

# Incidence and Impact of Totally Occluded Culprit Coronary Artery in Patients with Non-ST Segment Elevation Myocardial Infarction Acute Coronary Syndrome

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## ABSTRACT

**Background:** Significance of totally occluded culprit coronary artery in patients presenting with Non-ST segment Elevation myocardial infarction (NSTEMI) is underestimated.

**Purpose:** In this study, we aimed to assess the incidence and impact of totally occluded culprit artery on in-hospital and six months follow up outcomes of NSTEMI acute coronary syndrome (ACS) patients.

**Results:** This observational retrospective study was conducted on consecutive NSTEMI patients who presented to the Alexandria Main University hospital, Egypt between 1<sup>st</sup> June 2016 and 31<sup>st</sup> May 2017. All patients were managed with PCI within 72 hours of presentation. We excluded patients with cardiogenic shock, prior CABG, STEMI. Patients were divided into two groups according to pre-procedural culprit vessel Thrombolysis in Myocardial Infarction (TIMI) flow. Group 1: TIMI flow 0 total coronary occlusion included 112 patients (22.4%). Group 2: TIMI flow 1-3 non-total occlusion included 388 patients (77.6%). Group 1 patients had significantly higher incidence of smoking ( $P=0.01$ ), significantly higher level of cardiac enzymes ( $P<0.001$ ), significantly more collaterals ( $P<0.001$ ) and significantly more LCX and RCA as the culprit vessel ( $P<0.01$ ), while group 2 patients had significantly higher incidence of diabetes ( $P=0.02$ ) and significantly more LAD as the culprit vessel. There were no significant differences between two groups regarding to major adverse cardiac and cerebrovascular events (MACCE) in-hospital (5.3% vs. 1%,  $P=0.07$ ) but group 1 patients had significantly higher incidence of in-hospital arrhythmia (8.9% vs. 1%,  $P=0.007$ ). There were no significant differences regarding MACCE between two groups after 6 months follow-up (5.4% vs. 4.6%,  $P=0.24$ ).

**Conclusion:** Approximately 25% of NSTEMI patients have a totally occluded culprit artery. The presence of an occluded culprit artery did not significantly affect the clinical outcomes of NSTEMI patients either in-hospital or after six months follow up but was associated with significantly higher incidence of in-hospital arrhythmia.

**Keywords:** Non-ST segment elevation myocardial infarction; Coronary total occlusion; Electrocardiography; Coronary artery disease; Acute coronary syndrome

## INTRODUCTION

The spectrum of Acute Coronary Syndrome (ACS) including ST-segment elevation myocardial infarction (STEMI), non-ST segment elevation myocardial infarction (NSTEMI), and unstable angina have become leading cause of death globally [1-3]. In Middle East including Egypt, 64% of ACS patients present with NSTEMI and 36% present with STEMI according to the results of the ACCESS

registry [4].

Recent studies have shown that the incidence of NSTEMI has slightly increased over the last decade and have lower short-term mortality compared with STEMI patients, while at 1 or 2 years follow-up mortality rates become higher [5]. Based on electrocardiogram (ECG) ACS patients can be divided into STEMI patients with ST-segment elevation on ECG denoting total or near

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total occlusion of the culprit artery and necessitating immediate coronary angiography and revascularization or NSTEMI patients with ST segment depression or T wave inversion on ECG with early angiography and revascularization only if they have high risk [6,7].

Previous studies have shown that nearly 25% of NSTEMI patients present with a totally occluded coronary artery and two-thirds of the occlusions are already collateralized at the time of angiographic examination, (8,9) this was more common in patients presenting with either right coronary artery (RCA) or left circumflex artery (LCX) involvement, [8-14] which could be explained by the lack of ECG sensitivity in detecting acute ischaemia in the inferolateral and posterior walls.

The lack of classic ST-segment elevation on ECG in these subset of NSTEMI patients, despite the presence of totally occluded culprit artery lead to either delay in or no revascularization [15]. Currently the impact of totally occluded artery on the outcome of NSTEMI patients is still unclear, as previous studies had reported contradictory results. Some studies reported worse outcome for patients with totally occluded culprit artery [9,13,16] while other studies reported no significant difference in outcome [8,10,11,17]. In this study we aimed to evaluate the incidence and impact of totally occluded culprit artery on in-hospital and after six months follow up outcomes of NSTEMI patients.

## MATERIALS AND METHODS

### Study design

This is a retrospective observational study conducted on consecutive NSTEMI patients who presented to the Alexandria Main University hospital, Alexandria, Egypt between 1<sup>st</sup> June 2016 and 31<sup>st</sup> May 2017.

The inclusion criteria were established diagnosis of NSTEMI and candidates for PCI with invasive strategy performed within 72 hours of admission. The exclusion criteria were previous CABG, cardiogenic shock, previous PCI of same culprit vessel, STEMI and Left main coronary artery disease. The study population included 500 patients who were classified into two groups:

Group 1: Included 112 patients with totally occluded culprit vessel.

Group 2: Included 388 patients with non-totally occluded culprit vessel.

### Data collection

All patients' demographic data were collected including age, gender, comorbidities (hypertension, diabetes, dyslipidemia, prior ACS or PCI), and smoking. From laboratory data, we registered Troponin I, creatine kinase MB fraction (CK-MB), urea and creatinine levels on admission and peak levels during the hospital stay. ECG and Echocardiographic data including Ejection Fraction (EF), Wall Motion Abnormalities (WMA) and degree of Mitral regurgitation (MR) were also registered.

Among in-hospital treatments, we registered PCI procedure details including access site, procedure outcomes, complications, and the use of antithrombotic therapy (acetyl salicylic acid, clopidogrel, ticagrelor, heparin, enoxaparin and glycoprotein IIb/IIIa inhibitors). The culprit artery was identified primarily on angiographic findings with ECG and echocardiogram to support the assessment if needed. Totally occluded artery was defined as a lesion with 100% stenosis and a Thrombolysis In Myocardial Infarction (TIMI) flow 0 [18]. Baseline and at hospital discharge

GRACE and TIMI risk scores were calculated [19,20]. Baseline Syntax score and residual syntax score were also calculated [21].

### Clinical endpoint measurements

The primary clinical outcomes of the study were MACCE which was defined as a composite of death, re-infarction, need for revascularization, heart failure and cerebrovascular stroke either in-hospital or after six months follow up.

### Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS ver.20 Chicago, IL, USA) [22]. K-S test of normality was done to check for normality of quantitative variables. Normally distributed data were described using mean, Standard deviation, while not normally distributed data were described using median, range, and non-parametric tests were applied. We used number and percent to describe qualitative data. Independent Student t-test used to compare age between 2 groups. Mann Whitney U test used to compare non parametric quantitative parameters between 2 groups. Pearson Chi square used to compare 2 × 2 categorical variables, and Fisher's Exact test when if >20% of cells had expected cell count less than 5. And in >2 × 2 table we used Monte Carlo significance test if >20% of cells had expected cell count less than 5. Kaplan Meier survival curve was done for survival analysis of MACCE occurrence, with duration in days till occurrence, Log rank test used to compare survival between 2 groups. Any test was considered significant below or equal 0.05.

An informed consent was obtained from every patient or the legal guardians. The study was approved by the local ethics committee.

## RESULTS

### Patient's characteristics

Both patient groups (1 and 2) were well matched with respect to demographic data and clinical characteristics with no significant difference between them except for smoking which was significantly higher in group 1 (55.3% vs. 44.3%,  $P=0.01$ ) and Diabetes mellitus (DM) which was significantly higher in group 2 (25% vs. 41.7%,  $P=0.02$ ). Regarding the mean time from admission to PCI there was no statistically significant difference between the two groups ( $27.11 \pm 10.6$  hr vs.  $28.7 \pm 11.9$  hr,  $P=0.35$ ). The baseline characteristics of both groups are presented in Table 1.

### ECG, echocardiography and laboratory results

CK-MB and Troponin I levels were significantly higher in group 1 than in group 2 (92 vs. 35,  $p<0.001$  and 7.5 vs. 1.5,  $p<0.001$ ). There was no significant difference between two groups regarding other laboratory, ECG and echocardiography results. The baseline ECG, echocardiography and laboratory results of both groups are presented in Table 2.

### Grace risk score and TIMI risk score

There were no statistically significant differences between two groups as regard the GRACE risk score at admission, or TIMI risk score at admission (Table 3).

### Procedural characteristics of the studied population

With regard to the angiographic data, the incidence of multi vessel disease was not different between the two groups, group 1 patients had significantly higher percentages of LCX and RCA as the culprit vessel (55.4% and 23.2%), while group 2 patients had significantly higher percentages of LAD as the culprit vessel (53.1%). This was statistically significant  $P<0.001$ . Also there were

no significant difference between the two groups regarding the baseline Syntax score ( $11.68 \pm 6.05$  vs.  $6.79 \pm 3.24$ ,  $p = 0.12$ ) or the residual Syntax score ( $1.27 \pm 2.67$  vs.  $0.66 \pm 2.35$ ,  $p = 0.07$ ). The presence of collaterals was significantly higher in group 1 than in group 2 (73.2% vs. 4.6%,  $P < 0.01$ ).

All patients in the two groups were done through transfemoral approach, received Drug Eluting Stents (DES) and no patient had procedure related complications. Also, the antiplatelet treatment with clopidogrel or ticagrelor did not differ, but the use GP IIb/IIIa inhibitors was significantly higher in group 1 (23% vs. 3%,  $p = 0.04$ ). All data of the procedural characteristics of the studied population are summarized in Table 4.

### In hospital outcomes

Group 1 patients showed higher risk of cumulative MACCE than group 2 (5.3% versus 1%) but this was not statistically significant

( $p = 0.07$ ). Two patients in each group died while in-hospital mostly because of arrhythmia (ventricular fibrillation). The need for revascularization, the incidence of heart failure, re-infarction, ischemic cerebrovascular stroke (CVS) or bleeding was not different between groups. In hospital arrhythmia was significantly higher in group 1 compared to group 2 (8.9% vs. 1%,  $p = 0.007$ ). The data of in-hospital outcomes are summarized in Table 5.

### Six months follow up

There was no significant difference between the two groups regarding the composite MACCE endpoint after 6 months follow up (5.4% vs. 4.6%,  $p = 0.24$ ). Two patients in group 1 and 6 patients in group 2 died during follow up (1.8% vs. 0.02%,  $p = 1$ ). The need for revascularization, the incidence of heart failure, re-infarction, ischemic cerebrovascular stroke (CVS) or bleeding was not different between groups. The data of 6 months follow up outcomes are summarized in Table 6 (Figure 1).

**Table 1:** Baseline characteristics of the studied populations.

Age	Group 1 (n=112)		Group 2 (n=388)		Total sample	Test value(P )
Mean $\pm$ SD	56.54 $\pm$ 9.437		59.09 $\pm$ 9.686		57.53 $\pm$ 9.57	p=0.08
Sex	98	87.50%	302	77.8%	400 (80%)	p=0.11
Male	14	12.5%	86	22.2%	100 (20%)	
Female						
DM	8	7.14%	30	7.74%	228(45.6%)	*FEp=0.02
Insulin treated	28	25%	162	41.7%		
Orally treated						
HTN	56	50%	244	62.9%	300(60%)	p=0.08
Smoker	62	55.3%	172	44.3%	234 (46.8%)	* FEp =0.01
Current smoker	18	16.1%	30	7%	48 (9.6%)	
Former smoker						
Dyslipidemia	44	39.3%	120	30.9%	164 (32.8%)	p=0.24
CKD	4	3.6%	36	9.3%	40 (8%)	p=0.262
FH of CAD	24	21%	70	18%	94 (18.8%)	p=0.56
Hx of ACS	4	3.6%	32	8.2%	36 (7.2%)	p=0.378
Hx of PCI	8	7.1%	56	14.4%	64 (12.8%)	p=0.15
	Group 1(n=112)		Group 2 (n=388)			P
Admission to PCI (hr)	12-72		12-72			MWp = 0.35
Min. - Max.	27.11 $\pm$ 10.651		28.73 $\pm$ 11.956			
Mean $\pm$ SD.	24		24			
Median						
Killip class			40		93.3%	MWp=0.77
I	102	91.07 %	362		4.6%	
II	6	5.4 %	18		2.1%	
III	4	3.6 %	8			

$\chi^2$ : value for Chi square; t: Student t-test; MW: Mann Whitney test; \*: Statistically significant at  $p \leq 0.05$

**Table 2:** Baseline ECG, echocardiography and laboratory results of both groups.

	Group 1 (n=112)		Group 2 (n=388)		P
$\chi^2$ : value for Chi square; t: Student t-test; MW: Mann Whitney test; FEP: Fisher's Exact significance; *: Statistically significant at p $\leq$ 0.05	No. 2254	% 2254	No. 2254	% 2254	2254
Initial ECG					
Normal	64	57.1	238	61.3	p = 0.434
St depression	30	26.8	66	17	p = 0.102
T wave inversion	8	12.5	56	14.4	p = 0.7
Q waves	2	1.8	22	5.7	p = 0.3
Bundle branch	2	1.8	6	1.5	p = 1
Hb (g/dl)					
Min. – Max.	9.0 – 15.0		11.0 – 16.0		t <sup>p</sup> = 0.697
Mean $\pm$ SD.	13.20 $\pm$ 1.66		13.36 $\pm$ 1.44		
Median	13		13.25		

S.creatinine (mg/dl)					
Min. – Max.		0.60 – 3.20		0.60 – 1.70	
Mean ± SD.		1.03 ± 0.50		0.95 ± 0.23	
Median		0.9		0.95	
CKMB					
Median		92		35	
(Min-Max)		(5.0-125)		(5.5- 116)	
Troponin					
Median		7.5		1.5	
(Min-Max)		(0.5-35)		(0.5-45)	
ECHO					
EF					
Min-Max		35-75		30-70	
Mean ± SD		58.64± 7.44		59.19±7.616	
Median		60		60	
WMAS		52	46.4%	140	36.1%
p =0.16					
Mitral regurgitation					
No		92	82.1%	310	79.9%
Mild		20	17.9%	62	16%
Moderate		0	0%	12	3.1%
Severe		0	0%	4	1.5%

¶2: value for Chi square; t: Student t-test; MW: Mann Whitney test; \*: Statistically significant at  $p \leq 0.05$

**Table 3:** Grace risk score and TIMI risk score at admission of the studied population.

	Group 1		Group2		Test of significance	P
	(n = 112)		(n = 388)			
	No.	%	No.	%		
GRACE risk score						
Low	64	57.3	232	59.8	$\chi^2=2.67$	MC <sub>p</sub> =0.28
Intermediate	40	35.7	114	31.9		
High	8	7	32	8.3		
TIMI risk score						
Low	20	17.8	80	20.6	$\chi^2=1.567$	MC <sub>p</sub> =0.37
Intermediate	82	73.3	268	69.1		
High	10	8.9	40	10.3		

$\chi^2$ : value for Chi square; MC: Monte Carlo test; \*: Statistically significant at  $p \leq 0.05$

**Table 4:** Procedural characteristics of the studied population.

Group 1			Group 2		P value
(n=112)			(n=388)		
Number of diseased vessels					
One vessel CAD	32	28.6%	160	41.2%	‡2P=0.218
Two vessel CAD	52	46.4%	154	39.7%	
Three vessel CAD	28	25%	74	19.1%	
Culprit vessel					
LAD	24	21.4%	206	53.1%	‡2p=<0.001
LCX	62	55.4%	154	25.8%	
RCA	26	23.2%	74	21.1%	
Site of the lesion					
Proximal	28	50%	95	48.9%	‡2p=0.23
Mid	20	35.7%	74	37.2%	
Distal	8	14.3%	25	13.9%	
TIMI pre procedure					

0	112	100%	0	0%	2P = <0.001
I	0	0%	0	0%	
II	0	0%	64	16.5%	
III	0	0%	324	83.5%	
Use of GPIIa-IIIb antagonists	26	23%	14	3	p=0.04
Collaterals	82	73.2%	18	4.6%	2p = <0.01
TIMI III post procedure	110	98.2%	384	98.9%	p=0.36
Syntax score					
Mean $\pm$ SD	11.68 $\pm$ 6.05		6.79 $\pm$ 3.24		MW <sub>p</sub> =0.12
Median	10		7		
Min-Max	4.0-24.0		4.0-22.0		
Residual syntax score					
Mean $\pm$ SD	1.27 $\pm$ 2.67		0.66 $\pm$ 2.35		MW <sub>p</sub> =0.07
Median	0		0		
Min-Max	0-15		0-20		

$\chi^2$ : value for Chi square; MW: Mann Whitney test; \*: Statistically significant at  $p \leq 0.05$

**Table 5:** In hospital outcomes of the studied population.

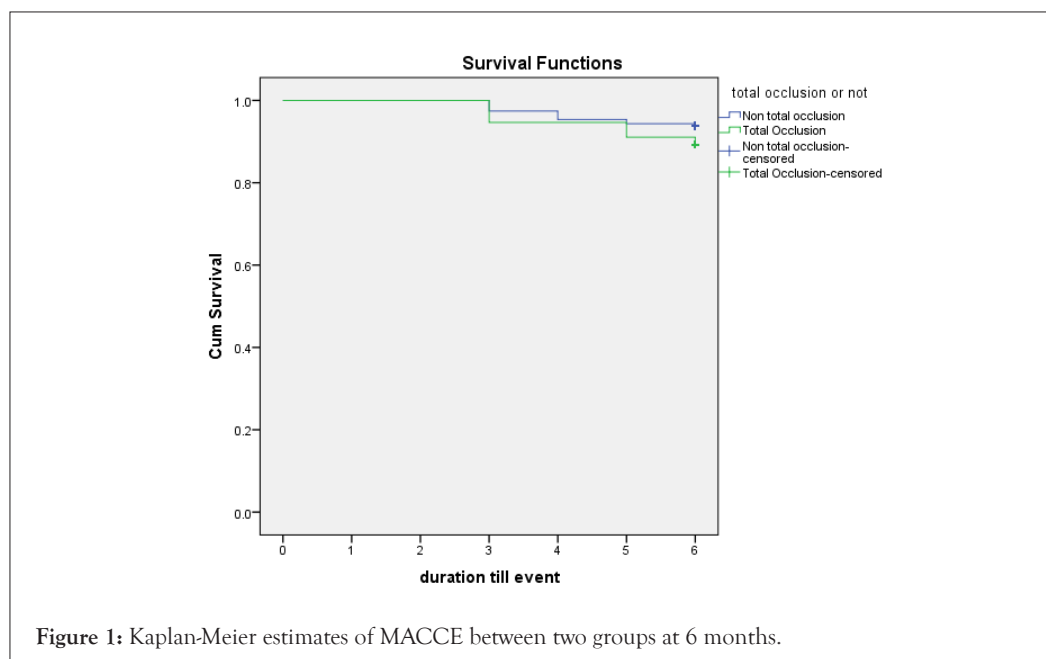
	Group 1 (n=112)		Group 2 (n=388)		P
	No.	%	No.	%	
Arrhythmias	10	8.9	4	1	*FEP=0.007
AF	4	3.5	2	0.5	
VF	6	5.4	2	0.5	
HF	4	3.5	16	0.04	FEP =1
Bleeding	6	5.4	2	0.5	FEP =0.06
Major	2	1.8	0	0	
Minor	4	3.6	2	0.5	
CIN	8	7.1	20	5.1	FEP =0.34
Local vascular complication	10	8.9	16	4.1	FEP =0.22
MACCE	6	5.3	4	1	FEP =0.07
Death	2	1.8	2	0.01	FEP =0.39
Re infarction	0	0	0	0	
Repeated revascularization	2	1.8	0	0	FEP =0.22
Stroke	2	1.8	1	0.01	FEP =0.39

FEP: Fisher's Exact significance; \*: Statistically significant at  $p \leq 0.05$

**Table 6:** 6 months follow up outcomes of the studied population.

	Group 1 (n=112)		Group 2 (n=388)		P
	No.	%	No.	%	
MACCE	6	5.4	18	4.6	p=0.24
Death	2	1.8	6	0.02	FEP=1
Re infarction	2	1.8	8	0.02	FEP=1
Repeated revascularization	2	1.8	4	0.01	FEP=0.53
Major bleeding	0	0	0	0	
Heart failure	2	1.8	6	0.02	FEP=1
Stroke	0	0	0	0	

FEP: Fisher's Exact significance; \*: Statistically significant at  $p \leq 0.05$



## DISCUSSION

The presence of an occluded culprit artery in NSTEMI patients cannot be diagnosed based on the clinical or electrocardiographic findings. The rationale beyond the absence of characteristic ST-segment elevation despite totally occluded artery in NSTEMI patients is still not understood. The lack of sensitivity of standard 12-lead ECG to detect changes of total occlusion in the inferolateral distribution [23-25], the presence of good collaterals, acute total occlusion in a territory with dual blood supply and chronic total occlusion misclassified as acute occlusion could be possible mechanisms [26].

The objective of this study was to evaluate the incidence and impact of totally occluded culprit artery on in-hospital and midterm follow up outcomes of NSTEMI patients. In our study the incidence of totally occluded culprit in NSTEMI patients was 23% which was similar to previous studies that reported an incidence of 25% [9-11]. The mean time from admission to PCI in the totally occluded culprit artery group in our study was  $27.11 \pm 10.6$  hr, this was similar to Kim, et al. [13] but contradicted by Kean soon, et al. [14] who reported longer time and Karwowski, et al. [12] who reported shorter mean time of chest pain to angiography in totally occluded group.

In this study the median of CKMB and Troponin I levels was significantly higher in the totally occluded artery group ( $p < 0.001$ ). This was similar to data from Jarosław Karwowski, et al. [12], Bahrmann, et al. [11] and Wang, et al. [10] that showed significantly higher CKMB and Troponin levels in the totally occluded culprit artery populations. Our findings can be summarized in showing significant involvement of RCA and LCX as culprit vessel in the totally occluded group as well as more collateral. This finding is compatible with other trials. Karwowski et al. [12] reported that in the totally occluded group, LCX represented the culprit vessel in 48.1% of patients and RCA in 29.5% of the patients. The incidence of MACCE either in-hospital or after six months follow up was similar among both groups but the incidence of in-hospital arrhythmia was significantly higher in the totally occluded group. These results are consistent with most studies addressing impact of totally occluded culprit artery in NSTEMI patients [8-14].

The current study was limited in several ways. Firstly, the current study was a retrospective, single center study. Secondly, patients with contraindication to PCI were excluded from the study and finally the relatively small sample size.

## CONCLUSION

Approximately 25% of NSTEMI patients have a totally occluded culprit artery. The presence of an occluded culprit artery did not significantly affect the clinical outcomes of NSTEMI patients either in-hospital or after six months follow up but was associated with significantly higher incidence of in-hospital arrhythmia. Further studies with bigger sample size and longer follow up duration are recommended.

## DECLARATIONS

### Ethics approval and consent to participate

An informed consent was obtained from every patient or the legal guardians. The study was approved by the local ethics committee

All author report no conflict of interest related to his manuscript.

## AVAILABILITY OF DATA AND MATERIALS

All data analyzed during this research are included in this published article.

## COMPETING INTERESTS

All authors declare that they have no competing interests.

## FUNDING

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## AUTHORS' CONTRIBUTIONS

SWA, THE, and MIL searched the literature, collected the data, performed the statistical analyses, and wrote the manuscript; SWA, AME, AMN, and THE contributed to conception, design, data interpretation, and supervision of the study. All authors read and approved the final manuscript.

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