ie, 1.50 ± 0.42 to 1.76 ± 0.52 mm, P = .04, at time instants of 29 and 30 in Figure 3). However, this improvement was more pronounced on a patient-specific level. In one example, we examined the regional LV wall motion in terms of regional CWD for a specific patient who experienced an improvement in LV function which is shown in Figure 4 and Table 3. Although there was no significant improvement in the average CWD characteristics in the septal and lateral LV regions following revascularization, the improvements in the LV endocardium-averaged CWD were seen mainly during the ejection phase of systole and in late diastole, in the apical LV region (see Table 3). Figure 5 summarizes the frequency of a given region of the LV being the most contractile wall region when the cardiac cycle was sampled into 30 equally spaced intervals, for this patient.

There were significant improvements in the LV ESV and LVEF with no significant changes in LV EDV for the cohort (n = 13) as a result of PCI. There was no improvement in LVDD following revascularization.

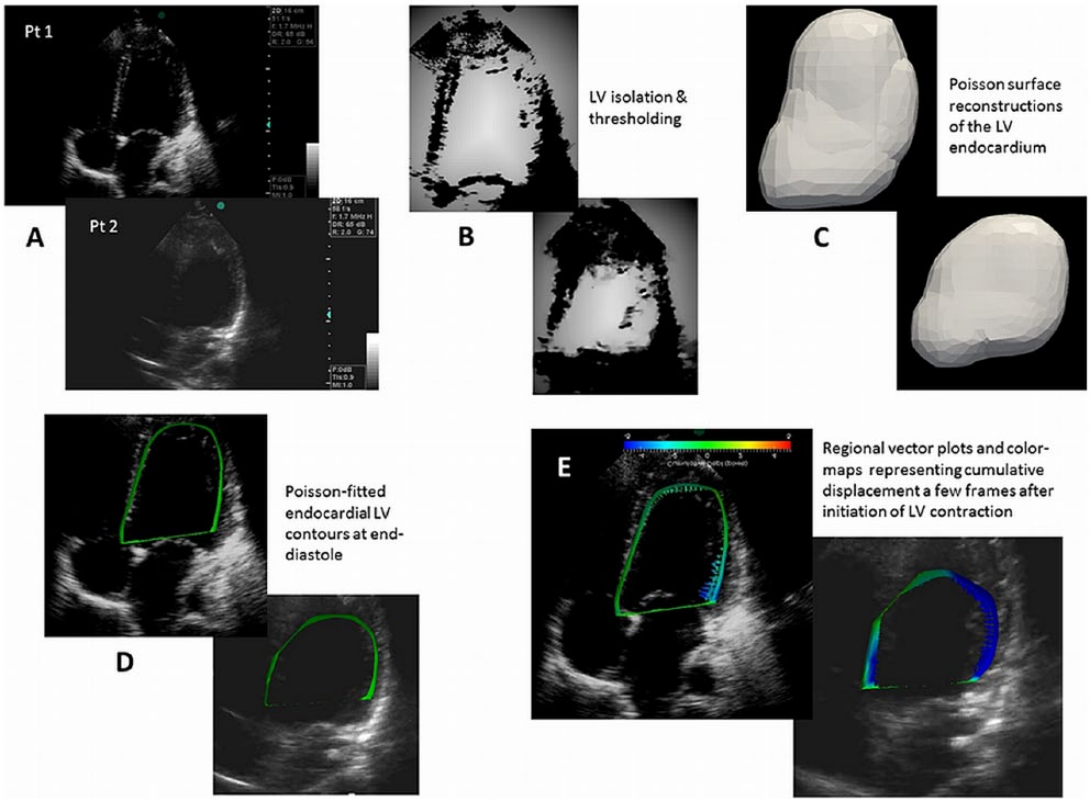

Figure 1. Automated LV segmentation from 4 chamber long axis echocardiographic images. (A) at each frame of a time series imaging sequence, followed by regional analysis of cumulative displacement from the end-diastolic phase (E). Representative segmentation results in the end-dyastolic phase (D) are the regional curvature outlines of Poisson surface reconstructions of an artificially extruded (ie normal to the image) 3D version of a thresholded active contour level set function (B) which was used to crop/isolate the original image frame and detect the LV region.

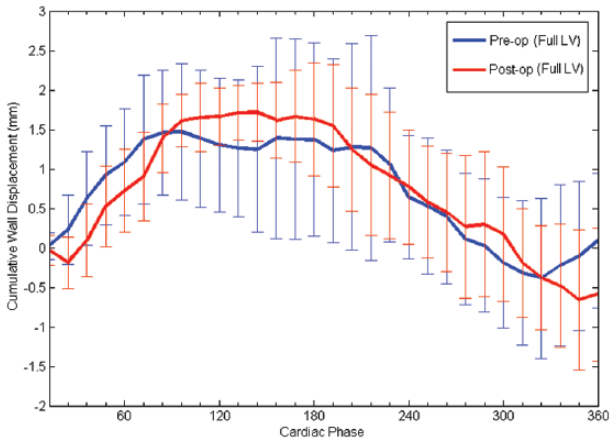

Figure 2. Average cumulative wall displacement (CWD) of the LV endocardium at baseline (blue) and after (red) percutaneous coronary interventions (PCI) following anterior-wall myocardial infarction.The error bars indicate standard deviation in the LV averaged CWD across the study cohort, before (blue) and after (red) PCI.

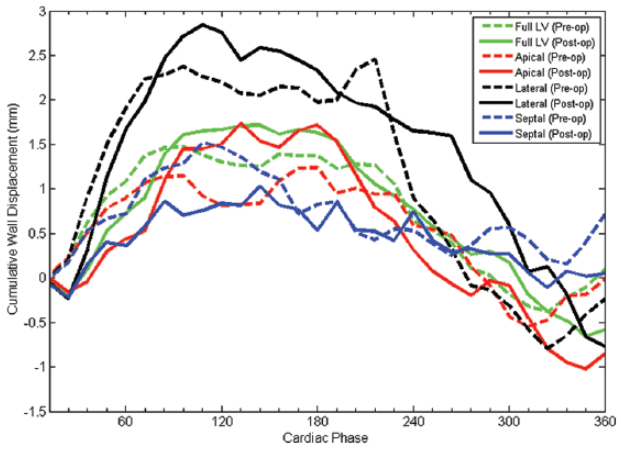

Figure 3. Regional average CWD in the septal, lateral and apical segments of the LV endocardiumpresented superimposed with theglobalLV averaged CWD at baseline (blue) following an anterior wall myocardial infarction and after (red) PCI.

Coronary anatomy

Coronary angiography performed in all patients revealed proximal occlusion of the left coronary artery (LAD) with distal LAD filling late through collaterals from the right coronary artery (RCA). Of the 13 patients, 9 had single-vessel disease affecting the LAD which was the IRA. In 3 patients, there was 2-vessel disease affecting the left circumflex coronary artery (LCX). In 1 patient, there was involvement of all 3 coronary arteries, with occlusion of LAD, and high-grade stenosis of LCX and proximal RCA. In 9 patients with single-vessel disease involving the LAD, there were collaterals from RCA in 4 patients and homolateral collaterals from the obtuse marginal

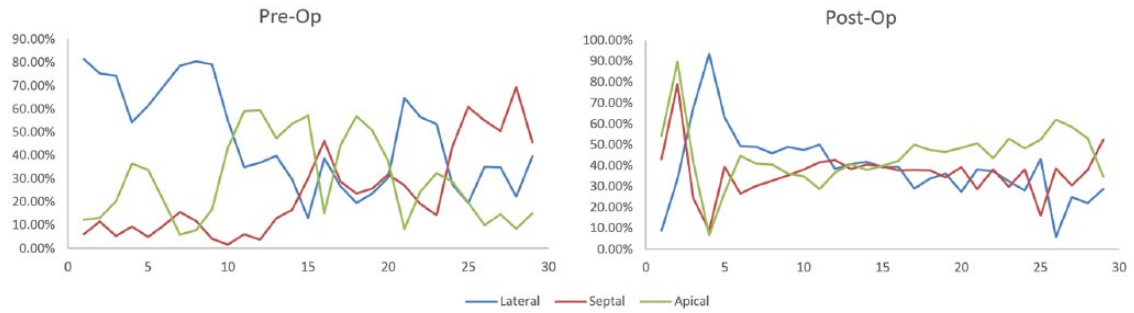

Figure 4. Comparison of regional LV-averaged CWD at baseline and after PCI for a patient-specific case where improvements in LV function were seen after PCI.

Table 3. Comparison of regional LV CWD before and after PCI for a patient-specific case where improvements in LV function were seen after PCI.

PHASE	PRE-PCI				POST-PCI			
	LATERAL, %	SEPTAL, %	APICAL, %	MOST CONTRACTILE WALL REGION	LATERAL, %	SEPTAL, %	APICAL, %	MOST CONTRACTILE WALL REGION
1	81.48	6.14	12.39	Lateral	8.86	43.12	54.18	Apical
2	75.32	11.51	13.16	Lateral	33.52	78.80	89.80	Apical
3	74.33	5.37	20.30	Lateral	67.53	24.50	41.56	Lateral
4	54.13	9.46	36.41	Lateral	93.33	8.94	6.82	Lateral
5	61.37	4.82	33.81	Lateral	62.95	39.49	27.02	Lateral
6	69.95	10.02	20.03	Lateral	49.33	26.58	44.51	Lateral
7	78.54	15.59	5.87	Lateral	48.93	30.31	40.95	Lateral
8	80.49	11.75	7.77	Lateral	45.84	32.69	40.43	Lateral
9	79.15	4.05	16.81	Lateral	48.91	35.23	36.10	Lateral
10	54.98	1.70	43.32	Lateral	47.42	38.14	34.81	Lateral
11	34.81	6.11	59.08	Apical	49.92	41.63	28.89	Lateral
12	36.81	3.76	59.43	Apical	38.29	42.60	36.67	Septal
13	39.71	12.84	47.45	Apical	40.80	38.36	40.63	Lateral
14	29.71	16.62	53.67	Apical	41.90	40.45	37.93	Lateral
15	13.01	29.94	57.05	Lateral	39.26	39.56	39.81	Apical
16	38.80	46.26	14.95	Septal	39.32	37.76	42.23	Apical
17	26.99	28.87	44.14	Apical	29.07	37.93	49.94	Apical
18	19.46	23.59	56.94	Apical	33.72	37.66	47.38	Apical
19	23.66	25.69	50.65	Apical	36.17	34.49	46.62	Apical
20	30.52	31.75	37.73	Apical	27.41	39.15	48.42	Apical
21	64.66	27.02	8.32	Lateral	38.21	28.82	50.62	Apical
22	56.52	19.15	24.32	Lateral	37.22	38.05	43.44	Apical
23	53.37	14.34	32.29	Lateral	32.57	29.89	52.88	Apical
24	27.52	43.78	28.70	Septal	28.15	38.21	48.33	Apical
25	19.42	60.81	19.76	Septal	43.16	15.96	52.38	Apical
26	35.13	54.95	9.92	Septal	5.90	38.61	62.03	Apical
27	34.90	50.45	14.65	Septal	24.83	30.42	58.46	Apical
28	22.32	69.33	8.35	Septal	22.13	37.91	53.15	Apical
29	39.50	45.55	14.96	Septal	28.69	52.49	34.55	Septal

Abbreviations: CWD, cumulative wall displacement; LV, left ventricular; PCI, percutaneous coronary intervention.

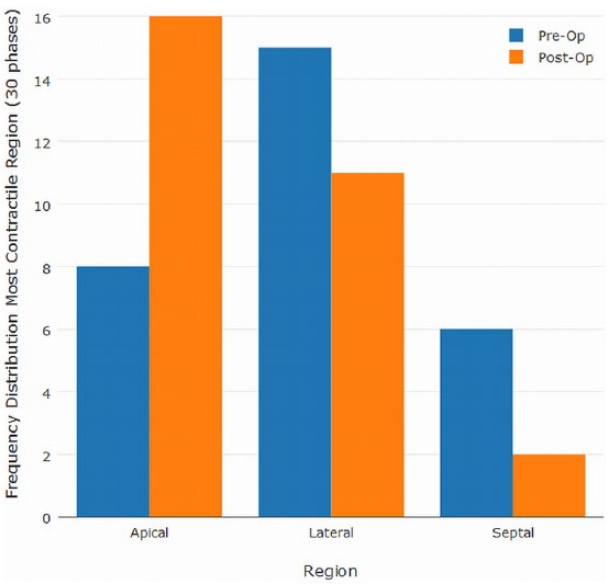

Figure 5. Comparison of the maximal contractile LV region at baseline and after PCI for a patient-specific case where improvements in LV function were seen after PCI.

in 5 patients. In 3 patients with 2-vessel disease, there were no collaterals.

Discussion

Lack of influence of late PCI on cardiac function and remodelling may explain the lack of clinical benefits of late PCI in terms of reduction in negative outcomes.[3–5] None of these randomized clinical trials on late PCI for an occluded IRA included infarct zone viability criterion as an inclusion for randomization to treatment, which may have influenced the results. Also, only few trials demonstrated improvements in cardiac systolic function after late PCI.[17–21] However, even in these trials, the effect on changes in LV size was not demonstrated.[3,14,15] As myocardial salvage is possible beyond the first 12-hour limit even when the IRA is totally occluded, we hypothesized that improvements in regional LV function are possible after late revascularization which may translate into beneficial clinical outcomes.[22–24]

The effects of revascularization on regional LV segments have not been adequately documented in longitudinal studies. These have been demonstrated in an experimental study, wherein early systole, a decline in systolic shortening, was noted compared with the uninvolved normal myocardium. In mid to late systole, shortening was observed in the ischaemic myocardium, which was due to persisting contractile activity which persisted beyond aortic valve closure extending into early diastole, decreasing diastolic compliance, and decreasing early diastolic filling.[16]

To test our hypothesis, we studied a pilot cohort of 13 patients who presented with anterior wall MI and underwent PCI beyond the first 12-hour limit. They all underwent PCI within 2 weeks of the index event. We studied the regional LV function by studying the CWDs before and after PCI which showed significant improvements in the IRA territory in all patients. Improvement in LV volume was also seen after late PCI. Although we did not demonstrate presence of myocardial viability by perfusion studies, none of our patients had extensive scarring of the infarct territory as evidenced by the presence of collateral circulation on angiography.

In this study, although global improvements in CWDs of the LV segments were not significant, the regional segmental displacements demonstrated improvements in the infarcted segments following revascularization resulting in synchronous contraction (Figure 2) reflected in the smaller standard deviations of the CWD curves following PCI. This was more pronounced on a patient-specific level (see Figure 4 and Table 3), validating our hypothesis that opening of the IRA especially the LAD is effective in improving regional LV function in the infarct territory. Late PCI resulted in reverse LV remodelling preventing infarct expansion and adverse remodelling. Furthermore, when the region of maximal contractility was compared before and after PCI, it was noted that more apical LV segments had maximal contractility after PCI (Figure 5).

Global LV systolic function improved following late PCI with improvements in LV size. Global CWDs did not show significant improvements following PCI. The cumulative displacement of the LV in the apical region improved significantly during the ejection phase of systole.

Following an anterior MI, the hypokinetic apex forms an ineffective fulcrum thereby leading to ineffective apical squeezing during systole.[25] Therefore, improvements in apical myocardial function alone results in improvements in global LV systolic function, even in the absence of global improvements in LV wall displacement. Late apical diastolic relaxation also significantly improved after revascularization indicating an improvement in apical untwisting favouring better LV filling. This was also evident in the synchronous contraction seen after PCI and also in more apical LV segments demonstrating maximal contractility after PCI (Figures 4 and 5).

Conclusions

Following an ST elevation anterior MI, late PCI with establishment of IRA patency results in reverse global LV remodelling with significant decreases in LV ESV and increases in LVEF. Improvements in regional apical LV CWD in the absence of improvements in global CWDs are seen which are responsible for the improvements in LV function. These findings in a pilot cohort tests the hypothesis that late revascularization leads to improvements in the infarct territory, limiting infarct expansion and adverse LV remodelling.

Author Contributions

SMA and PGM were jointly responsible for the concept, analysis and drafting the manuscript. KV was responsible for overall guidance and critical revision of the manuscript. AM and

SBL were responsible for analysis of the data. FF was responsible for guidance advice and critical evaluation of the manuscript.

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