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Research Article

NATURAL HISTORY OF ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION WITH TOTAL OCCLUSION OF INFARCT-RELATED ARTERY DURING SIX-MONTH FOLLOW-UP WITH OPTIMUM MEDICAL THERAPY

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ABSTRACT

Objective: Fate of ST-segment elevation myocardial infarction (STEMI) patients on optimum medical therapy (MED) who remain asymptomatic following myocardial infarction (MI) within 24 h, electrically and hemodynamically stable regarding their clinical status, left ventricular function, with totally occluded infarct-related artery.

Methods: One hundred patients whose angiography performed 3–28 days after STEMI, showed total occlusion of the infarct-related artery with poor or absent ante-grade flow, were put on optimum MED in the absence of contraindication and followed up for 6 months.

Results: At 1st month, among 100 patients, 46 (46%) patients were asymptomatic. About 43 (43%) patients were presented with shortness of breath on exertion (SOBE) and rest 11 (11%) had both chest pain and shortness of breath. In subsequent visit at 6 months, 46% of patients were asymptomatic and rest presented with SOBE, none of them presented with significant chest pain.

Conclusion: In spite of optimum MED, patients with total occlusion of infarct-related artery and non-viable myocardium developed progressive remodeling. Collateral flow is not adequate to prevent remodeling. Remodeling causes gradually progressive heart failure symptoms. The patient usually did not present with chest pain. Shortness of breath was predominant symptoms in follow-up in this group of patients.

Keywords: ST-segment elevation myocardial infarction, Infarct-related artery, Optimum medical therapy.

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INTRODUCTION

The late open-artery hypothesis tells after myocardial infarction (MI), mechanical recanalization of a persistently occluded artery even at a time too late for myocardial salvage should decrease left ventricular (LV) remodeling and improve longer outcome [1]. Depending on the collateral circulation, myocardium may remain alive for a long period after sudden occlusion of an artery [2]. Even after successful thrombolysis, reocclusion but without reinfarction prevents salvaged myocardium from achieving contractility, with resultant ill yield for LV function and remodeling [3]. An opened-up infarct-related artery during discharge was associated with better outcomes [4-6]. Several randomized trials of small or modest sample sizes compared percutaneous coronary intervention (PCI) versus medical therapy (MED) for total occlusion late after MI [7-11]. Although no definite results are found, betterment in LV function hinted that the late opening of arteries after MI should be sincerely considered. However, in occluded artery trial (OAT), the PCI carried out in stable patients 3–28 days after MI did not reduce the occurrence of death, reinfarction, or heart failure (HF). In addition, there was an inclination toward excess reinfarction in the PCI arm during follow-up [12]. The total occlusion study of Canada 2 substudy of OAT also found no benefit of the PCI strategy in LV function [13]. These results have put a real challenge to the late open artery hypothesis and its clinical implications. As per 2013 ACC/AHA guideline for the management of ST-segment elevation MI (STEMI), the benefits of routine, that is, non-ischemia-driven, PCI of an angiographically significant stenosis in a patent infarct artery 24 h after STEMI are less well established. Delayed PCI of a totally occluded infarct artery 24 h after STEMI should not be undertaken in clinically stable patients without evidence of severe ischemia [14].

Aims and objectives

The aims of this study were as follows:

1. Fate like death, MI, HF New York Heart Association (NYHA) Class III or IV
2. Remodeling, functional outcomes such as LV ejection function, right ventricular ejection function, chamber dimensions, and diastolic function
3. Evaluation of coronary anatomy in selected patients regarding status of ante grade flow, collateral circulation, lesion progression, or new lesion formation.

METHODS

This prospective observational study was conducted with 100 patients admitted in the cardiology ward of R.G. Kar Medical College and Hospital from March 2017 to August 2018. Patients were eligible for enrollment if coronary angiography, performed 3–28 days after STEMI, showed total occlusion of the infarct-related artery with poor or absent ante grade flow, defined as a Thrombolysis in MI (TIMI) flow Grade of 0 or 1. The qualifying period of 3–28 days was based on calendar days; day 1 was the day of the onset of symptoms. Diagnostic ST elevation in the absence of LV hypertrophy or left bundle-branch block (LBBB) as defined by the European Society of Cardiology/ACCF/AHA/World Heart Federation Task Force for the Universal Definition of MI as new ST elevation at the J point in at least 2 contiguous leads of ≥2 mm (0.2 mV) in men or ≥1.5 mm (0.15 mV) in women in leads V2–V3 and/or of ≥1 mm (0.1 mV) in other contiguous chest leads or the limb leads [7].

The majority of patients had evolved electrocardiogram (ECG) evidence of Q-wave infarction in contiguous. New or presumably new LBBB has been considered a STEMI equivalent. ST depression in ≥2 precordial leads (V1–V4) was taken as transmural posterior wall STEMI. MI in the presence of LBBB has been determined from Sgarbossa criteria (≥3 points taken as MI) [15].

1. ST-elevation of ≥1 mm and concordant with the QRS complex (5 points)
2. ST-segment depression ≥1 mm in lead V1, V2, or V3 (3 points)
3. ST elevation ≥5 mm and discordant with the QRS complex (2 points).

Patients with NYHA Class III or IV HF, in cardiogenic shock, with serum creatinine concentration higher than 2.5 mg/dL, angiographically significant left main or three-vessel coronary artery disease, with angina at rest or exertion, dynamic ECG changes in convalescent period were excluded from the study.

Patients who met the inclusion and exclusion criteria and who were either mechanically (mechanically stable means no features of pump failure, no requirement of inotrope, absence of acute mitral regurgitation (MR), ventricular septal rupture or absence of pulmonary edema, LV failure) or electrically stable (electrically stable means there was no evidence of bradyarrhythmia like complete heart block or advanced 2nd-degree heart block or evidence of tachyarrhythmia like ventricular tachycardia) were put on optimal MED. At the time of discharge, all the patients with STEMI received guideline-directed MED. Every patient got dual anti-platelet therapy (aspirin 75 mg and clopidogrel 75 mg) throughout the period of study if there was no contraindication. Every patient received angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (if intolerant to ACEI) if not contraindicated; beta-blocker (metoprolol succinate extended-release 12.5/25/50/75/100 mg) was given if not contraindicated. High-intensity statin (40–80 mg atorvastatin) was given to every patient until unless contraindicated. Loop diuretic was given if there were features of congestion. Mineralo corticoid receptor antagonist was given to those who were having features HF, diabetes, or HF with ejection fraction (EF) ≤40%. Insulin was given to diabetic patient. Nitrate was given to reduce chest pain symptom. The study population was evaluated at 1-month, 3-month, and 6-month intervals. History taken as symptoms of angina, palpitation, dyspnea, fatigue (as per NYHA classification) [16], h/o hospitalization, fatal or non-fatal MI. Pulse (rate, rhythm, volume, equality, special character), blood pressure, neck veins, pedal edema, precordium, added heart sound, murmur, chest examination, gastrointestinal system examination were done. ECG (rate, rhythm, axis, arrhythmia, chamber enlargement, and diagnosis of STEMI as per guideline), and echocardiography (2D, M-mode, and color Doppler, tissue Doppler imaging) were performed [17]. Standard apical 4 chambers, 2 chambers, 3 chambers, parasternal long axis, parasternal short axis at basal, mid and apical level were examined. The interventricular septum was kept as horizontal as possible in line with anterior wall of aorta. Measurements were taken at the level of mitral leaflet tip perpendicular to LV cavity. End diastolic linear dimension was taken at the onset of ECG QRS complex. End systolic dimension was taken just before mitral valve opening. LV EF was measured by M-mode (Teichholz method), modified Simpson bi-pane disk method, and visual eyeballing. Left atrial volume calculated from area length method from apical 4 chambers and apical 2 chambers views at end systole.

Trans mitral Doppler-E/A ratio measured. On tissue Doppler imaging e' velocity (average of medial and lateral e' velocity is measured), E/e' ratio was taken. Right ventricular function assessment was done in patients with inferior wall MI (IWMI) and right ventricular MI. Following parameters were taken into consideration – (i) fractional area shortening in apical 4 chambers view, normal value being >35%, (ii) tricuspid annular plane systolic excursion in apical 4 chambers view, normal being >17 mm, (iii) pulsed tissue Doppler S', normal being >9.5 cm/s (iv) myocardial performance index by tissue Doppler method, normal being >0.54. All patients of STEMI meeting inclusion criteria had been undergone coronary angiography by radial or femoral route whichever found suitable. For the left coronary artery, following projections were taken: A. anteroposterior, B. left anterior oblique (LAO)-caudal, C. LAO-cranial, D. right anterior oblique (RAO)-caudal, and E. RAO-cranial. For the right coronary artery (RCA), following projections were taken: A. LAO45, B. LAO-cranial, and C. RAO 30.

TIMI flow is classified into the following:

- TIMI 0 flow (no perfusion) refers to the absence of any ante-grade flow beyond a coronary occlusion
- TIMI 1 flow (penetration without perfusion) is faint ante-grade coronary flow beyond the occlusion, with an incomplete filling of the distal coronary bed
- TIMI 2 flow (partial reperfusion) is delayed or sluggish ante-grade flow with complete filling of the distal territory
- TIMI 3 is normal flow which fills the distal coronary bed completely.

The following scale (Rentrop classification) was used to grade the filling of collateral channels [18].

0=no visible filling of any collateral channels;

I=collateral filling of branches of the vessel to be dilated without any dye reaching the epicardial segment of that vessel (that is, RCA injection showing retrograde filling of septal branches to their origin from the left anterior descending (LAD) artery, without visualization of the latter occluded artery);

2=partial collateral filling of the epicardial segment of the vessel being dilated; and

3=complete collateral filling of the vessel being dilated

Coronary angiography in follow-up visit was done in patients who had angina chest pain, hemodynamic alteration, or deterioration of LV function.

Biochemical test – Troponin I (By ROCHE card test), complete hemogram, renal profile, estimated glomerular filtration rate, data were analyzed by standard statistical method by applying Statistical Packages for the Social Sciences-19 software.

RESULTS AND ANALYSIS

A total of 102 patients were enrolled two patients could not be traced after discharge following first admission with STEMI. Rest 100 patients were meticulously followed up. Every patient has been undergone coronary angiography and discharged with optimum MED. Every patient was evaluated at 1 month, 3 months, and 6 months clinically, and echocardiographically 11 patients (11%) were undergone repeat coronary angiography in 1st visit due to significant chest pain (CCS II or more). No angiography was done in any patient on further visit due to the absence of chest pain. Table 1 shows among all patients, 54 (54%) were anterior wall MI (AWMI), 35 (35%) were IWMI, and rest (11%) were IWMI with right ventricular involvement. Among all STEMI patients, 46 (46%) patients received thrombolytic with streptokinase, rest were non-thrombolysed either due to late presentation or the presence of absolute contraindication. During the time of 1st admission, 57 (57%) patients had moderate regional wall motion abnormality (RWMA), and rest (43%) had severe RWMA. Among 100 patients of STEMI and among 46 patients of IWMI (including RVMI), 23 patients showed poor right ventricle (RV) function on echocardiography, although on further, visit all the 23 patients RV function recovered well. On angiography during 1st admission, LAD remained the infarct-related artery (IRA) in 54%, RCA in 35%, and left circumflex in rest of the cases. TIMI 0 flow in IRA was found in 54% of cases and TIMI I was found in the rest of the cases. Collaterals were found in 68 patients (68%) and amongst them, Grade 1 was in 22 (22%), Grade 2 in 34 (34%), and Grade 3 in 12 (12%) of cases. Double and multi-vessel disease (presence of significant epicardial coronary artery disease other than IRA) was found in 55 (55%) of cases. During 2nd visit at 1st month, among 100 patients,

Table 1: Frequency distribution of different parameter of study population

Time	Parameter	Value	Frequency (%)
Admission	AWMI	54	54
	IWMI	35	35
	IWMI+RV involvement	11	11
	Thrombolysed	46	46
	Non-thrombolysed	54	54
	Moderate RWMA	57	57
	Severe RWMA	43	43
	LAD	54	54
	RCA	35	35
	LCx	11	11
	Grade I collateral	22	22
	Grade II collateral	34	34
	Grade III collateral	12	12
At 1 month follow-up	No SOB	46	46
	SOB	43	43
	SOB+Chest pain	11	11
	NYHA Class I	46	46
	NYHA Class II	34	34
	NYHA Class III	20	20
	Mild RWMA	46	46
	Moderate RWMA	22	22
	Severe RWMA	32	32
At 3 months follow-up	No SOB	46	46
	SOB	54	54
	SOB+Chest pain	0	0
	NYHA Class I	46	46
	NYHA Class II	21	21
	NYHA Class III	33	33
	Mild RWMA	46	46
	Moderate RWMA	20	20
	Severe RWMA	34	34
At 6 months follow-up	No SOB	46	46
	SOB	54	54
	SOB+Chest pain	0	0
	NYHA Class I	46	46
	NYHA Class II	20	20
	NYHA Class III	34	34
	Mild RWMA	46	46
	Moderate RWMA	11	11
	Severe RWMA	43	43

MI: Myocardial infarction, AW: Anterior wall, IW: Inferior wall, RV: Right ventricle, LAD: Left anterior descending, LCx- Left circumflex, RCA: Right coronary artery, RWMA: Regional wall motion abnormality, SOB: Shortness of breath, NYHA: New York heart association

46 (46%) patients were asymptomatic. About 43 (43%) patients were presented with shortness of breath on exertion (SOBE), and the rest 11 (11%) had both chest pain and shortness of breath. Regarding NYHA class 46 (46%) had NYHA Class I, 34 (34%) had NYHA Class II, and 20 (20%) had NYHA Class III symptoms. About RWMA 46 (46%) patients had mild RWMA, 22 (22%) had moderate RWMA, and the rest (32%) had severe RWMA. Regarding MR at 1 month 35% had no MR, 44% had grade 1 MR and the rest 21% had grade 2 MR. In next visit at 3 months, 46% of patients were asymptomatic, and the rest presented with SOBE; none of them presented with significant chest pain. Among this 46% of patients, 21% had NYHA Class II and 33% had Class III symptoms. About RWMA 46% had mild RWMA, 20% had moderate RWMA, and rest (34%) had severe RWMA. Regarding MR at 3 month 30% had no MR, 42% had Grade 1 MR and rest 28% had Grade 2 MR. In subsequent visit at 6 months, 46% of patients were asymptomatic, and rest presented with SOBE, none of them presented with significant chest pain. Among this 46% of patients, 20% had NYHA Class II and 34% had Class III symptoms. About RWMA 46% had mild RWMA, 11% had moderate RWMA, and the rest (43%) had severe RWMA. Regarding MR at 3 months, 27% had no MR, 41 had Grade 1 MR and rest 32% had Grade 2 MR. Fig. 1 shows Kaplan-Meier survival analysis curve

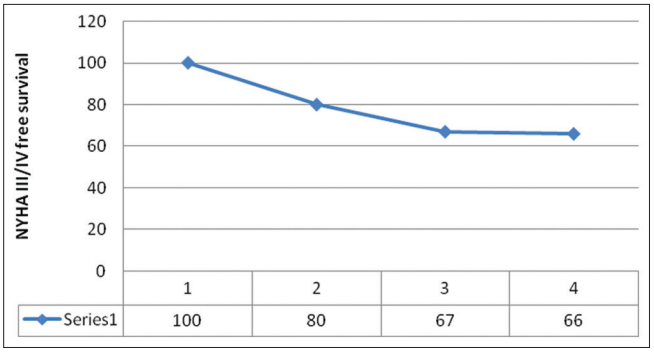

Figure 1: Kaplan-Meier survival analysis for patients developed class III/IV heart failure

showing rate of progression of symptoms of HF due to progressive remodeling. To start with 100 patients at 6 months, 66 patients survived from the development of NYHA Class III/IV HF symptoms. Table 2 shows during the period of 6 months follow-up readmission due to cardiovascular reason other than for coronary angiography in 2nd visit was in 9 patients (9%) and non-fatal MI occurs in 4 patients (4%). Chi-square test among patients with readmission with types of MI, which shows all the readmission happens in AWMI patients (p=0.4). Chi-square test among non-fatal MI with different types of MI, which shows 2 in AWMI and 2 in IWMI with RVMI patients (p=0.02). Table 2 shows no correlation between thrombolysis and readmission (p=0.5) or non-fatal MI (p=0.04). Table 3 shows one sample t-test was done among progression of change of EF, left ventricular internal diameter in diastole (LVIDd), left ventricular internal diameter in systole (LVIDs), e' and E/e' in successive follow-up. All of the parameters show a statistically significant correlation (p<0.005). ANOVA test among LVIDd, LVIDs, e', E/e' in separate visits with different types of MI which shows mean LVIDd in AWMI in follow-up visit 51±1.68, 58.4±5.69, 62±6.14 and 64.71±6.41, in IWMI 47.35±.95, 46.21±3, 48.97±1.425, 49±2.37, in IWMI+RVMI 44±1, 46±1.02, and 46±2, 46.5±2.87. These changes are found to statistically significant (p<0.05). Mean LVIDs in AWMI in follow-up visit 36.53±1.01, 44±6, 47±6.32 and 50.95±8.24, in IWMI 32±1.66, 33.38±1.28, 35.68±1.24, 35.6±1.22, in IWMI+RVMI 34±1, 32±1.02, 32±2, 33.22±2.87 mean e' in AWMI in follow-up visit 8.4±0.4, 7.2±0.4, 6.6±0.4 and 6±0.4, in IWMI 12±0.95, 12.2±0.3, 13.97±0.425, 12±0.37, in IWMI+RVMI 12±1, 13±1.02, 12±0.13, 12±2.87. Mean E/e' in AWMI in follow-up visit 16±1.6, 24±1.7, 27±1.6 and 28±1.4, in IWMI 10±0.95, 11±0.3, 13±1.425, 12±0.37, in IWMI+RVMI 10.2±12±1.02, 11±1.2, 12±1.87. Similarly the changes in LVIDs, E/e' and e' were all found to be statistically significant (p<0.005).

DISCUSSION

Pfeffer and Braunwald pointed that an acute MI, especially the large one, can make changes in the geometry of both the infarcted and non-infarcted areas of heart [19]. This remodeling can harm the function of ventricle and the prognosis for survival. In this study, the 100 patients, although were stable hemodynamically and electrically at the time of recruitment, developed LV remodeling, deterioration of systolic dysfunction with gradual diminution of EF, as well as diastolic dysfunction on further visit, which were found to be statistically significant. OAT study showed a bigger chance of ventricular remodeling was found to be in AWMI patient; here, it had been seen that maximum LV dilatation, maximum left atrium (LA) dilatation, maximum deterioration of e', as well as elevation of E/e' were found in AWMI patient [12]. OAT study also told that preponderance of chest pain reduced gradually. In this study also, it has been seen in 3rd and 4th visit no patient presented with angina. Horie *et al.* [7] showed 10 times more incidence of HF in comparison to PCI group. In this study also, there was significant remodeling of the left ventricle in conservative treatment. Tayebjee *et al.*, said occluded coronary artery causes increase mortality and morbidity. Without reopening individuals have

Table 2: Cross tabulation and Chi-square test among different types of AMI with readmission and non-fatal AMI

Parameter	AWMI		IWMI		IWMI+RVMI		p
Non-fatal MI	Yes	No	Yes	No	Yes	No	0.02
	2	52	0	35	2	9	
Readmission	Yes	No	Yes	No	Yes	No	0.4
	9	45	0	35	0	11	

Table 3: Change in different echo parameter on follow-up visit

Parameter	N	Mean	Standard deviation	p (One-way ANNOVA)
EF (at admission)	100	44.13	3.974	<0.005
EF (at 1 month)	100	43.32	8.069	
EF (at 3 months)	100	43.55	8.841	
EF (at 6 months)	100	42.72	10.006	
LVIDd (at admission)	100	49.26	2.990	<0.005
LVIDd (at 1 month)	100	52.89	7.680	
LVIDd (at 3 months)	100	55.82	8.333	
LVIDd (at 6 months)	100	57.52	9.445	
LVIDs (at admission)	100	34.73	2.407	<0.005
LVIDs (at 1 month)	100	39.07	7.121	
LVIDs (at 3 months)	100	41.84	8.045	
LVIDs (at 6 months)	100	43.67	10.206	
e'(at admission)	100	10.02	1.837	<0.005
e'(at 1 month)	100	9.47	2.556	
e'(at 3 months)	100	9.48	3.221	
e' (at 6 months)	100	9.37	3.113	
E/e' (at admission)	100	13.41	3.321	<0.005
E/e' (at 1 month)	100	18.59	6.809	
E/e' (at 3 months)	100	21.03	7.622	
E/e' (at 6 months)	100	21.03	7.823	
LA (at admission)	100	32.36	2.402	<0.005
LA (at 1month)	100	38.34	4.159	
LA (at 3 months)	100	39.57	4.288	
LA (at 6 months)	100	40.87	4.453	

EF: Ejection fraction, LVIDd: Left ventricular internal diameter in diastole, LVIDs: Left ventricular internal diameter in systole, LA: Left atrium

a poorer prognosis [23]. However, collateral circulation can protect and preserve myocardium around the time of coronary occlusion, contribute to better outcome and reduction of symptoms. In this study also, collaterals were found in 68% of patients which may contribute to the survival of the patients. Thune and Solomon [20] hinted an acute MI causes a loss of contractile fibers, which not only reduces systolic function but also impairs diastolic function. In this study also, there were statistically significant systolic and diastolic dysfunction found on subsequent follow-up. Hochman *et al*. showed 2166 patients with no reduction in major cardiovascular events during a mean follow-up of 3 years [12]. There was also more chance of non-fatal MI in PCI group. In this study in conservative management, there was less trend of non-fatal infarct (4%). Ioannidis and Katritsis showed PCI does not seem to confer any benefits when used for late revascularization of occluded arteries after MI in stable patients [21]. Elmariah *et al.* [22] showed that recent studies have hinted reduced benefit with late reperfusion [22]. Moreover, better medical treatment of STEMI has drastically reduced morbidity and mortality. In this study also, only 46% of patients received thrombolysis as per guideline, in spite of all the patients (100) survived at least up to 6 months, although some developed symptoms (54%) but good number of patients remained asymptomatic (46%), and the development of symptoms were not to be found statistically significant.

SUMMARY AND CONCLUSION

There was no mortality found during this period of study. There was a 9% incidence of readmission and a 4% incidence of non-fatal MI only. About 68% of patients had collaterals. Although few patients presented with chest pain after 1 month, there was no complaint of chest pain on subsequent visit. The patients of IWMI who had RV involvement also during admission did well with conservative management. There was no further evidence of RV systolic dysfunction on follow-up visit. The patient gradually developed features of LV remodeling and LA enlargement, more pronounced with AWMI presented more with HF symptoms. Following conclusions could be made from this study:

1. Collateral flow and OMT are not adequate to prevent remodeling
2. Remodeling causes gradually progressive HF symptoms
3. Patients usually did not present with chest pain; shortness of breath was predominant symptoms in follow-up.

Limitations of the study

1. Small study population with short period of observation
2. No control population was taken with revascularization with PCI.

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Nil.

AUTHOR'S CONTRIBUTION

Equal contribution for all the authors for data collection, statistics, and manuscript writing.

CONFLICTS OF INTEREST

There were no conflicts of interest in this study.

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