The Impact of Timing of Percutaneous Coronary Intervention on the Prognosis of Non-ST Segment Elevation Myocardial Infarction Patients

Ann. Ital. Chir., 2025 96, 3: 339–344
https://doi.org/10.62713/aic.3339

Tianzhu Li[1,†], Nimin Lu[2,†], Yingxue Dong[1]

[1]Department of Cardiovascular, The First Affiliated Hospital of Dalian Medical University, 116014 Dalian, Liaoning, China
[2]Department of Cardiovascular, The First Affiliated Hospital of Jinzhou Medical University, 121001 Jinzhou, Liaoning, China

AIM: To study the effect of timing of percutaneous coronary intervention (PCI) to prognosis of Non-ST segment elevation myocardial infarction (NSTEMI) patients.

METHODS: 295 Patients were derived from our hospital who were diagnosed as NSTEMI and accepted PCI therapy in 24 hours from admission during March 2017 to May 2020. According to results of coronary angiography, patients with NSTEMI were divided into culprit artery occlusion (CO, n = 117) and non-culprit artery occlusion (N-CO, n = 178) two groups and then according to timing of PCI into three categories: <6 h, 6–12 h and 12–24 h from admission. We defined major adverse cardiovascular events (MACE) in 1 year follow.

RESULTS: In this study, with earlier time to PCI, the incidence of MACE was lower in NSTEMI patients with CO. The incidence of MACE was higher in the CO group than in the N-CO group (25.8% vs. 36.8%, $p = 0.046$). The incidence of MACE was 11.8% in T1 (<6 h) group (n = 50), less than 29.4% in T2 (6–12 h) group (n = 30) and 43.4% in T3 (12–24 h) group (n = 215), with a statistically significant difference ($p = 0.044$). However, this phenomenon does not occur in N-CO group. As the duration of PCI increased, patient survival decreased progressively over the course of follow-up in NSTEMI with CO ($p = 0.048$).

CONCLUSIONS: Our study found that early PCI improves the prognosis of NSTEMI patients with culprit artery occlusion.

Keywords: Non-ST segment elevation myocardial infarction; culprit artery; occlusion

Introduction

Acute myocardial infarction (AMI) is categorized into ST segment elevation myocardial infarction (STEMI) and Non-ST segment elevation myocardial infarction (NSTEMI), and it was previously believed that STEMI occurs mainly due to the interruption of blood flow caused by acute thrombosis in the coronary arteries, resulting in transmural ischemia of the entire myocardium, which manifests itself on the electrocardiogram as ST-segment elevation of the leads corresponding to the ischemic region of the myocardium, whereas NSTEMI occurs due to the subendocardial ischemia of the endocardium caused by incomplete occlusion of the coronary arteries, and therefore it does not manifest as ST-segment elevation on the electrocardiogram. However, in clinical practice, complete occlusion of the offender vessel also occurs in about 1/3 of patients with NSTEMI, which is often associated with a larger area of myocardial necrosis and a worse prognosis compared with patients without complete occlusion [1].

Percutaneous coronary intervention (PCI) is an important therapeutic modality in the treatment of myocardial infarction and is aimed at restoring myocardial blood supply. Current guidelines recommend that the timing of interventional intervention in patients with Non-ST segment elevation-Acute coronary syndrome (NSTE-ACS) be determined according to risk stratification [2]. Patients who develop offender vessel occlusion often experience a delay in intervention because of the absence of electrocardiography (ECG) specific manifestations, which may be an important reason for the poor prognosis of these patients.

Theoretically, early PCI to open the vessel in patients with NSTEMI combined with artery occlusion of the offender vessel can block the progression of myocardial necrosis and reduce complications. However, there is no evidence to confirm the benefit of early intervention in NSTEMI patients with combined culprit artery occlusion. In this study, we retrospectively analyzed the data of NSTEMI patients in a single center, and analyzed the prognosis of NSTEMI patients with combined culprit artery occlusion with different timing of PCI, aiming to confirm that early PCI can improve the prognosis of these patients.

Submitted: 25 April 2024 Revised: 14 October 2024 Accepted: 14 November 2024 Published: 24 February 2025
Correspondence to: Yingxue Dong, Department of Cardiovascular, The First Affiliated Hospital of Dalian Medical University, 116014 Dalian, Liaoning, China (e-mail: dongyingxue_0113@sina.com).
†*These authors contributed equally.*

Table 1. Comparison of clinical characteristics among different time of PCI group of NSTEMI patients.

	N-CO (n = 178)	CO (n = 117)	F/χ^2/Z	p-value
Age (years)	62.6 ± 10.8	61.9 ± 11.4	0.527	0.599
Male (%)	126 (70.8)	88 (75.2)	0.695	0.405
Hypertension (%)	117 (65.7)	81 (69.2)	0.392	0.531
Diabetes mellitus (%)	62 (34.8)	39 (33.3)	0.070	0.791
Smoke (%)	90 (50.6)	58 (49.6)	0.028	0.868
LDC-C (mmol/L)	2.92 ± 0.92	2.84 ± 0.70	0.498	0.443
eGFR (mL/min)	83.8 ± 29.2	82.6 ± 17.8	0.414	0.679
LVEF (%)	51.8 ± 16.1	50.9 ± 13.6	0.768	0.619
CK-MB (U/L)	57.15 (24.2, 90.1)	33.45 (19.5, 47.4)	–8.03	0.005
cTnT (ng/L)	628 (401, 855)	925 (402, 1449)	87.34	0.000
IRA (%)			5.152	0.076
LAD	92 (51.7)	47 (40.2)		
LCX	51 (28.7)	35 (29.9)		
RCA	35 (19.7)	35 (29.9)		
Time of PCI (%)			4.395	0.109
T1 (<6 h)	33 (18.5)	17 (14.5)		
T2 (6–12 h)	13 (7.3)	17 (14.5)		
T3 (12–24 h)	132 (74.2)	83 (70.9)		
MACE (%)	46 (25.8)	43 (36.8)	3.988	0.046

PCI, percutaneous coronary intervention; NSTEMI, Non-ST segment elevation myocardial infarction; CO, culprit artery occlusion; N-CO, non-culprit artery occlusion; LDC-C, Low-Density Lipoprotein Cholesterol; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; CK-MB, Creatine kinase-MB; cTnT, Cardiac Troponin T; IRA, Infarct-Related Artery; LAD, Left Anterior Descending artery; LCX, Left Circumflex artery; RCA, Right Coronary Artery; MACE, major adverse cardiovascular events.

Materials and Methods

Patients were derived from The First Affiliated Hospital of Dalian Medical University who were diagnosed as NSTEMI and accepted PCI therapy in 24 hours from admission during March 2017 to May 2020. All participants provided written informed consents to participate in the study. The study population comprised all patients admitted with NSTEMI.

Study Population

The study population consisted of patients from March 2017 to May 2020 with the diagnosis of NSTEMI. Patients were diagnosed with NSTEMI based on the presence of chest pain and elevated troponin levels without persistent ST-segment elevation [1]. Coronary angiograms were interpreted by two or more experienced cardiologists, and the culprit artery was identified as least one of the following conditions: a lesion that could explain the change of the electrocardiogram; the presence of a fresh thrombus; and significant relief of the patient's symptoms after the intervention. According to timing of coronary angiography, patients with NSTEMI were divided into culprit artery occlusion (CO) and non-culprit artery occlusion (N-CO) two groups and according to timing of PCI into three categories: <6 h from admission; 6–12 h from admission; and 12–24 h from admission. We defined major adverse cardiovascular events (MACE) as mortality, recurrent myocardial infarction (MI), stent thrombosis, ischemia-driven urgent revascularization, and cerebrovascular event in 1-year follow up. All patients who underwent PCI were medicated postoperatively according to guidelines, which included at least 2 antiplatelet agents, statin. This study was approved by the Ethics Committee of The First Affiliated Hospital of Dalian Medical University (PJ-KS-KY-20-067). Signed written informed consents were obtained from the patients and/or guardians. This study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki.

Statistical Analysis

In the evaluation of data distribution normality, tests such as the Shapiro-Wilk test or the Kolmogorov-Smirnov test with Lilliefors correction were utilized. When comparing groups with non-normal distributions, non-parametric statistical methods were employed. The Mann-Whitney U test was chosen for such comparisons due to its robustness in handling non-normal data and its ability to test for differences in median values between two independent groups. The continuous variables were represented as mean ± standard deviation or median (P25, P75), and the categorical variables were expressed as number (percentage). The continuous variables were analysed using Analysis of Variance

Table 2. Comparison of clinical characteristics and MACE between N-CO group and CO group of NSTEMI patients.

	T1 (n = 50)	T2 (n = 30)	T3 (n = 215)	F/χ^2/Z	*p*-value
Age (years)	63.7 ± 10.6	64.7 ± 11.7	61.6 ± 11.0	1.462	0.233
Male (%)	35 (70.0)	23 (76.7)	156 (72.6)	0.418	0.811
Hypertension (%)	32 (64.0)	19 (63.3)	147 (68.4)	0.568	0.753
Diabetes mellitus (%)	16 (32.0)	9 (30.0)	76 (35.3)	0.468	0.791
Smoke (%)	23 (46.0)	18 (60.0)	107 (49.8)	1.521	0.467
LDC-C (mmol/L)	3.04 ± 0.87	2.81 ± 0.63	2.86 ± 0.86	1.051	0.351
eGFR (mL/min)	80.7 ± 20.4	82.5 ± 20.6	84.0 ± 26.8	0.362	0.696
LVEF (%)	51.3 ± 13.2	45.7 ± 16.8	52.2 ± 15.1	2.469	0.086
cTnT (ng/L)	764.25 (662.7, 865.8)	847.65 (762.3, 933.0)	667.3 (552.3, 782.3)	0.872	0.419
IRA (%)				7.420	0.115
LAD	32 (64.0)	14 (46.7)	93 (43.3)		
LCX	10 (20.0)	10 (33.3)	66 (30.7)		
RCA	8 (16.0)	6 (20.0)	56 (26.0)		
CO	17 (34.0)	17 (56.7)	83 (38.6)	4.395	0.111
CK-MB (U/L)	32.9 (20.5, 45.3)	44.5 (30.1, 58.9)	55.25 (40.0, 70.5)	6.452	0.011

Table 3. Comparison of MACE among different time of PCI in CO group of NSTEMI patients and in N-CO group of NSTEMI patients.

	T1	T2	T3	χ^2	*p*-value
CO group (number)	17	17	83		
MACE (%)	2 (11.8)	5 (29.4)	36 (43.4)	0.038	0.044
N-CO group (number)	33	13	132		
MACE (%)	9 (27.3)	3 (23.1)	34 (25.8)	0.088	0.957

(ANOVA) followed by Tukey's Honest Significant Difference (HSD) for post-hoc testing when significant differences were found. Categorical variables were analyzed using Chi-squared tests and Fisher's exact tests where appropriate. Differences between continuous variables were assessed for normally distributed data using independent samples *t*-tests. The proportional hazards assumption was evaluated by Kaplan-Meier (K-M) survival curves. To assess the survival probability of patients in each subgroup, Kaplan-Meier survival curves were generated. The survival analysis was conducted using the log-rank test to compare differences between the groups. The median survival times and the corresponding 95% confidence intervals (CIs) were calculated for each subgroup. Statistical significance was determined with a p-value < 0.05.

All statistical analyses were performed using IBM SPSS Statistics software (version 23.0; IBM Corp., Armonk, NY, USA) with 2-sided p value of 0.05 for statistical significance assessment for all analyses.

Results

Comparison of Clinical Characteristics and MACE between N-CO Group and CO Group of NSTEMI Patients

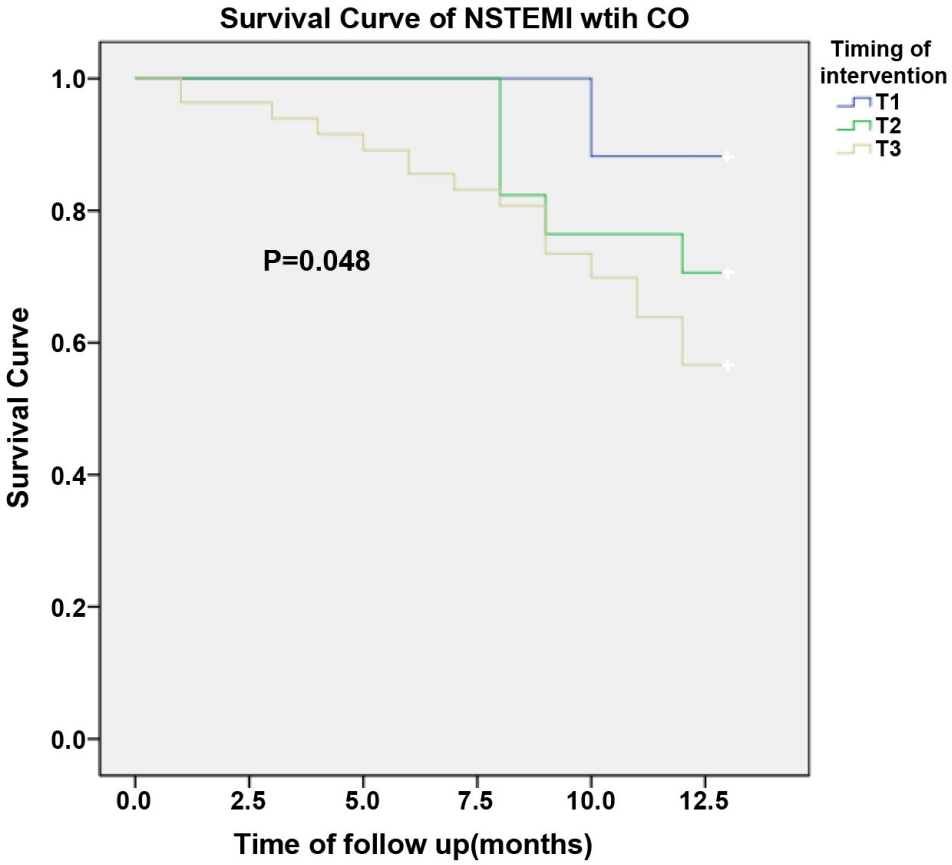
A total of 295 people were included in this study, 117 (39.7%) patients were into CO group. There were no statistical differences between the two groups in terms of gender, age, hypertension, diabetes mellitus, smoke, Low-Density Lipoprotein Cholesterol (LDL-C), estimated glomerular filtration rate (eGFR), left ventricular ejection fraction (LVEF), Infarct-Related Artery (IRA) and time of PCI. The level of Creatine kinase-MB (CK-MB) was lower in CO group than NCO group, and the level of Cardiac Troponin T (cTnT) were higher in CO group than NCO group, indicating more myocardial injury in CO group. (25.8% vs. 36.8%, $p = 0.046$). See Table 1.

Comparison of MACE among Different Time of PCI in CO Group of NSTEMI Patients and in N-CO Group of NSTEMI Patients

In this study, In the T1, T2, and T3 groups, there were no statistically significant differences in the comparison of baseline characteristics, except CK-MB (Table 2). With earlier time to PCI, the incidence of MACE was lower in NSTEMI patients with CO. The incidence of MACE was 11.8% in T1 group, less than 29.4% in T2 group and 43.4% in T3 group, with a statistically significant difference ($p = 0.044$). But this phenomenon does not occur in N-CO group (Table 3).

Survival Analysis with Kaplan-Meier Curve in CO Group of NSTEMI Patients

By Kaplan-Meier (K-M) survival curve analysis, As the duration of PCI increased, patient survival decreased progressively over the course of follow-up in NSTEMI with CO ($p = 0.048$, Fig. 1). The median survival times for the subgroups (T1, T2, T3) were as follows:



Number at risk / Time point	T1	T2	T3
0 months	17	17	83
2.5 months	17	17	81
5.0 months	17	17	79
7.5 months	17	14	77
10.0 months	15	12	74
12.5 months	15	10	70

Fig. 1. The K-M curve in CO group in different timing of PCI in NSTEMI patients. SPSS (version 23.0, IBM Corp., Armonk, NY, USA); K-M, Kaplan-Meier.

T1: Median survival time = 10.0 months.
T2: Median survival time = 12.5 months.
T3: Median survival time = 30.3 months.

Discussion

Current guidelines recommend that the NSTE-ACS determine the timing of PCI based on risk stratification rather than coronary anatomy. Therefore, all patients with NSTEMI are at least high-risk and should undergo PCI within 24 h. However, current interventions for NSTEMI fall short of the guidelines in many regions, and the very high-risk patients in whom the guidelines call for PCI within 2 h are usually also combined with very high surgical risks and complications. There is a study showing that the majority of very high-risk patients don't get very early PCI like the guidelines recommend [3]. Similar to STEMI, NSTEMI patients with culprit artery occlusion are relatively clinically stable early in the course of their disease and can be considered to benefit more from early PCI treatment.

Comorbid artery occlusions are common in patients with NSTEMI, and two meta-analyses [1,4] have shown that artery occlusion occurs in 25%–34% of patients with NSTEMI and that there is an elevated risk of cardiovascular events and death in the short and long term, compared to patients with NSTEMI who do not develop occlusions. Myocardial injury markers such as troponin and CK-MB were at higher levels in patients with artery occlusion than in non-occluded patients, suggesting that occlusion of the offender vessel is usually accompanied by a larger infarct size, and that NSTEMI patients with artery occlusion of the offender vessel are often delayed in undergoing interventional intervention because of the absence of the typical electrocardiographic manifestation of ST-segment elevation, compared with those who did not undergo a complete occlusion of the vessel. The time from symptom onset to coronary angiography or percutaneous coronary intervention (PCI) was similar (31.3 h vs 34.2 h) [1]. Clinical risk stratification of NSTEMI patients with artery occlusion in offenders was similar to that of patients with non-artery occlusion, with Kiliip classification, GRACE score, and Thrombolysis In Myocardial Infarction (TIMI) score not differing from those of patients with non-occlusion, and the absence of significant high-risk manifestations was also an important reason for delayed interventional intervention in these patients. Another study with a 36-month follow-up showed that also in the presence of artery occlusion of the offender, the mortality rate was significantly higher in patients with STEMI than in those with NSTEMI, but in patients with NSTEMI, the presence or absence of artery occlusion did not affect the long-term prognosis [5]. Meyers *et al*. [6] categorized patients with acute myocardial infarction into offenders with artery occlusion and found that the prognosis of patients without ST-segment elevation but with artery occlusion was similar to that of STEMI. A polish study [7] showed that Killip classification, prehospital cardiac arrest, and intraprocedural cardiac arrest in NSTEMI patients with artery occlusion were intermediate between those with STEMI and NSTEMI patients without artery occlusion, which may be related to delayed intervention and Left Circumflex artery (LCX) occlusion. There are no studies confirming that NSTEMI patients with combined culprit artery occlusion can benefit from early intervention.

The results of this study show that In NSTEMI patients with culprit artery occlusion, prognosis is related to the timing of PCI, and early PCI reduces the incidence of MACE. However, this phenomenon does not occur in the N-CO group. In the CO group, significantly elevated troponin may be associated with larger infarct size, and these patients may benefit more from PCI therapy. A systematic review [8] showed that early intervention can reduce mortality in high-risk patients. On the other hand, patients with NSTEMI often have a longer duration of illness and have a lower in-hospital mortality rate and a poorer long-term prognosis compared to STEMI [9]. A study by Menon *et al*. [10] showed no difference in outcomes between interventional and pharmacologic conservative treatment in patients with artery occlusion for patients with stable NSTEMI.

There is no method for early identification of artery occlusion in offenders, and some scholars have proposed that NSTEMI patients can be judged by the Survival After Veno-Arterial Extracorporeal Membrane Oxygenation (SAVE) score [11] to determine whether there is acute occlusion of the offender's vessel, and a SAVE score of $\geq$3 can be considered to have acute occlusion of the vessel and undergo urgent interventional therapy, but this scoring system is based on extrapolations of a large number of previous studies, and it has not yet been confirmed in a clinical cohort.

But our results confirm that early intervention in NSTEMI patients with combined offender vessel occlusion improves 1-year prognosis, but there are many limitations: (1) this is a retrospective study without randomized grouping, and it is possible that patients with offender vessel occlusion, who have more pronounced early symptoms and more typical ischemic manifestations on electrocardiograms, have a greater likelihood of obtaining early PCI, which may bias the results; (2) NSTEMI patients have more combined multibranch lesions and chronic total occlusion (CTO), and there is difficulty in correctly identifying patients, which may make the grouping error. bias; (3) NSTEMI patients combined with more multibranch vasculopathy and CTO, and there is difficulty in correctly identifying the offender vessel, which may make the grouping of patients in error, and thus better methods are needed to identify patients with offender vessel occlusion before coronary angiography.

Conclusions

Our study found that early PCI improves the prognosis of NSTEMI patients with culprit artery occlusion, yet further

large-scale, randomized studies are needed to confirm these findings.

Availability of Data and Materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions

TL: Conceptualization, Methodology, Investigation, Formal Analysis, Software, Writing-original draft. YD: Conceptualization, Methodology, Investigation, Visualization, Writing-Review & Editing. NL: Methodology, Investigation, Supervision. All authors have been involved in revising it critically for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of The First Affiliated Hospital of Dalian Medical University (PJ-KS-KY-20-067). Signed written informed consents were obtained from the patients and/or guardians. This study was performed in accordance with the ethical standards as laid down in the 2013 Declaration of Helsinki.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

References

[1] Khan AR, Golwala H, Tripathi A, Bin Abdulhak AA, Bavishi C, Riaz H, *et al*. Impact of total occlusion of culprit artery in acute non-ST elevation myocardial infarction: a systematic review and meta-analysis. European Heart Journal. 2017; 38: 3082–3089.

[2] Collet JP, Thiele H, Barbato E, Barthélémy O, Bauersachs J, Bhatt DL, *et al*. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. European Heart Journal. 2021; 42: 1289–1367.

[3] Lupu L, Taha L, Banai A, Shmueli H, Borohovitz A, Matetzky S, *et al*. Immediate and early percutaneous coronary intervention in very high-risk and high-risk non-ST segment elevation myocardial infarction patients. Clinical Cardiology. 2022; 45: 359–369.

[4] Hung CS, Chen YH, Huang CC, Lin MS, Yeh CF, Li HY, *et al*. Prevalence and outcome of patients with non-ST segment elevation myocardial infarction with occluded "culprit" artery - a systemic review and meta-analysis. Critical Care (London, England). 2018; 22: 34.

[5] Karwowski J, Gierlotka M, Gąsior M, Poloński L, Ciszewski J, Bęćkowski M, *et al*. Relationship between infarct artery location, acute total coronary occlusion, and mortality in STEMI and NSTEMI patients. Polish Archives of Internal Medicine. 2017; 127: 401–411.

[6] Meyers HP, Bracey A, Lee D, Lichtenheld A, Li WJ, Singer DD, *et al*. Comparison of the ST-Elevation Myocardial Infarction (STEMI) vs. NSTEMI and Occlusion MI (OMI) vs. NOMI Paradigms of Acute MI. The Journal of Emergency Medicine. 2021; 60: 273–284.

[7] Terlecki M, Wojciechowska W, Dudek D, Siudak Z, Plens K, Guzik TJ, *et al*. Impact of acute total occlusion of the culprit artery on outcome in NSTEMI based on the results of a large national registry. BMC Cardiovascular Disorders. 2021; 21: 297.

[8] Jneid H. Merits of Invasive Strategy in Diabetic Patients With Non-ST Elevation Acute Coronary Syndrome. Journal of the American Heart Association. 2017; 6: e005773.

[9] Kilickap M, Erol MK, Kayikcioglu M, Kocayigit I, Gitmez M, Can V, *et al*. Short and Midterm Outcomes in Patients With Acute Myocardial Infarction: Results of the Nationwide TURKMI Registry. Angiology. 2021; 72: 339–347.

[10] Menon V, Ruzyllo W, Carvalho AC, Almeida de Sousa JM, Forman SA, Jaworska K, *et al*. Infarct artery distribution and clinical outcomes in occluded artery trial subjects presenting with non-ST-segment elevation myocardial infarction (from the long-term follow-up of Occluded Artery Trial [OAT]). The American Journal of Cardiology. 2013; 111: 930–935.

[11] Tziakas D, Chalikias G, Al-Lamee R, Kaski JC. Total coronary occlusion in non ST elevation myocardial infarction: Time to change our practice? International Journal of Cardiology. 2021; 329: 1–8.