Journal of Advances in Medicine and Medical Research

32(21): 99-106, 2020; Article no.JAMMR.62614
ISSN: 2456-8899
(Past name: British Journal of Medicine and Medical Research, Past ISSN: 2231-0614, NLM ID: 101570965)

Stenting versus Pharmacological Therapy in Treatment of Single Vessel Intermediate Culprit Lesion Stenosis in Acute St-Segment Elevation Myocardial Infarction

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMMR/2020/v32i2130699
Editor(s):
(1) Dr. Chan-Min Liu, Xuzhou Normal University, China.
Reviewers:
(1) Shweta Patil, Maharashtra University of Health Sciences, India.
(2) Mustafa Yurtdaş, Istanbul Atlas University, Turkey.
Complete Peer review History: http://www.sdiarticle4.com/review-history/62614

Original Research Article

Received 01 September 2020
Accepted 05 November 2020
Published 19 November 2020

ABSTRACT

Background: Primary percutaneous coronary intervention (PCI) with stent implantation has been the standard therapy in acute ST-segment elevation myocardial infarction (STEMI) patients. Compared with medical treatment alone, stent implanting can achieve larger lumen gain and helps to reduce the re-occlusion risk of the infarct-related artery.
Purpose: The aim of this study was to compare the effectiveness of stenting of single vessel intermediate culprit lesion stenosis to pharmacological treatment alone in acute STEMI patients.
Methods: This study was prospective comparative interventional case series. It included 60 patients admitted to coronary care unit of our University hospital with acute STEMI. All patients were subjected to detailed history taking, clinical examination, 12 leads ECG, echocardiography and cardiac catheterization and angiography (TIMI flow and corrected TIMI frame count (CTFC) was reported. Patients selected were those with intermediate culprit lesion (40-70%) single vessel stenosis.
Patients were divided into 2 groups:

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Group A: 30 patients who underwent stenting of the culprit lesion in addition to standard pharmacological treatment.
Group B: 30 patients who received pharmacological treatment and no stenting (Glycoprotein II b/IIIa inhibitor in addition to the standard pharmacological treatment).
Patients were followed up for 12 months and major adverse cardiac events (MACE) were reported (death, myocardial infarction, coronary re-vascularization, stroke and hospitalization because of heart failure).
Results: 63.3% of group A patients reported complete ST segment resolution versus 30% of group B (P=0.034). TIMI Flow showed statistically significant difference in group A compared to group B regarding (P value=0.005) Group A reported slow fast blood flow (CTFC<60) in 1 patient (3.3%) while in group B it was reported in 5 patients (16%). There was a statistically significant difference between the 2 groups regarding CTFC (P value=0.029). At 12 months follow up, MACE were reported in one patient of group A versus 4 patients of group B (P value >0.05).
Conclusion: Stent implantation reported better immediate efficacy and safety results among acute STEMI patients with single vessel intermediate culprit lesion stenosis and favourable effects in reducing MACE.

Keywords: STEMI; intermediate stenosis; culprit lesion; primary PCI; MACE.

1. INTRODUCTION

Coronary artery disease (CAD) is the leading cause of mortality and morbidity in the world. The basic principle of treating acute ST-segment elevation Myocardial infarction (STEMI) is to achieve effective myocardial Reperfusion [1] Primary percutaneous coronary intervention (PCI) with stent implantation has been the standard therapy in acute STEMI patients .Stent implantation can achieve larger lumen gain and helps to reduce the Re-occlusion risk of the infarct-related artery (IRA) [2].

Prior pathology studies have demonstrated that about 35% of the Culprit lesions have diameter stenosis of less than 70%.The net acute Lumen gain in intermediate stenosis lesion is less than those with Significant stenosis lesions. In addition, stenting might increase the risks of no-reflow phenomenon, PCI related small MI, side branch occlusion, stent thrombosis and stent restenosis. stenting might cause additional interventional no reflow risks. Effective antithrombotic therapy which includes aspiration thrombectomy as well as intracoronary tirofiban is one of importance in treating high thrombotic burden lesions [3].

2. PATIENTS AND METHODS

The study included 60 patients admitted to Cardiology Department of Tanta University with acute ST-segment elevation Myocardial infarction. The duration of the research from November 2017 to May 2019.

Patients divided into 2 groups:

Group A: 30 Patients underwent stenting of intemediate stenosis.

Grorip B: 30 Patients underwent Non Stenting and Pharmalogical treatment

2.1 Inclusion Criteria

1- Patients aged between I8-80 years old
2- Patients with acute ischemic chest pain of more than 30 min ST-segment Elevation of more than 0.1 mV in at least two contagious leads or new left bundle-branch block on the ECG and troponin level elevation
3- Time from symptom onset of less than 12 hours
4- Single vessel disease intermediate stenosis culprit lesions (40%-70% diameter reduction).

2.2 Exclusion Criteria

1- Patients with stenosis more than 70years or less than 40%
2- Rescue PCI after thrombolysis
3- Patients with hemodynamic instability at admission (cardiogenic shock)
4- Multiple organ failure

All patients were subjected to the following

2.2.1 History

- Personal history:-Age, sex, occupation , residence and the presence of symptoms (typical chest pain, dyspnea and sweating)

- Presence of risk factors as hypertension diabetes mellitus, smoking, addiction and renal impairment
- Past history of premature coronary artery disease

2.2.2 Full Clinical examinations including

- General examination:- vital signs:- heart rate ,blood pressure and respiratory rate
- Signs of heart failure /hemodynamic instability according to kliip classification
- Signs of comorbities:- hepatic or renal insufficiency

2.2.3 Twelve leads surface ECG

Routine 12-lead ECG was done for the patients to detect changes suggestive of STEMI. ECGs would be recorded on admission 30,60 minutes and post invasive procedure. ST-segment Elevation of more than 0.1 mV in at least two contagious leads or new left bundle-branch block. A 12-lead ECG used to determine the coronary artery that is most likely affected by an ischemic event.

2.2.4 Echocardiographic examination

Measurements, including ejection fraction, assessment of diastolic function, assessment of mitral regurgitation were performed

2.2.5 Cardiac catheterization (Primary percutaneous intervention for Infarct related artery (IRA)

All patients underwent primary coronary angiography (CAG), door to angiography time was less than one hour. CAG was performed with the use of 6 F or 7 F sheath via trans-radial or trans-femoral approach.

Angiographic characteristics, which include the thrombolysis in myocardial infarction (TIMI) coronary blood flow and thrombus burden, were assessed and recorded. In high thrombus burden lesions, thrombus debulking therapy (manual aspiration thrombectomy or intracoronary administration of glycoprotein IIb/IIIa inhibitor) was done when necessary, and was at the discretion of the cardiologist.

In patients who received manual aspiration thrombectomy, adequate thrombectomy was carried out to obtain normal coronary blood flow. The thrombectomy device was a 6-French (crossing profile, 0.068 in) Export Aspiration Catheter (Medtronic Cardio Vascular, Santa Rosa, CA, USA).

As for the use of glycoprotein II b/III an inhibitor, intravenous tirofiban administration was selectively used, with 0.4 μg/kg per min for 30 min. In high thrombus burden lesions or in case of no re-flow phenomenon, tirofiban was intracoronary administrated with bolus dose of 15 μg/kg, followed by intravenous administration with maintenance dose of 0.1 μg/kg per min for 24–48 h. intracoronary nitrates administration was recommended to obtain maximal epicardial vessel vasodilation.

Coronary blood flow was graded according to the Thrombolysis inMyocardial Infarction (TIMI) grading system. Normal coronary bloodflow was defined as TIMI 3 flow [4]. 'Ihrombus burden was assessed andclassified with TIMI thrombus grades, large thrombus burden lesionswere defined as thrombus Grade 4-5 and small thrombus burden asthrombus Grade 0-3 [5].

Patients' angiographic and intervention procedural records were collected and analyzed. Quantitative coronary angiography (QCA) was used to assess angiographic characteristics. Corrccted TIMI ftame count (CTFC) was used to further assess the coronary blood flow. CTFC < 23 frarnes showed nomal fast coronary blood flow; CTFC > 23 but <40 frames was taken as a little slow but still nomal blood flow; CTFC > 40 frames represents slow re-flow; if the CTFC >60 frames, the blood flow was actually quite slow [6].

2.3 Criteria for Assessment of Patients

Patients whose CAG confirmed to be with single vessel intermediate (40%–70%) stenosis culprit lesions

Group A: 30 Patients would undergostandard primary PCI with stent implantation (stenting group)

Patients who were allocated to the stenting group received standard primary PCI with stent implantation, with or without balloon dilation. Types of instruments and intervention strategies were left to the operators.

No re-flow phenomenon is a common complication after stenting and can be managed by injection of intracoronary vasodilator as:-

Verapamil 50 to 1000 Microgram, Adenosine 24 Microgram to 4milligram also can be managed by injection of intracoronary antithrombotic as tirofiban

Group B: 30 Patients would undergo Non Stenting and Pharmalogical Treatment and PCI (thrombectomy) but without dilatation or stenting.

Patients assigned to the non-stenting group received neither stent implantation nor balloon dilation. Because in the non-stenting group, stent implantation is not intended, balloon dilatation alone is avoided for fear of risks of coronary dissection and endothelial injury after balloon dilatation. For patient safety consideration, during hospitalization, patients assigned to non-stenting group would be considered for urgent CAG and stent implantation in case of refractory angina, re-infarction, malignant ventricular arrhythmia, worsening heart failure, severe hypotension and cardiac shock. Perioperative events and complications were evaluated and recorded.

2.4 Post Procedural Therapy

Both groups received optimized pharmacologic therapy. Post invasive procedure, patients were continued on a maintenance dose of ticagrelor (180 mg/day) or clopidogrel (75 mg/day) for 12 months and Aspirin (100 mg/day) lifelong.

2.5 Follow Up

Follow up clinic visits occurred at 2 weeks, 30 days, 6 months and 1 year for assessment of occurrence of clinical end points and adverse events.

2.6 Statistical Analysis of the Data

The analysis was calculated by SPSS version 25. The qualitative parameters were described by number of frequency and percentage while the quantitative variables were described by mean, standard deviation and range. In addition, the comparison of independent quantitative variables was calculated by Anova with Tukey test in post hoc analysis. However, comparison between two qualitative variables was done by Chi square, Fisher's exact fisher and Monte Carlo tests.

3. RESULTS

This study was prospective comparative interventional case series. It will include 60 patients admitted to Cardiology Department of Tanta University with acute ST-segment elevation Myocardial infarction.

3.1 Observation of the Study

3.1.1 Age, sex distribution

The age of the studied patients ranged from 18 years to 80 years with the mean 52.9 ± 15.57 years. There were 2 patients (≤ 25 years) 51 of the patients aged (35-65 y) and 7 of the patients aged > 65 years. They were 45 males (75%) and 15 females (25%).

3.1.2 Special habits

There were 40 smokers (66.7%) and 20 non-smokers (33.3%) (P-value 0.01*).

3.1.3 Diabetes mellitus

This study included 40 patients with diabetes meillitus, 30 males and 10females. Their age ranged from 30 to 65 years.

3.2 Hypertension

This study included 50 patients with hypertension, 42 males and 8 females. Their age ranged from 25 to 70 years

Table 1. Distribution of diabetic patients among the study population

DM			Stenting	Non stenting	Total
+ve		N	21	19	40
		%	70.0%	63.3%	66.7%
-ve		N	9	11	20
		%	30.0%	36.7%	33.3%
Total		N	30	30	60
		%	100.0%	100.0%	100.0%
Chi-square	X^2	0.300			
	P-value	0.584			

Table 2. Distribution of hypertensive patients among the study population

HTN			Stenting	Non stenting	Total
+ve		N	24	26	50
		%	80.0%	86.7%	83.3%
-ve		N	6	4	10
		%	20.0%	13.3%	16.7%
Total		N	30	30	60
		%	100.0%	100.0%	100.0%
Chi-square	X^2	0.480			
	P-value	0.488			

Table 3. Distribution of myocardial infarction cases among the study population

		Stenting	Non stenting	Total
Anterior	N	19	20	39
	%	63.3%	66.7%	65.0%
Inferior	N	4	2	6
	%	13.3%	6.7%	10.0%
Lateral	N	7	8	15
	%	23.3%	26.7%	25.0%
Total	N	30	30	60
	%	100.0%	100.0%	100.0%

Table 4. Distribution of IRA among the study population

IRA		Stenting	Non stenting	Total
Diagonal	N	3	5	8
	%	10.0%	16.7%	13.3%
LAD	N	17	15	32
	%	56.7%	50.0%	53.3%
RCA	N	3	2	5
	%	10.0%	6.7%	8.3%
CX	N	7	8	15
	%	23.3%	26.7%	25.0%
Total	N	30	30	60
	%	100.0%	100.0%	100.0%

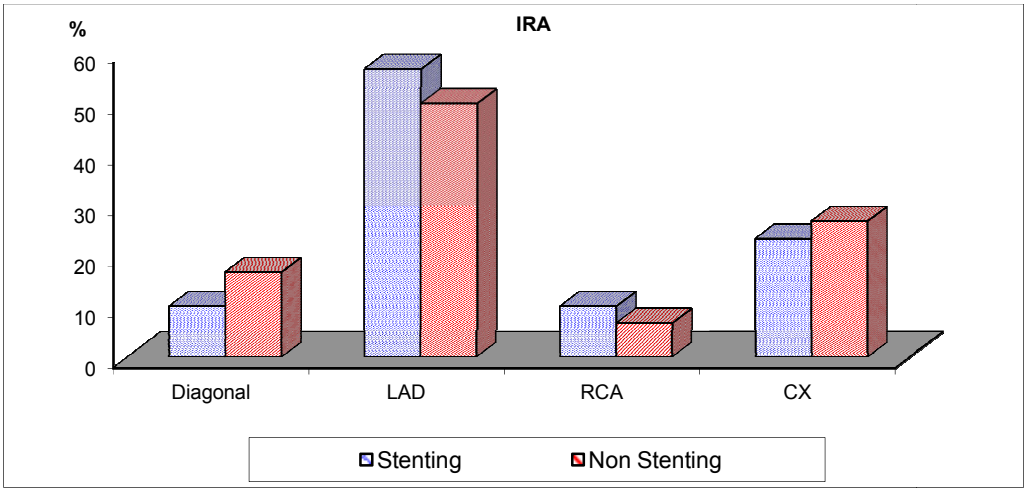

Fig. 1. Bar chart showing distribution of IRA among the study population

3.3 Twelve Leads Surface ECG

The results revealed that 39 patients (65%) had ST segment elevation in anterior Leads (v1: v4), while 6 patients(10%) had segment elevation in inferior Leads (LII,III: Avf), while 15 patients(25%) had segment elevation in lateral Leads (LI, AVL ,V4:V6)

3.4 Cardiac Catheterization (Primary Percutaneous Intervention for Infarct Related Artery (IRA)

As for the use of glycoprotein II b/III an inhibitor, intravenous tirofiban administration was selectively used, with 0.4 μg/kg per min for 30min. In high thrombus burden lesions or in case of no re-flow phenomenon, tirofiban was intracoronary administrated with bolus dose of 15 μg/kg, followed by intravenous administration with maintenance dose of 0.1 μg/kg per min for 24–48 h.

The presented angiographic and intervention procedural data are based on the assessment of QCA. The mean time from symptom onset was 5.73 ± 2.3 h. The mean door to angiography time was 54.8 ± 9.2 min. Overall, the initial angiographic finding (before thrombectomy) showed that the mean diameter stenosis is 84.6% ± 17.4%.

In stenting group, direct stent implantation was performed in 17 (57.7%) patients. The other 13 (42.3%) patients received balloon pre-dilation before stenting. All implanted stents were drug eluting stents. Post balloon dilation was performed in 18 (61.7%) patients. In non-stenting group, neither balloon dilatation nor stent implantation was performed.

It is noticeable that 3 (11.1%) patients who were allocated in the non-stenting group were with small thrombus burden lesions (TIMI thrombus Grade ≤ 3 class). This might be associated with early spontaneous myocardial reperfusion after anti-thrombus pharmaceutical therapy. These 3 (11.1%) patients just received CAG, with no aspiration thrombectomy nor other invention therapies performed.

3.5 Immediate Invasive Effects and Intra-Procedure Complications

Post invasive procedure, the residual minimal luminal diameter (MLD) was 3.33 ± 0.49 mm in the stenting group versus 1.89 ± 0.92 mm in the non-stenting group, $P< 0.01$. Normal fast blood flow (CTFC < 23) was achieved in 48.3% of the patients in stenting group versus 39.4% in the non-stenting group. Meanwhile, slow blood flow was more common in the stenting group (16.9%), compared with the non-stenting group (10.6%), $P = 0.01$.

As for the myocardial reperfusion assessed by ECG, the two groups had similar PCI to post-procedural ECG time, which was 41 min (interquartile range, 24–63) in the stenting group, and 39 min (interquartile range, 21–58) in the non-stenting group, $P = 0.39$. In the stenting group, 55.7% of the patients were found with complete ST-segment resolution on ECG, compared with 39.4% of the patients in the non-stenting group, $P< 0.01$. In the stenting group, 56.4% of the patients had no persistent ST-segment deviation, as compared with 42.1% in the non-stenting group, $P = 0.03$ While, 22.7% of the patients in the stenting group versus 20.9% in the non-stenting group had no pathologic Q waves on ECG, $P = 0.73$.

Table 5. Post procedural corrected TIMI flow (corrected TIMI frame count)

CTFC			Stenting	Non Stenting	Total
< 23		N	16	7	23
		%	53.3%	23.3%	38.3%
23 – 40		N	10	17	27
		%	33.3%	56.7%	45.0%
> 40 – 60		N	3	1	4
		%	10.0%	3.3%	6.7%
> 60		N	1	5	6
		%	3.3%	16.7%	10.0%
Total		N	30	30	60
		%	100.0%	100.0%	100.0%
Chi-square	X^2	9.003			
	P-value	0.029*			

As for the peri-operative complication, overall, no death occurred during invasive procedure, no patient experienced non-protocol pre-discharge catheterization. In the stenting group, one patient happened flow limiting dissection after balloon pre-dilation and one patient happened acute side branch occlusion after stent implantation. The two patients' problems were resolved during primary PCI. In the non-stenting group, no acute vessel occlusion occurred.

4. DISCUSSION

The present study might provide a second look at the no stent strategy in the modern era. The main finding of this study is that, for acute STEMI patients with single vessel disease and intermediate (40%–70%) stenosis of the culprit lesion before or after aspiration thrombectomy and/or intracoronary tirofiban (15 μg/kg) were enrolled, stent implanting has better efficacy and safety in reducing MACCE rates during 12 months follow up. Stenting and non-stenting treatments are associated with similar all cause death, ischemia driven admission and bleeding rates at 12 months. First, in the present study, acute STEMI which were caused by plaque erosion and plaque rupture were studied as a whole. Compared with ruptured plaque, the eroded plaque has smaller necrotic core and more smooth muscle cells and proteoglycan-rich matrix [7]. The patients enrolled in EROSION trial were more stable than our study. Second, the present study had longer follow-up time (12 months) than the EROSION trial (one month). Third, in the present study, only acute STEMI patients with single vessel intermediate stenosis (40%–70% diameter reduction) culprit lesions were enrolled, stenting was found to have less MACCE rate during long term follow-up.

The DANAMI 3-DEFER trial compared the different strategies between conventional and deferred stenting in STEMI patients. Patients who were allocated to the deferred PCI group received repeat CAG 48 h later. Stent implantation was intended, unless the residual stenosis was < 30%. The conclusion is that routine deferred stenting failed to reduce adverse events compared with the conventional stenting strategy [8]. In the present study, unless non-protocol catheterization caused by ischemia was needed, patients in the non-stenting group did not receive routine deferred stenting.

A few studies have evaluated the different strategies between PCI and conservative pharmacotherapy in treating ACS patients. Legutko J, et al. [9] have studied the borderline coronary lesions in ACS patients, and concluded that PCI and medical therapy yield similar clinical outcomes. Prati and colleges demonstrated that STEMI with plaque erosion could be managed with effective anti-thrombotic therapy without stenting [10].

Several factors might influence the clinical prognosis of these patients. First, the acute lumen gain was larger in the stenting group than the non-stenting group. Second, in patients who were free from no/slow reflow complications, stenting helped to achieve better myocardium reperfusion effect than non-stenting. As for the reperfusion therapy of STEMI, both the epicardial blood flow restoration and myocardium reperfusion are important [11]. Third, besides reperfusion strategies, other factors of age, cardiac function, among others, also might influence patients' clinical outcomes. In the multivariate analysis, older age, compromised left ventricular function (LVEF<50%) and no/slow reflow phenomenon were associated with higher MACCE rates. Pharmacologic therapy plays an important role too. The benefits of aspirin and β blocker were independent of the reperfusion strategy.

5. LIMITATIONS

This study has several limitations. First, for fear of increasing total ischemic time during primary PCI, intravascular ultrasound and optical coherence tomography were not used for objective evaluation of lesions. Second, the present finding could not be generalized to acute STEMI patients with multi-vessel diseases. Also, the conclusion could not be extended for the strategy of stable angina or non-ST segment elevation ACS. Third, deferred stenting was not studied. Fourth, larger studied with longer-term follow-up are warranted.

6. CONCLUSION

In the management of single vessel intermediate stenosis culprit lesions in acute STEMI, stent implantation has better efficacy and safety in reducing MACCE during clinical follow up. Further study and long-term data are warranted.

CONSENT

An informed consent was taken from all participants.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/62614