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Research Brief

A study of unprotected left main intervention in the ACS population 2013–2018



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ABSTRACT

Objectives: Our objectives were to evaluate the outcomes of left main percutaneous coronary interventions in Acute Coronary Syndrome population.

Methods: This is a retrospective & observational study. Primary endpoint is a composite of death, stent thrombosis/MI, target lesion revascularization. Secondary endpoints include individual components of the primary events analyzed separately.

Results: Seventy five patients, two year follow – up data was analyzed. The primary event analysis showed that the Elective Double Stent (EDS) group had a higher primary events (36% vs. 14%, p value – 0.008, Hazard ratio – 0.76 (0.51–1.15, 95% CI), in secondary event analysis stent thrombosis (ST)/ Myocardial infarction (MI) rates were higher in EDS group (8% Vs 36%, p Value – 0.008, Hazard ratio-0.63(0.35–1.14, 95%CI), there is no difference in target lesion revascularization (TLR) and death rates in both the groups.

Conclusions: The provisional strategy is better than EDS in treatment of left main bifurcation lesions in the ACS population.

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What we know?

- Randomized trials and guidelines have shown equipoise between percutaneous coronary intervention and coronary artery bypass grafting (CABG) in the management of stable patients with left main stenosis and less complex anatomy, but ACS population were excluded from these studies.
- Contemporary data in this population is mainly from British cardiovascular interventional society (BCIS)⁹ and acute Myocardial Infarction in Switzerland (AMIS)¹⁰ plus registries.

But they show contrasting results in the mortality rates more overlong term follow-up was not there in these studies.

What this study adds to the current knowledge.

- This study found that in LM angioplasties are done more in the ACS population when compared to stable heart disease population.
- This is the first study to show the long term outcomes of the Provisional, EDS strategies in the ACS population undergoing distal LM bifurcation angioplasty.
- Analysis of primary outcomes (death, TLR, and MI/stent thrombosis) shows that the EDS group had a greater number of primary outcome events in long term. Difference is observed only after a mean gap of 20 months.
- This study also found that there are a greater number of stent thrombosis events in the EDS group when compared to the provisional strategy in the long term. There is no difference in

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other secondary outcomes events like the deaths and TLR in both the groups.

1. Introduction

Left Main percutaneous interventions have the potential to cause major ischemic injuries and hence it is a challenge for specialists. Unlike patients with stable angina,^{1–3} limited data is available on outcomes of patients undergoing unprotected Left Main percutaneous interventions presenting as acute coronary syndromes (ACS) including STEMI.^{4–8}

Contemporary data in this population is mainly from British cardiovascular interventional society (BCIS),⁹ and acute Myocardial Infarction in Switzerland (AMIS),¹⁰ registries, but they show contrasting results in the mortality rates and long term follow-up data is not available in these registries. Hence the objective of this study is to evaluate the outcomes of individuals undergoing UPLM (Un-Protected Left Main) intervention with various bifurcation treatment strategies in the ACS population.

2. Methodology

This is a retrospective observational single-center study. The data is derived from a patient's database of a tertiary hospital where they underwent UPLM angioplasty from April 2013–July 2018. Among the total of 4327 angioplasties done, 100 consecutive patients underwent UPLM angioplasty. Among those 100, ACS population accounted for 75, they constituted the study population, 5 patients did not have the long term follow up. Of the remaining seventy individuals, 67 had left main lesion involving distal bifurcation, hence their data was used for final analysis.

Both groups were analyzed separately. All interventions were performed according to current standard guidelines. Decisions to treat bifurcation lesions by either provisional or EDS strategy were

made by the individual operators. All patients data was analyzed after two years of follow-up. Mean duration of follow up is 3 yrs.

Study endpoint and definitions: The primary endpoint of the study is defined as death, myocardial infarction, stent thrombosis, or target lesion failure with repeat revascularization. Secondary endpoints constitute the individual components of the primary endpoint analyzed separately.

Statistical analysis: Data of all the patients were entered in the excel sheet. All this data analysis was done with IBM SPSS trial version23.

3. Results

ACS UPLM intervention were done in 75 patients, of them 5 did not had the long-term follow-up data, among them 67 patients had left main lesions involving the distal bifurcation, hence their data was considered for the final analysis.

Baseline clinical characteristics and the angiographic data in provisional and EDS are shown in Table 1. Majority of the patients with Killips class I at the time of presentation underwent the EDS strategy (8% Vs 63%, *p* value - < 0.0001). Most of those in higher Killips class (Killip class III) underwent the provisional strategy (Killips class III – 46% Vs 9%, *p* value – 0.04). TIMI III flow before the beginning of the procedure was seen more in the EDS group (Provisional Vs EDS – 32% Vs 72%, *p* value – 0.005) (Table 2). No member in the EDS group had TIMI 0 or TMI I flow at the beginning of the procedure, whereas they constituted 17% of the Provisional group. Inotropic support was needed at the time of admission more in Provisional group of patients (53% Vs 9%, *p* value – 0.017), mean syntax score in provisional group is 22.65, EDS group had a mean syntax score of 25.36 (Table 2), although the difference is not statistically significant. Along with distal left main angioplasty, only 14% (n = 10) underwent angioplasty in the remaining vessels, majority were done in LAD (Left anterior descending artery). Majority of the population underwent through femoral route (5% Vs 24%), MCS (mechanical circulatory support) devices were not used

Table 1
Baseline clinical & angiographic characteristics. All variables are shown as percentages with actual numbers shown in brackets. Only 67 patients had left main lesion involving the distal bifurcation.

	Total (n = 67)	Provisional strategy (56)	EDS (11)	<i>p</i> – VALUE
Age		57.77	60.90	0.467
Male sex	70 (49)	71 (40)	81 (9)	0.477
Smoking	10 (7)	14 (6)	9 (1)	0.872
HTN	57(40)	57 (32)	72 (8)	0.335
DM	51(36)	48 (27)	81 (9)	0.040
Hyperlipidemia	2(2)	–	18 (2)	0.000
LV EF %	46%	46%	49%	0.470
<i>Killips class during Presentation</i>				
Killip class I	17 (12)	8 (5)	63 (7)	<0.0001
Killip class II	32 (22)	33 (19)	27 (3)	0.667
Killip class III	38 (27)	46 (26)	9 (1)	0.048
Killip class IV	8 (6)	10 (6)	0 (0)	0.000
Cardiogenic shock during presentation	1(1)	1(1)	0	00000
<i>Clinical Presentation</i>				
ACS		80 (56)	15 (11)	0.546
MI (STEMI)		37 (26)	28 (4)	0.875
No of patient receiving TLT before procedure		14 (10)	18 (2)	0.608
Angiographic characteristics				
<i>MEDINA classification</i>				
111	37(25)	33(19)	54(6)	0.196
110	30(21)	35(20)	9 (1)	0.081
101	1(1)	0	9(1)	–
011	2(2)	1(1)	9(1)	0.193
001	0	0	0	–
010	25(18)	28(16)	18(2)	0.477
100	0	0	0	0

ACS – acute coronary syndrome, STEMI – ST segment elevation myocardial infarction, HTN -hypertension, DM – diabetes mellitus.

Table 2

Baseline procedural characteristics of the study population. All variable are depicted as percentages with actual numbers shown in the bracket. Of the total 70 patients undergoing left main angioplasty only 67 had left main lesion involving distal left main bifurcation, their data was analyzed.

	Total	Provisional	EDS	p value
<i>TIMI flow</i>				
TIMI 0 flow	2 (2)	3 (2)	0	–
TIMI I flow	11 (8)	14 (8)	0	–
TIMI II flow	44 (31)	50 (28)	27 (3)	0.166
< TIMI III flow	58 (41)	67 (38)	27 (3)	0.028
TIMI III flow	37 (26)	32 (18)	72 (8)	0.005
Inotropic support	44(n = 31)	53(n = 30)	9(n = 1)	0.017
<i>No. of stents per patient</i>				
1 stent per patient	40(28)	50(28)	0	–
2 stents per patient	38(27)	35(20)	63(7)	0.084
≥3 stents per Patient	17(12)	14(8)	36(4)	0.050
<i>Guiding catheter</i>				
6F	40(28)	44 (25)	21 (3)	0.285
7F	55(39)	55 (31)	72(8)	0.2855
8F		0	0	0
<i>Radial artery Access</i>				
Femoral access	24(14)	21 (15)	14 (2)	0.808
Rotational atherectomy	75(53)	78 (44)	81 (9)	0.808
FFR	2(2)	1 (1)	9 (1)	0.193
IVUS guidance	1(1)	1 (1)	0	0.0000
OCT guidance	25(18)	25 (14)	36 (4)	0.436
Thrombectomy	1(1)	1 (1)	0	0.000
IABP/MCS	0	0	0	0.0000
Procedural failure	1(1)	1 (1)	0	0.0000
Cutting balloon	10(7)	12 (7)	0	0.00
Xience stent (Abbott)	78(55)	80 (45)	90 (10)	0.404
Vascular concepts (Pronova)	14(10)	16 (9)	9 (1)	0.552
Mean Maximum LM Stent diameter	3.57	3.56	3.59	0.887
Mean Post dilation balloon diameter	4.28	4.33	4.18	0.084
Mean stent length	41.59	40.14	56.54	0.0097
Mean number of stents per patient	1.77	1.69	2.36	0.015
Mean syntax score	22.56	22.65	25.36	0.242
Final kissing Inflation	14(10)	12 (7)	27 (3)	0.427
Final POT	82(58)	87 (49)	72 (8)	0.427
Side branch treatment in provisional strategy patients			Stent strategy in EDS Patients	
Side branch struts Opened	12(21)		T stent	18 (2)
Kissing inflation	7 (12)		TAP	9(1)
Side branch stent implantation	5 (3)		DK crush	54 (6)
Side branch stent technique			Cullote	18 (2)
T stent, TAP	5 (3)		Crush/Mini crush	0
Cullote, Reverse crush technique	–			

IVUS- intravascular ultrasound, OCT-optical coherence tomography, IABP- intra aortic balloon pump, MCS – mechanical circulatory support, FFR-fractional flow reserve.

in any patient, FFR was used in 1%, OCT was used in 1%, IVUS was used in 25% of patients, right dominant circulation was seen in majority of the population (80% Vs 19%), one patient was referred for emergency CABG as the distal flow could not be established, one patient underwent CPR during the procedure, thrombosuction was not used this cohort of population.

Mean stent length is high in the EDS group (56.54) when compared to the Provisional group (40.14, p value = 0.0097). Mean post dilation balloon size in LM is high in the Provisional group (4.33) compared to EDS group (4.18 p value = 0.084). All other risk factors, clinical characteristics, and procedural characteristics were equally matched in both groups.

3.1. Outcomes

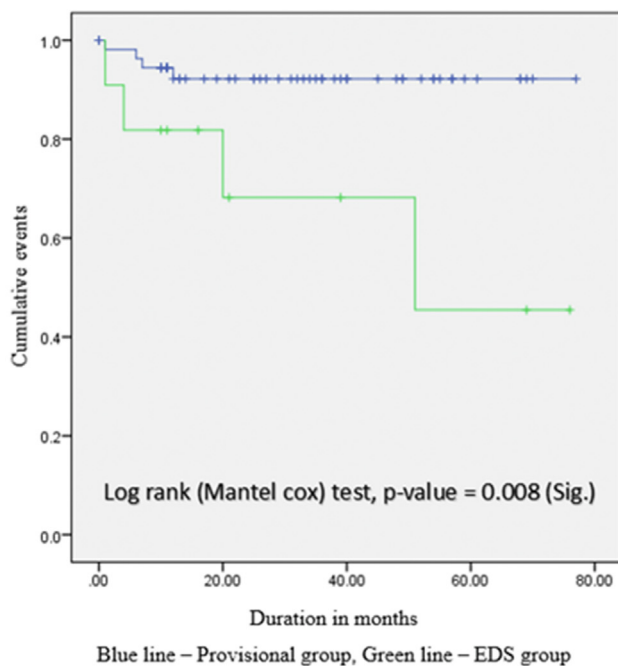
In hospital mortality rate was 2.8% ($n = 2$) in provisional group, no in hospital events in EDS group. There was no statistically significant difference in one month (5% Vs 9%, p value = 0.63) or 6 months or one year event rates in both the groups (7.14% vs. 18.1%, p value = 0.24, 10% Vs 18%, p value = 0.48 respectively). The primary outcome analysis (death, MI, ST, TLR) after 2 years of follow-up (Fig. 1) showed that the EDS group had a higher primary outcome events than the provisional group (36% vs. 14%, p value = 0.037,

Hazard ratio = 0.76 (0.51–1.15, 95% CI)). Individual components of the primary outcome, death rates (10% vs. 18%, p value = 0.467, Hazard ratio=0.88 (0.58–1.34, 95% CI)), target lesion revascularization (TLR) (3% Vs 9%, p Value = 0.363, Hazard ratio=0.79(0.35–1.77, 95% CI)), were not statistically significant, except for Stent thrombosis/MI at two year. (8% vs. 36%, p Value = 0.008, Hazard ratio= 0.63(0.35–1.14, 95%CI)).

4. Discussion

The present study found that after two years of follow-up, the provisional group had a smaller number of primary outcome events and a smaller number of stent thrombosis/MI events. There is no difference between deaths and TLRs in the two groups. This study found that those who were sick (higher Killip class, more number of STEMI at presentation, and those who were on inotropes) at the time of presentation and those with complex lesions and less than TIMI III flow were treated by Provisional strategy. Those who had higher comorbidities like DM, higher age were treated with EDS strategy. Even though primary outcome events are more in the EDS strategy after two years of follow-up, a significant difference could not be established during one year of follow-up. This lack of difference in the early period may be due to the fact the provisional

Comparison of stent thrombosis in provisional and EDS groups of ACS patients



Comparison of primary outcomes in provisional and EDS groups of ACS patients

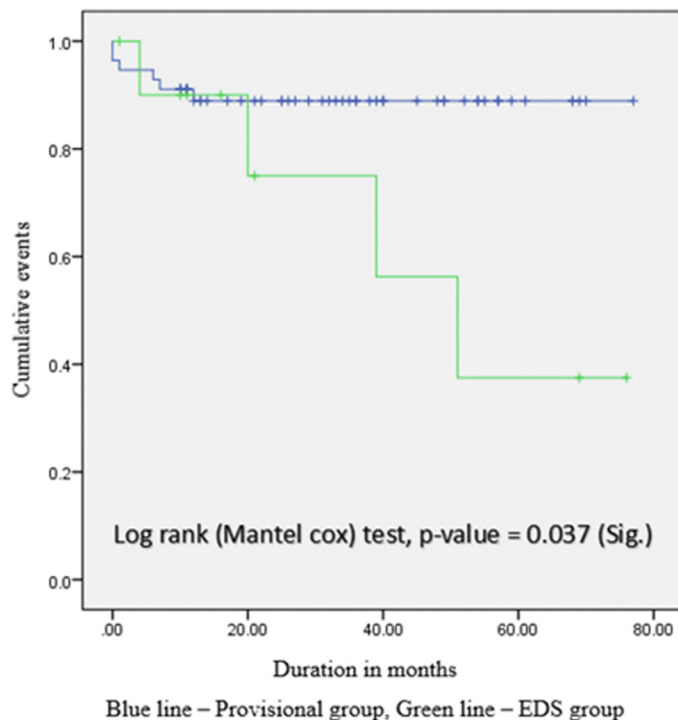


Fig. 1. a. Kaplan–Meier in the provisional group in long term. b. Kaplan–Meier curves show that primary outcomes are less in the provisional group and there is statistically significant difference in between two groups.

group had a higher percentage of sick patients than the EDS group (those with flow less than TIMI III at the time of angioplasty, those having STEMI, higher Killip class & more usage of ionotropes at the time of presentation). This negated the early benefits of the provisional strategy.

In the present study, side branch struts were opened in 20% of patients, final kissing inflation was done in 12% of patients and side branch stent implantation was done in only 5% of the patients. This is comparable to studies done by Hyeon-Cheol Gwon et al¹¹ (results from COBIS registry) & David E. Kandzari et al¹² (technical analysis from EXCEL trial), where they found that MACE is increased in those undergoing KBI, side branch stent implantation. All these factors contributed to lower rates of stent thrombosis in the provisional strategy.

A higher number of primary outcome events after two years of follow-up is mainly driven by a greater number of stent thrombosis events in the EDS strategy group. Factors like lesion length/stent length were shown to be associated with the risk of stent thrombosis in various studies. Studies done by Airoidi et al,¹³ Lakovou et al¹⁴ and Giustino G et al¹⁵ have found that the mean stent length is one parameter that is strongly associated with stent thrombosis. The longer stent length is correlated to extensive atherosclerosis, complex anatomic features, and multivessel disease. All these features have well known correlation with post PCI adverse events.^{16,17}

Imaging guidance (IVUS) was used in 36% of the population undergoing the EDS strategy. It was done in 25% of the provisional patient population (25% vs 36%, p value = 0.436). Studies done by Kensuke Takagi et al¹⁸ found that when IVUS guidance was used in above 60% of the subjects, the EDS strategy can be as good as the provisional strategy.

When STEMI subgroup and distal LM true bifurcation lesion (Medina 111, Medina 011) patients were separately analyzed, it showed that the primary outcome events and secondary outcome events are not statistically different between the provisional and EDS groups. Those present with cardiogenic shock had a high mortality rate this is in line with studies done by Hochman JS, et al¹⁹ (SHOCK trial). All of them underwent the provisional strategy with high in hospital event rates.

LM bifurcation lesions presenting with ACS are complex, majority of the data is from small observational studies & AMICS¹⁰, BCIS⁹ registries. They included patients with LM bifurcation lesions in the ACS population. Angioplasty in this population was associated with higher event rates and the follow-up in these studies was relatively short. There is even limited data regarding different treatment strategies used to treat this population. Hence it is very important to investigate the impact of different treatment strategies in this population. The present study showed that long term outcomes would be better when a majority of the population undergo provisional strategy.

5. Conclusion

Provisional strategy improves the long term outcomes in ACS patients undergoing LM angioplasty.

6. Limitations

This is a retrospective, single center observational study. Some baseline and angiographic characteristics were unfavorable to the EDS group compared with the provisional group, this may have significantly affected the results.

Declaration of competing interest

Nil.

Acknowledgement

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