Index Admission of Percutaneous Coronary Intervention versus Pharmaco-invasive Strategy for Patients with Acute ST-Elevation Myocardial Infarction: A Tertiary Centre-based Study

Muaath Ahmed H. Mohammed*, W Isa WYH, Z Yusof

Cardiology Unit, Department of Medicine, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia.

ABSTRACT

INTRODUCTION: Pharmaco-invasive strategy is a standard of care in patients with ST-elevation myocardial infarction (STEMI), but the optimal timing may not be achieved due to limitations. Thus, a large number of patients underwent percutaneous coronary intervention (PCI) at a later timing during their index hospitalisation. However, small evidence is available on the outcome of this strategy. This study aimed to compare the clinical outcomes of delayed PCI during index admission with a pharmaco-invasive strategy for patients with STEMI. **MATERIAL AND METHODS:** This retrospective cohort study was conducted at a tertiary centre. Medical records of all STEMI patients who were treated by PCI from January 2013 to March 2018 were retrieved. The clinical outcomes of the study were the rate of major adverse cardiac event (MACE) and major bleeding at 30 days and 6 months post PCI. **RESULTS**: A total of 91 STEMI patients were analysed. Twenty-nine (31.9%) patients were treated by pharmaco-invasive strategy, and 62 (68.1%) patients underwent PCI during their index admission. At 30 days post PCI, the rates of MACE in the pharmaco-invasive and PCI during index admission group were 10.7% and 10.3%, respectively (p=0.958). The rates at 6 months were 8.3% and 7.8% (p=0.942). The rates of major bleeding at 30 days were one (3.6%) and none (p=0.151). By contrast, the rate at six months was only one (2.0%) for the PCI during index admission group. **CONCLUSIONS**: PCI during index admission may had similar clinical outcomes to pharmaco-invasive strategy.

INTRODUCTION

Acute myocardial infarction (MI) is a major health problem globally and constitutes about 25-40% of ST-segment elevation myocardial infarction (STEMI). The primary treatment of patients with STEMI is reperfusion therapy with either pharmacological reperfusion (fibrinolysis) or mechanical reperfusion.[1] Substantial evidence from several studies has shown that mechanical reperfusion is superior to fibrinolytic therapy; therefore it remains the best choice for acute MI.[2] Pharmaco-invasive strategy is defined as the administration of fibrinolytic therapy followed by performing angiography and percutaneous coronary intervention (PCI) within 3–24 h after initiation of fibrinolytic therapy.[1] The early revascularisation by pharmaco-invasive or primary PCI (PPCI) strategies is still a major obstacle in healthcare centres, especially in developing countries, and many STEMI patients worldwide may have missed it. Therefore, delayed PCI has become the third PCI option. However, the evidence for delayed PCI benefits and timing still requires further studies.[3] In Malaysia, 81% of STEMI patients (n = 8190) received fibrinolysis as reperfusion therapy. Fibrinolysis has been the major reperfusion strategy for those who were presented to non-PCI capable centres. PPCI is still at a low rate due to a limited number of PCI capable centres and cost. It was delivered only for 16.4% of STEMI patients, and 33.4% of patients underwent PCI during their index admission.[4,5] Very few studies have been conducted on reperfusion therapy outcomes in Malaysia.[6] Therefore, the present study aimed to compare the rate of major adverse cardiac event

(MACE) and major bleeding amongst STEMI patients who were treated by PCI during index admission versus pharmaco-invasive strategy.

METHODOLOGY

Study design and population
A retrospective cohort study was conducted at Hospital University Sains Malaysia, a tertiary care centre in the east coast of Peninsular Malaysia. All STEMI patients aged 18 years or more treated by pharmaco-invasive strategy or PCI during index admission were included. The medical files of these patients were retrieved from January 2013 to March 2018. The STEMI diagnosis was clearly written in the medical records, and the diagnosis was verified based on the presence of at least two out of these criteria: symptoms, ECG changes and serum cardiac biomarkers.[7,8] Patients who were treated by primary PCI were excluded. The patients were divided into two groups depending on the types of PCI strategy. The first group contained patients for whom PCI was done as part of pharmaco-invasive strategy. This strategy was defined as the first administration of fibrinolysis followed by PCI up to 48 h from the STEMI onset. The 48 h cut off was chosen based on the favourable outcomes from three studies.[9-11] The second group consisted of patients for whom PCI was performed after 48 h up to 28 days of STEMI onset and during their index hospitalisation.

Operational definition
MACE was defined as an event of one or more of the following: cardiac death, stroke, recurrent MI, re-hospitalisation due to heart failure or repeated coronary revascularization.[12] Any death in and out of the hospital associated to the ischemic heart disease presentation or sudden cardiac death was defined as cardiac death.[13] The definition of stroke was the appearance of new neurological deficits lasting for > 24 h with evidence of brain ischemia or haemorrhage by brain imaging.[14] Any documented readmission with MI diagnosis was defined as recurrent MI.[15] Patient readmission with the primary diagnosis of heart failure and length of hospitalisation of at least 24 h was defined as re-hospitalisation due to heart failure.[16] Repeated revascularisation denoted the need for

PCI or coronary artery bypass grafting in subsequent hospitalisations.[17] Major bleeding was defined as development of intracranial bleeding, bleeding requiring hospitalisation, and reduction in haemoglobin > 2 g/dL or requiring blood transfusion due to bleeding.[18]

Data collection
The patients' demographics and baseline characteristics, coronary risk factors, coronary angiogram parameters, and PCI outcomes were obtained from a review of medical records. All data were recorded using a standardized data collection form.

The rate of MACE and major bleeding at 30 days and 6 months post PCI were the clinical outcomes evaluated in this study. The clinical outcome-related data were collected by reviewing patients' follow up notes and through phone calls.

Statistical Analysis
The Statistical Package for Social Science (SPSS) version 24 was used for all statistical analyses. Categorical variables were described by frequency and percentage and analysed using chi-square test. Normally distributed continuous variables were presented as mean (standard deviation) and compared using the Student t-test. A 2-sided P-value of less than 0.05 was considered significant.

RESULTS

A total of 168 STEMI patients were screened. Amongst them, 2 underwent primary PCI, and 75 had their PCI after discharge. Thus, 91 STEMI patients were included in this study. Twenty-nine patients (31.9%) were treated by pharmaco-invasive strategy, and 62 patients (68.1%) underwent PCI during the index admission. In the pharmaco-invasive group, the mean hours from administering fibrinolytic therapy until the PCI procedure were 26.4 (12.7). In the PCI during the index admission group, the median days from STEMI onset until PCI was 3.0. A total of 98.9% of stents used were drug-eluting types. For coronary risk factors, smoking was the most frequent risk factor reported amongst STEMI patients. The distribution of other risk factors between study

groups was insignificantly different. Most patients had an anterior MI and commonly presented with Killips class 1.

Table 1 shows the baseline characteristics of the patients and coronary risk factors.

Variables	Pharmaco-invasive strategy n = 29	PCI during index admission n = 62	p-value
Age	53.1±12.4	57.1±10.1	0.111
Gender /Male	26 (89.7)	52 (83.9)	0.462
Coexisting conditions:			
Smoking	16 (59.3)	39 (67.2)	0.473
Dyslipidaemia	17 (58.6)	27 (43.5)	0.846
Hypertension	13 (44.8)	29 (46.8)	0.862
Diabetes Mellitus	13 (44.8)	20 (32.3)	0.245
History of CKD	1 (3.4)	9 (14.5)	0.116
Previous CAD	2 (6.9)	9 (14.5)	0.229
History of CVA	0 (0.0)	1 (1.6)	0.492
Previous angioplasty	0 (0.0)	2 (3.2)	0.328
Anterior MI	19 (65.5)	37 (59.7)	0.781
Killips class 1	16 (55.2)	31 (50.0)	0.420
Giving fibrinolysis	29 (100.0)	50 (80.6)	0.011
DNT (min)	78.7± 144.7	83.9± 187.8	0.900
Heart rate, beat/min	79.8± 26.37	87.71± 24.03	0.842
Blood Pressure, mm Hg Systolic BP	135.2+ 24.0	134.7 + 30.2	0.932
Diastolic BP	87.0± 25.4	80.3 ± 20.3	0.186
Body Mass Index	25.5± 3.3	26.0 ± 5.4	0.656

Values are mean ± SD, n (%), CKD: Chronic Kidney Disease, CAD: Coronary Artery Disease, CVA: CerebroVascular Accident, MI: Myocardial Infarction, DNT: Door Needle Time.

Angiographic and Procedural Results

The majority of patients in this study have a single vessel disease, and left anterior descending artery was the most common culprit. TIMI flow grade 3 post PCI was achieved in all patients of the pharmaco-invasive group and in 98.8% of PCI during index admission group (p=0.336). Table 2 presents these results.

Clinical Outcomes

The rates of MACE at 30 days post PCI in the pharmaco-invasive group and PCI during the index admission group were 10.7% and 10.3%, respectively (p = 0.958). The rates

Table 2. Angiographic parameters of the patients

Variables	Pharmaco-invasive strategy n = 29	PCI during index admission n = 62	p-value
No of diseased vessels			0.174
Single vessel disease	15 (51.7)	22 (35.5)	
LAD			
RCA	2 (6.9)	2 (3.2)	
LCX	0 (0.0)	4 (6.5)	
2 Vessel disease			
LAD+RCA	8 (27.6)	13 (21.0)	
LAD+LCX	0 (0.0)	9 (14.5)	
RCA+LCX	1 (3.4)	5 (8.1)	
3 Vessel disease			
LAD+RCA+LCX	3 (10.3)	7 (11.3)	
Culprit artery			0.142
LAD	22 (75.9)	37 (59.7)	
RCA	7 (24.1)	19 (30.6)	
LCX	0 (0.0)	6 (9.7)	
TIMI flow post PCI			0.336
0	0 (0.0)	0 (0.0)	
1	0 (0.0)	0 (0.0)	
2	0 (0.0)	2 (3.2)	
3	28 (100.0)	60 (98.8)	

Values are mean + SD, n (%), CKD: Chronic Kidney Disease, CAD: Coronary Artery Disease, CVA: CerebroVascular Accident, MI: Myocardial Infarction, DNT: Door Needle Time.

of cardiac death were 3.4% and 1.7% (p=0.595). Re-hospitalisation due to heart failure, reinfarction, and repeated PCI were high in PCI patients during the index admission group but non-statistically significant. Major bleeding occurred only in one patient (3.6%) of the pharmaco-invasive group (p=0.151). Table 3.1 shows these results.

Table 3.1 The rate of MACE and major bleeding at 30 days post PCI

Variables	Pharmaco-invasive strategy n = 29	PCI during index admission n = 62	p-value
MACE	3 (10.7)	6 (10.3)	0.958
Cardiac death	1 (3.4)	1 (1.7)	0.595
Stroke	1 (3.6)	1 (1.8)	0.603
Re-infarction	0 (0.0)	1 (1.6)	0.658
Re-hospitalization due to HF	3 (10.7)	6 (10.3)	0.958
Repeated revascularization PCI	0 (0.0)	1 (1.7)	0.485
CABG	0 (0.0)	0 (0.0)	
Major bleeding	1 (3.6)	0 (0.0)	0.151

Values are n (%), MACE: Major Adverse Cardiac Event, HF: Heart Failure, PCI: Percutaneous Coronary Intervention, CABG: Coronary Artery Bypass Graft

At 6 months, the rate of MACE was 8.3% in the pharmaco-invasive and that was 7.8% in the PCI during the index admission group (p = 0.942). Cardiac death and stroke were only reported for patients in the PCI during the index admission group. Only one patient (2.0%) in the PCI during index admission group developed major bleeding at 6 months post PCI (p = 0.485). Table 3.2 shows these results.

Table 3.2 The rate of MACE and major bleeding at 6 months post PCI

Variables	Pharmaco-invasive strategy n = 29	PCI during index admission n = 62	p-value
MACE	2 (8.3)	4 (7.8)	0.942
Cardiac death	0 (0.0)	2 (3.6)	0.325
Stroke	0 (0.0)	1 (2.0)	0.485
Re-infarction	0 (0.0)	0 (0.0)	
Re-hospitalization due to HF	2 (8.3)	4 (8.0)	0.961
Repeated revascularization PCI	0 (0.0)	0 (0.0)	
CABG	0 (0.0)	0 (0.0)	
Major bleeding	0 (0.0	1 (2.0)	0.485

Values are n (%), MACE: Major Adverse Cardiac Event, HF: Heart Failure, PCI: Percutaneous Coronary Intervention, CABG: Coronary Artery Bypass Grafting

DISCUSSION

The European Society of Cardiology (ESC) recommended PPCI as a class I reperfusion strategy to treat STEMI patients.[19] However, this treatment should be delivered with a door-to-balloon time of < 90 min.[1] The advantages of PPCI over fibrinolytic therapy disappear when the door-to-balloon time is more than 120 min.[20] PPCI is an ideal reperfusion strategy but may be unavailable in many centres; thus, the pharmaco-invasive strategy is an alternative option.[21] Studies have revealed that the application of PCI within 24 h of fibrinolysis decreased the composite endpoints of death, ischemia and reinfarction within 30 days of PCI.[22] However, in developing countries, even the 24 h period is insufficient to arrange for PCI due to various factors, such as manpower, logistic/lack of PCI centres and cost.[23] In consideration of the limitations, PCI during index admission is a favourable option. This delayed stenting strategy was supported by Wu et al. [24] who reported that the application of PCI 12 h up to 28 days

after STEMI (including those who had been discharged and come back as an elective procedure) was significantly more effective than standard medical therapy and showed satisfactory short- and long-term mortality outcomes. One meta-analysis has shown that delayed PCI for STEMI patients improved the long-term survival rate at 2.8 years of follow-up instead of the medical therapy (6.3% vs. 8.4%, the odds ratio for death was 0.49, 95% CI 0.26–0.94).[25] Another study has shown that such treatment prevented the left ventricular remodelling and improved clinical outcomes.[2] In this study, 91/168 STEMI patients had either pharmaco-invasive or index admission PCI. They accounted for 54.2% of all STEMI patients admitted at this centre between January 2013 and March 2018. Amongst them, the majority were in the PCI during the index admission group. This situation can be explained by that all these PCI were done during office hours only and the cardiac laboratory was closed during the weekend due to short of manpower and cost. This study suggested that the PCI during index admission had comparable outcomes to the pharmaco-invasive strategy.

Based on occluded artery trial (OAT) and other clinical trials, ESC recommended against PCI between 3-28 days after STEMI onset.[19] In the OAT trial, 2166 STEMI patients were randomised between 3-28 days of STEMI onset to late PCI (median 8 days) versus conservative treatment. The results showed no difference in the rate of the composite end point of death, reinfarction or heart failure. The results were 17.2 and 15.6 (p = 0.20) after 4 years of follow up.[27] In this trial, a low rate of drug-eluting stent implantation was noted. It was used only for 8% of the patients. The Southwest German Interventional Study in Acute Myocardial Infarction (SIAM III) was the first trial comparing pharmaco-invasive strategy with delayed PCI strategy. In this trial, 197 STEMI patients were randomised to early PCI strategy (PCI within 6 h of STEMI onset) and delayed PCI (within 2 weeks of STEMI onset) after administration of full-dose reteplase. The investigators found that the combined endpoints of mortality, ischemic events, reinfection and need for revascularisation at 30 days post PCI were 8.5% in the immediate stenting group and 30.9% in the delayed stenting group (p<0.001); the rates were 25.6% and 50.6% (p<0.001) at 6 months.[28] The investigators in this trial

used only a bare metal stent. In the current study, 98.9% of the stents used were drug-eluting type. These differences in the findings can be explained by the type of stents used. Using bare metal stents is no longer a favourable option per current STEMI guidelines. The latest guidelines recommend against the use of bare metal stents unless in a few exceptional situations, such as when the risk of bleeding from prolonged antiplatelet usage outweighs the revascularisation benefits. The latest generation of drug-eluting stents and bioresorbable vascular scaffold polymers show higher efficacy and safety outcomes than bare metal stents.[29]

Furthermore, the patients in the OAT and SIAM III trials took an average of 8 and 12 days, respectively, to undergo PCI, which was considerably longer than that in the current study. Yazici et al. 30 compared the outcomes of early PCI < 3days (12 hr–3 days) to late PCI > 3 days, and they found that the MACE incidence at 1 year of follow up was insignificantly different between both groups (21.6% versus 11.1%, p=0.163). These results are consistent with the findings of the present study. Notably, most Yazicis' study patients had a high percentage of TIMI flow grade 3 before PCI procedure. Thus, this situation may explain the similar favourable clinical outcomes between both study groups. Yip et al. 31 examined the ideal time of PCI for STEMI patients. They concluded that PCI's performance on more than 4 days post MI was harmless and associated with a great success rate. Locally, the National Cardiovascular Database registry's annual report showed that the patients who underwent PCI during their hospitalisation had a better outcome regardless of any duration of even up to 1 year after the initial presentation. The reported death rate at 1 year for those who did not receive PCI was 21.5% versus 13.1% for those who had.[4] The current findings may provide some evidence for this observation. Major bleeding is a widespread complication after PCI as multiple antithrombotic drugs are commonly used.[32] In the present study, the incidence of major bleeding was insignificantly different between both study groups. Only one patient in the pharmaco-invasive group had major bleeding at 30 days, and one patient in the PCI during the index admission group developed major bleeding at 6 months post PCI. Scheller et al. 28 reported similar

findings. The rate of major bleeding in the early stenting was 9.8% versus 7.4% in the delayed PCI strategy (p=0.374). Extra caution must be exercised when interpreting this outcome because of the small number of events. The present study provided a positive indication for the STEMI patients' reperfusion who could not receive the early recommended reperfusion strategies due to multiple factors. This study has some limitations. Because of being single-centred and retrospective, it does not reflect the real world. Another limitation is its small number of patients.

CONCLUSION

The study suggested that PCI during index admission might have similar clinical outcomes to the pharmaco-invasive strategy.

REFERENCES

1. O'Gara, P.T., F.G. Kushner, D.D. Ascheim, D.E. Casey, M.K. Chung, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association

Task Force on Practice Guidelines. Journal of the American College of Cardiology, 2013. 61(4): e78-e140.

2. Nielsen, P.H., M. Maeng, M. Busk, L.S. Mortensen, S.D. Kristensen, et al. Primary angioplasty versus fibrinolysis in acute myocardial infarction: long-term follow-up in the Danish acute myocardial infarction 2 trial. Circulation, 2010. 121(13): 1484-1491.

3. Zheng, W., C.-M. Yu, J. Liu, W.-X. Xie, M. Wang, Y.-J. Zhang, et al.Patients with ST-segment elevation of myocardial infarction miss out on early reperfusion: when to undergo delayed revascularization. Journal of geriatric cardiology: JGC, 2017. 14(8): 524.

4. W.A Wan Ahmad, Annual Report of the NCVD ACS Registry, 2014 – 2015.Kuala Lumpur, Malaysia. National Cardiovascular Disease Database, 2017.

5. Ahmad, W.A.W., Annual Report of the NCVD-ACS Registry, 2011-2013. Kuala Lumpur, Malaysia. National Cardiovascular Disease Database, 2015.

6. Seong, A.C. and C.K.M. John, A review of coronary artery disease research in Malaysia. Med J Malaysia, 2016. 71: 43.

7. Malaysia, M.o.H., Clinical practice guidelines: management of acute ST segment elevation myocardial infarction, in Clinical Practice Guidelines (CPG) 2014: Secretariat : Putrajaya.

8. Antman, E.M., M. Hand, P.W. Armstrong, E.R. Bates, L.A. Green, et al.2007 Focused update of the ACC/AHA 2004 guidelines for the management of patients with ST-elevation myocardial infarction: a report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines: developed in collaboration with the Canadian Cardiovascular Society endorsed by the American Academy of Family Physicians: 2007 Writing Group to review new evidence and update the ACC/AHA 2004 guidelines for the management of patients with ST-elevation myocardial infarction, writing on behalf of the 2004 writing committee. Circulation, 2008. 117(2): 296-329.

9. Ellis, S.G., W.W. O'neill, E.R. Bates, J.A. Walton, E.G. Nabel, et al. Coronary angioplasty as primary therapy for acute myocardial infarction 6 to 48 hours after symptom onset: report of an initial experience.

Journal of the American College of Cardiology, 1989. 13(5): 1122-1126.

10. Nakabayashi, T., T. Hayashi, Y. Inoue, A. Ikeda, H. Morii, N. Naito, et al. Percutaneous transluminal coronary angioplasty performed 24-48 hours after the onset of acute myocardial infarction improves chronic-phase left ventricular regional wall motion. Angiology, 2000. 51(4): 281-288.

11. Bodí, V., E. Rumiz, P. Merlos, J. Nunez, M.P. López -Lereu, et al. One-week and 6-month cardiovascular magnetic resonance outcome of the pharmacoinvasive strategy and primary angioplasty for the reperfusion of ST-segment elevation myocardial infarction. Revista Española de Cardiología (English Edition), 2011. 64(2): 111-120.

12. Kip, K.E., K. Hollabaugh, O.C. Marroquin, and D.O. Williams, The problem with composite end points in cardiovascular studies: the story of major adverse cardiac events and percutaneous coronary intervention. Journal of the American College of Cardiology, 2008. 51(7): 701-707.

13. Hicks, K.A., H.J. Hung, K.W. Mahaffey, R. Mehran, S.E. Nissen, et al. Standardized definitions for cardiovascular and stroke end point events in clinical trials. Clinical Data Interchange Standards Consortium, 2014.

14. Sacco, R.L., S.E. Kasner, J.P. Broderick, L.R. Caplan, J. Connors, et al. An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association/ American Stroke Association. Stroke, 2013. 44(7): 2064-2089.

15. Gershlick, A.H., A. Stephens-Lloyd, S. Hughes, K.R. Abrams, S.E. Stevens, et al. Rescue angioplasty after failed thrombolytic therapy for acute myocardial infarction. New England Journal of Medicine, 2005. 353(26): 2758-2768.

16. Glossary, C., http://cdisc.org/ therapeutic, 2014.

17. Cutlip, D.E., S. Windecker, R. Mehran, A. Boam, D.J. Cohen, et al.Clinical end points in coronary stent trials: a case for standardized definitions. Circulation, 2007. 115(17): 2344-2351.

18. Pacing, C.C., Defibrillation and Resynchronization Therapy 2017(fifth edition).

19. Ibanez, B., S. James, S. Agewall, M.J. Antunes, C. Bucciarelli-Ducci, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). European heart journal, 2017. 39(2): 119-177.

20. Pinto, D.S., P.D. Frederick, A.K. Chakrabarti, A.J. Kirtane, E. Ullman, et al.Benefit of transferring ST-segment–elevation myocardial infarction patients for percutaneous coronary intervention compared with administration of onsite fibrinolytic declines as delays increase. Circulation, 2011: CIRCULATIONAHA. 111.018549.

21. Rashid, M.K., N. Guron, J. Bernick, G.A. Wells, M. Blondeau, et al. Safety and efficacy of a pharmacoinvasive strategy in ST-segment elevation myocardial infarction: a patient population study comparing a pharmacoinvasive strategy with a primary percutaneous coronary intervention strategy within a regional system. JACC: Cardiovascular Interventions, 2016. 9(19): 2014-2020.

22. D'souza, S.P., M.A. Mamas, D.G. Fraser, and F. Fath-Ordoubadi, Routine early coronary angioplasty versus ischaemia-guided angioplasty after thrombolysis in acute ST-elevation myocardial infarction: a meta-analysis. European heart journal, 2010. 32(8): 972-982.

23. Mehta, S., C.B. Granger, T.D. Henry, C.L. Grines, A. Lansky, et al. Reducing system delays in treatment of ST elevation myocardial infarction and confronting the challenges of late presentation in low and middle-income countries. Indian heart journal, 2017. 69 (Suppl 1): S1.

24. Wu, X., D. Yang, Y. Zhao, C. Lu, and Y. Wang, Effectiveness of percutaneous coronary intervention within 12 hours to 28 days of ST-elevation myocardial infarction in a real-world Chinese population. PloS one, 2013. 8(3): e58382.

25. Abbate, A., G.G. Biondi-Zoccai, D.L. Appleton, P. Erne, A.W. Schoenenberger, et al.Survival and cardiac remodeling benefits in patients undergoing late percutaneous coronary intervention of the infarct-related artery: evidence from a meta-analysis of randomized controlled trials. Journal of the American College of Cardiology, 2008. 51(9): 956-964.

26. Fan, Y., X. Bai, Y. Chen, G. Shen, Q. Lu, et al. Late Percutaneous Coronary Intervention Prevents Left Ventricular Remodeling and Improves Clinical Outcomes in Patients With ST‐Elevation Myocardial Infarction. Clinical cardiology, 2015. 38(2): 82-91.

27. Hochman, J.S., G.A. Lamas, C.E. Buller, V. Dzavik, H.R. Reynolds, et al. Coronary intervention for persistent occlusion after myocardial infarction. New England Journal of Medicine, 2006. 355(23): 2395-2407.

28. Scheller, B., B. Hennen, B. Hammer, J. Walle, C. Hofer, et al. Beneficial effects of immediate stenting after thrombolysis in acute myocardial infarction. Journal of the American College of Cardiology, 2003. 42(4): 634-641.

29. Neumann, F.-J., M. Sousa-Uva, A. Ahlsson, F. Alfonso, A.P. Banning, et al.2018 ESC/EACTS Guidelines on myocardial revascularization. European heart journal, 2018.

30. Yazici, G.E., M. Erden, G.A. Tacoy, B.B. Yavuz, S. Turkoglu, et al. The optimal time of elective percutaneous coronary intervention for stable patients after ST elevation myocardial infarction. Angiology, 2009. 60(1): 67-73.

31. Yip, H.-K., C.-J. Wu, C.-H. Yang, H.-W. Chang, S.-M. Chen, et al. Delayed Post-Myocardial Infarction Invasive Measures, Helpful or Harmful?: A Subgroup Analysis. Chest, 2004. 126(1): 38-46.

32. Boden, W.E., K. Eagle, and C.B. Granger, Reperfusion strategies in acute ST-segment elevation myocardial infarction: a comprehensive review of contemporary management options. Journal of the American College of Cardiology, 2007. 50(10): 917-929.