The Egyptian Journal of Hospital Medicine (October 2024) Vol. 97, Page 3932-3937

Routine Early Coronary Angioplasty versus Ischaemia-Guided Coronary Angioplasty after Successful Thrombolysis in Patients with Acute Anterior STEMI

Amir Wadie Andrawes
Department of Cardiovascular Medicine, Faculty of Medicine, Ain Shams University, Egypt
Corresponding author: Amir Wadie Andrawes, **Mobile:** (+2) 01008880048, **E-mail:** amir-wadie@hotmail.com

ABSTRACT

Background: The recommended reperfusion treatment for individuals suffering from acute ST-elevation myocardial infarction (STEMI) is primary percutaneous coronary intervention (PCI). However, few hospitals offer 24-hour personnel for PCI procedures, and many lack PCI facilities. If primary PCI cannot be completed in a timely manner, thrombolytic treatment is given to eligible patients because reperfusion is a crucial strategy to reduce mortality and severe cardiovascular events in STEMI care, and the benefit is time-dependent.

Objective: To compare routine early coronary angioplasty with ischaemia-guided angioplasty after successful thrombolysis in patients with acute anterior STEMI.

Patients and methods: The study enrolled 100 patients presented to the Emergency Department of Ain Shams University hospitals and the National Heart Institute with acute anterior STEMI divided into two groups: Group A received routine early coronary angioplasty within 24 hours after thrombolysis, while Group B received ischaemia-guided angioplasty based on stress myocardial perfusion imaging.

Results: Group A showed significantly lower rates of recurrent chest pain and need for urgent intervention compared to Group B, with no significant differences in heart failure, arrhythmias, major bleeding, or mortality during hospitalization. At three months, Group A had non-significantly lower rates of recurrent chest pain, need for urgent intervention, readmission, and mortality compared to Group B. The study highlights the importance of timely intervention, with Group A having an average time from thrombolytic initiation to angiography and subsequent PCI of 15 hours compared to 22 days in Group B. Group B achieved better Thrombolysis in Myocardial Infarction (TIMI) flow grades post-PCI, which may have offset the benefits of early intervention observed in Group A.

Conclusion: Routine early invasive strategy after successful thrombolysis is associated with improved clinical outcomes compared to ischaemia-guided management, emphasizing the importance of timely intervention.

Keywords: MACCE; PCI; Thrombolysis; Myocardial perfusion; TIMI flow; Clinical outcomes.

INTRODUCTION

The recommended reperfusion treatment for individuals with acute STEMI is primary PCI. Few hospitals, however, offer 24-hour personnel for PCI operations, and many lack PCI facilities. If primary PCI cannot be completed in a timely manner, eligible patients are given thrombolytic treatment because reperfusion is a crucial technique to reduce mortality and severe cardiovascular events in STEMI care, and the benefit is time-dependent [(1)].

Prior to discharge, it was customary to evaluate the patient's risk of further cardiac adverse events if they had undergone thrombolytic treatment and showed evidence of effective reperfusion. Rescue PCI is recommended for patients with failed reperfusion [(2)].

Left ventricular function and the degree and grade of myocardial ischaemia were the two most crucial factors utilized to assess both short-term and long-term risk after myocardial infarction [(3)]. With an IIa class of recommendation (level of evidence A), the ESC guidelines advise an early routine coronary angiography 3–24 hours following effective thrombolysis [(4)].

This study aimed to compare routine early coronary angioplasty in patients with acute anterior STEMI after successful thrombolysis versus ischaemia-guided coronary angioplasty regarding the major adverse cardiac events (death, non-fatal MI, recurrent ischaemia, heart failure and stroke).

PATIENTS AND METHODS

The study included 100 patients with acute anterior STEMI treated with streptokinase at Ain Shams University hospitals and National Heart Institute, and National Heart Institute between January 2013 and January 2015.

Patients were randomly placed into two groups: Group A received a routine invasive coronary angiography within 24 hours post-thrombolysis, while group B underwent an ischaemia-based strategy with stress myocardial perfusion imaging within 30 days followed by CA if residual ischaemia was detected.

Inclusion criteria: Patients with acute anterior STEMI who received successful thrombolytic therapy within 12 hours of chest pain onset.

Exclusion criteria: Non-anterior STEMI, contraindications to thrombolytic therapy, presentation after 12 hours of symptom onset, and failed thrombolysis requiring rescue PCI.

The study assessed various parameters, including cardiac risk factors, echocardiographic findings, and in-hospital outcomes, to compare the effectiveness of these strategies in managing STEMI. Key findings included:

Received: 03/06/2024
Accepted: 04/08/2024

- **Patient Assessment:** Detailed history, physical examination, ECG, and laboratory investigations were conducted for all patients.
- **Thrombolytic Therapy:** All patients received streptokinase within 12 hours of chest pain onset.
- **Echocardiography:** Evaluation of Lt. ventricular dimensions, volumes, ejection fraction, and regional wall motion anomalies.
- Coronary Angiography: Performed within 24 hours for Group A and within one month for Group B if residual ischaemia was detected by MPI.
- **Outcomes:** Monitored in-hospital complications such as heart failure, arrhythmias, bleeding, and mortality. Follow-up included major adverse cardiac and cerebrovascular events (MACCE) and echocardiographic examination after three months.

Ethical approval:

The Ethics Committee of Ain Shams University's Faculty of Medicine, Cardiology Department 9/2012, accepted this study, and all patients gave their written informed permission before being included in the study. The study adhered to the Helsinki Declaration throughout its execution.

Statistical analysis

On an IBM compatible computer, SPSS version 20.0 was used to tabulate and analyze the obtained data. Data Presentation: Continuous numerical data as mean and standard deviation (SD), categorical data as frequency and percentages. Comparisons: Unpaired t-test for numerical data, Pearson chi-squared or Fisher's exact test for categorical data. $P \leq 0.05$ and $P \leq 0.01$ were used to determine whether the results were significant or highly significant.

Risk Analysis

Relative risk calculation for adverse outcomes, cumulative incidence of MACCE, multivariate binary logistic regression for management strategy and MACCE incidence, multivariate linear regression for management strategy and ejection fraction at 3 months.

RESULTS

Both groups had similar age (mean 55 years) and sex distribution (Group A: 68% male, Group B: 64% male). No significant differences were found in the presence of risk factors like hypertension, diabetes mellitus, dyslipidemia, smoking, and family history of CAD between the groups.

Stress myocardial perfusion scans in Group B showed that 94.1% of patients had good viability, and 91.2% had peri-infarct ischaemia, guiding the decision for angioplasty (Figure 1).

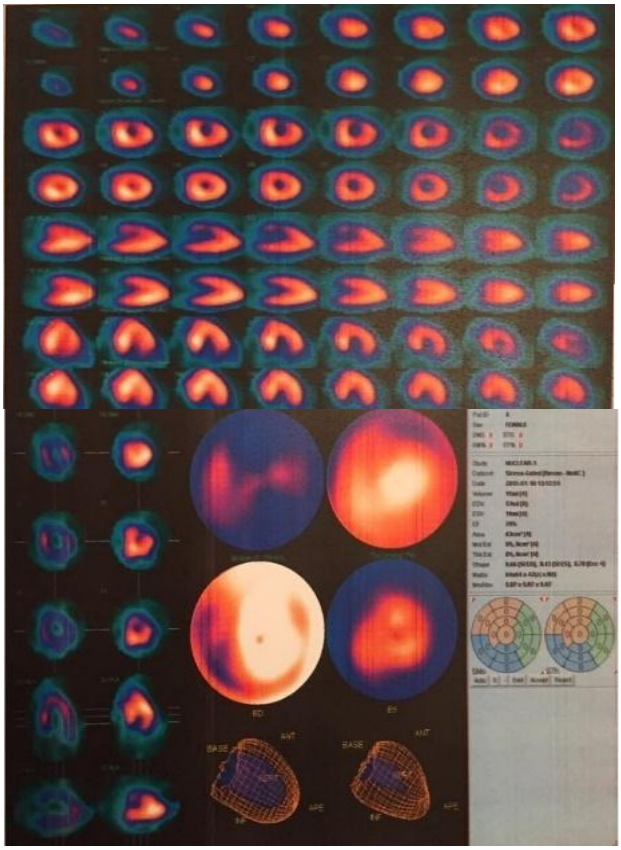

Figure (1): Nuclear study of patient No. 48 in group B showing reversible anterior ischaemia (LAD territory).

There weren't statistically significant differences between both groups regarding the site of the lesion in LAD, the number and of stents used in each patient, complications during procedure, associated significant lesions in the non-culprit vessels (Figure 2).

Figure (2): Case No. 3 in group A before and after stenting of the LAD.

The difference was statistically significant between both groups regarding the average time interval from fibrinolytic initiation to angiography and subsequent PCI (P<0.001), and the pre and post procedure TIMI-flow grade (p<0.05) (Figure 3).

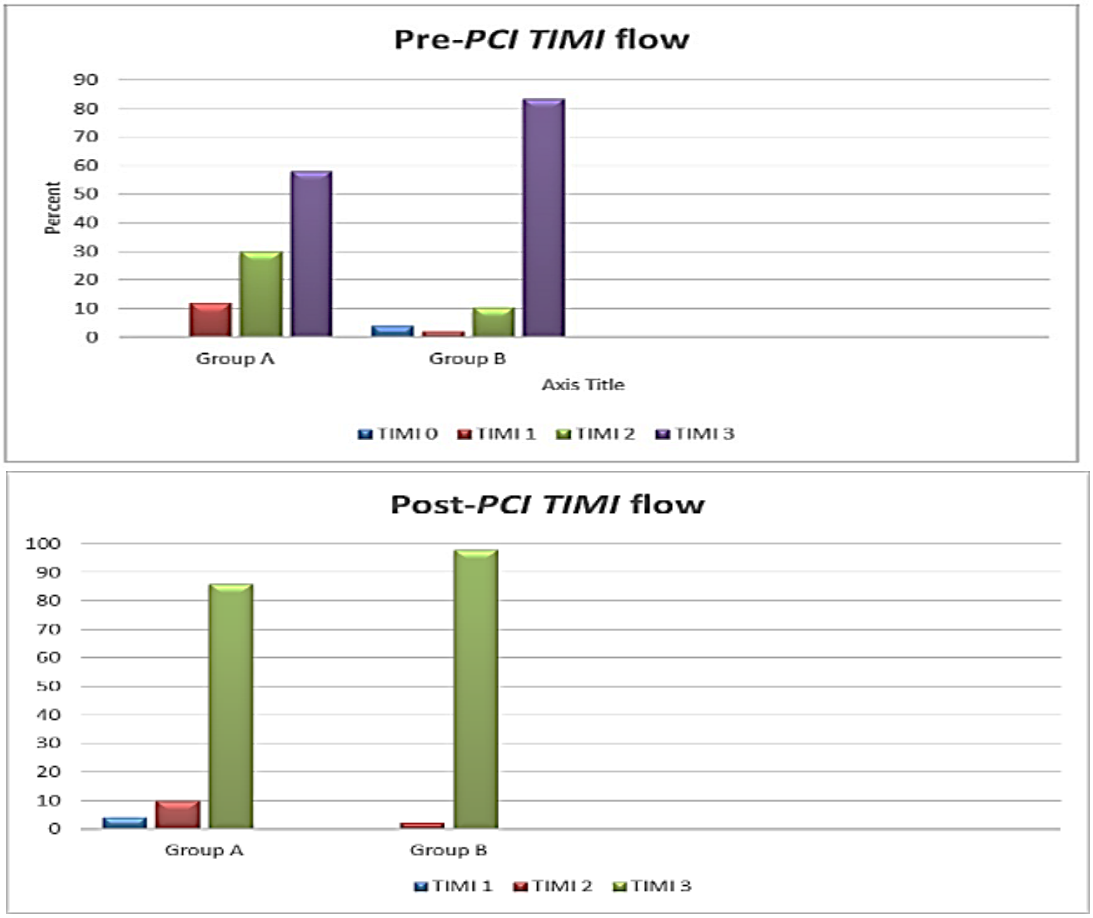

Figure (3): Normal TIMI grade 3 flow was achieved in 43 patients (86 %) in group A and in 47 patients (97.9 %) in group B.

Group A had significantly lower rates of recurrent chest pain and need for urgent re-intervention. No significant differences were found in heart failure, arrhythmias, major or minimal bleeding, in-hospital mortality, or stroke between the groups. Group A had a shorter hospital stay (Table 1).

Table (1): In-hospital outcome measures in both study groups

Variable	Group A (n=50)	Group B (n=50)	p-value
• Recurrent chest pain	1 (2.0%)	9 (18.0%)	**0.008¶** (HS)
• Urgent (re)intervention	1 (2.0%)	13 (26.0%)	**<0.001¶**(HS)
• Heart failure	2 (4.0%)	4 (8.0%)	0.678§ (NS)
• Arrhythmia Nil Frequent PVCs NSVT VT CHB	 48 (96.0%) 1 (2.0%) 1 (2.0%) 0 (0%) 0 (0%)	 45 (90.0%) 2 (4.0%) 1 (2.0%) 1 (2.0%) 1 (2.0%)	 0.710§ (NS)
• Stroke	0 (0%)	0 (0%)	-
• CIN	1 (2.0%)	0 (0%)	1.000§ (NS)
• Major bleeding	1 (2.0%)	0 (0%)	1.000§ (NS)
• Minimal bleeding	5 (10.0%)	1 (2.0%)	0.204§ (NS)
• In-hospital mortality	0 (0%)	1 (2.0%)	1.000§ (NS)
• Hospital length of stay (days)	3 (3 – 3)	4 (3 – 5)	**<0.0001¥** (HS)

Data are presented as number (%) or median (interquartile range). ¶Pearson chi-squared test, §Fisher's exact test, §Mann-Whitney test.
n= Number of patients in the group, P= Probability of chance (Significance), NS= Non-significant, HS= Highly significant.

Overall, the routine invasive strategy resulted in better in-hospital outcomes and shorter hospital stays compared to the ischaemia-based strategy. At the 3-month follow-up, patients who received early mechanical revascularization showed lower, but not statistically significant, rates of recurrent chest pain, need for urgent intervention, readmission, and mortality compared to those who did not receive early angioplasty. Both groups had similar rates of heart failure (4%). No cases of arrhythmias or stroke were reported in either group (Table 2).

Table (2): Outcome measures at 3-months in both study groups

Variable	Group A (n=50)	Group B (n=49)	p-value
Recurrent chest pain within 3 months	0 (0%)	3 (6.2%)	0.118¶(NS)
Urgent intervention within 3 months	0 (0%)	3 (6.2%)	0.118¶(NS)
Heart failure within 3 months	2 (4.0%)	2 (4.2%)	1.000¶ (NS)
Arrhythmia within 3 months	0 (0%)	0 (0%)	-
Stroke within 3 months	0 (0%)	0 (0%)	-
Three-months mortality	0 (0%)	1(2.04%)	0.495¶(NS)
Readmission within 3 months	1 (2.0%)	3 (6.2%)	0.362¶ (NS)

Data are presented as number (%), ¶Fisher's exact test**,** n= Number of patients in the group. P= Probability of chance (Significance), NS= Non-significant.

During hospitalization: Group A had significantly fewer MACCE. At 3 months: No significant difference in MACCE was found. Cumulative incidence: Group A had significantly fewer MACCE by the end of follow-up (Table 3).

Table (3): Incidence of MACCE during hospitalization and at 3-months and the cumulative incidence of MACCE in both study groups.

Variable	Group A (n=50)	Group B (n=50)	p-value
MACCE during hospitalization	3/50 (6.0%)	13/50 (26.0%)	**0.012¶** (S)
MACCE at 3-months	2/50 (4.0%)	6/49 (12.2%)	0.160¶(NS)
Cumulative incidence of MACCE by end of follow-up	3/50 (6%)	17/50 (34%)	**<0.001¶**(HS)

Data are presented as ratio (valid %), ¶ Fisher's exact test, n= Number of patients in the group. P= Probability of chance (Significance), NS= Non-significant, S=Significant, HS=Highly significant.

Risk Analysis

The ischaemia-based strategy had a higher relative risk for MACCE during hospitalization and cumulative incidence but not at 3 months (Table 4).

Table (4): Risk analysis for the occurrence of MACCE during hospitalization and at 3-months and the cumulative incidence of MACCE.

Index	MACCE during hospitalization	MACCE at 3-months	Cumulative incidence of MACCE
Relative risk (RR)*	4.33	3.1	5.67
95% CI for RR	1.31 to 14.28	0.65 to 14.43	1.77 to 18.13
z statistic	2.410	1.414	2.923
p-value¶	**0.016** (S)	0.157 (NS)	**0.004** (HS)
Number needed to harm (NNH)	5.0 (Harm)	12.13 (Harm)	3.57
95% CI for NNH	16.20 (Harm) to 2.96 (Harm)	5.30 (Harm) to 42.20 (Benefit)	2.34 to 7.51

*Ischaemia-based strategy is referenced to routine early revascularization strategy, ¶Z-test. P= Probability of chance (Significance). NS= Non-significant. HS=Highly significant.

Multivariate Analysis:

The ischaemia-based strategy and time to thrombolytic therapy were independent predictors of MACCE during hospitalization (Figure 4).

Time to thrombolytic therapy was the only independent predictor of MACCE at 3 months (Figure 5). (Figure 3).

No significant predictors for EF at 3 months were identified.

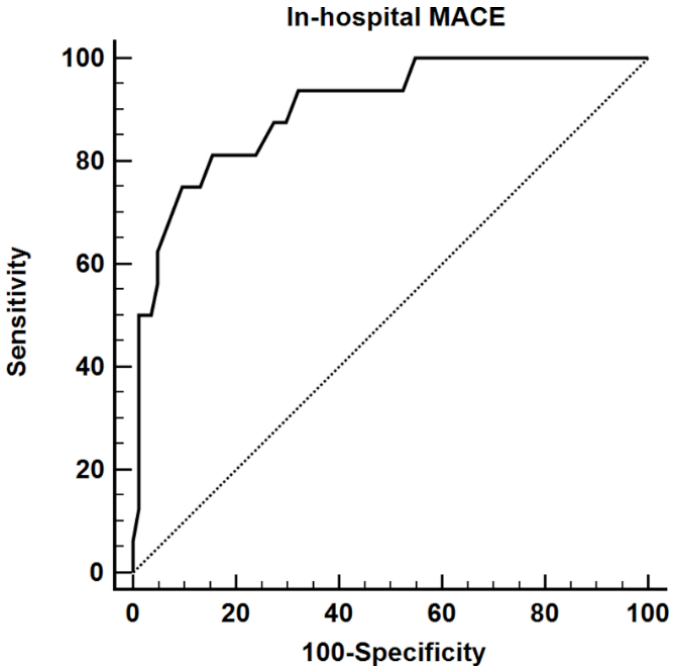

Figure (4): ROC curve derived from the multivariate binary logistic regression model for prediction of MACCE during hospitalization.

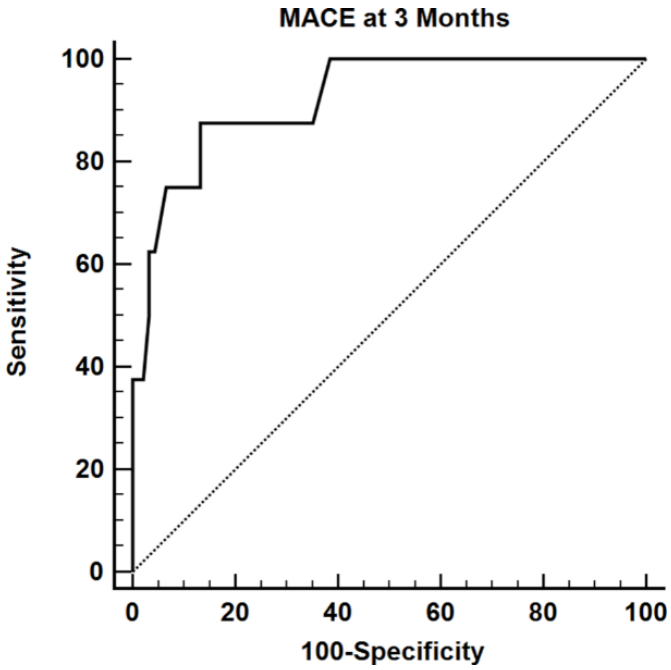

Figure (5): ROC curve derived from the multivariate binary logistic regression model for prediction of MACCE at 3-months.

DISCUSSION

Acute STEMI is caused by the breakdown of a coronary artery plaque, which results in thrombus development and arterial obstruction [(5)]. Timely reperfusion treatment, whether pharmacological or catheter-based, is critical for restoring coronary flow, limiting myocardial damage, and improving outcomes [(6)].

Primary PCI is the recommended reperfusion technique because it is more successful in lowering mortality than fibrinolytic treatment[(7)]. However, many hospitals lack PCI facilities, making thrombolytic therapy a necessary alternative when timely PCI is not feasible[(4)].

After thrombolytic therapy, patients are assessed for future cardiac risks. Those with failed reperfusion require rescue PCI[(2)]. The two most significant indicators utilized to determine short-term and long-term risk after MI were LV function and the amount and severity of myocardial ischaemia [(4)].

Earlier studies showed limited benefits of routine PCI post-thrombolysis. However, with advancements in stents and pharmacotherapy, recent studies support early routine angioplasty for better outcomes[(8)].

For patients who have successfully undergone thrombolysis, current guidelines advocate early routine coronary angiography (3-24 hours post-thrombolysis) [(9)].

Our study showed that routine early PCI significantly reduced recurrent ischaemia and urgent re-intervention compared to ischaemia-guided strategies. Studies like TRANSFER-AMI and GRACIA-1 support early PCI for better outcomes [(10,11)]. Early PCI does not significantly increase bleeding risks compared to ischaemia-guided management [(12)].

We concluded that routine early PCI within 24 hours post-thrombolysis is more effective than a watchful waiting strategy, reducing the incidence of adverse cardiac events without significantly increasing bleeding risks.

A meta-analysis of five fibrinolytic studies found that patients with TIMI grade 3 flow had considerably improved LV function and clinical outcomes than those with lower TIMI grades. TIMI grade 3 flow was the best predictor of survival [(13)].

In the current study Group A: 86% achieved TIMI grade 3 flow, 10% achieved TIMI grade 2, and 4% achieved TIMI grade 1. Group B: 97.9% achieved TIMI grade 3 flow, 2.1% achieved TIMI grade 2.

The better TIMI flow in Group B might have offset the benefits of early intervention, resulting in no significant differences in ventricular function, mortality, or heart failure between the groups. The longer time to PCI in Group B (22 days) compared to Group A (15 hours) might explain the differences in TIMI flow.

Group A had a shorter hospital stay, likely due to rapid risk stratification from early angiography.

Early revascularization showed better outcomes compared to ischaemia-guided strategy. Time between symptom onset to thrombolytic therapy was the only independent predictor for MACCE at 3 months, emphasizing the "Time is muscle" hypothesis. STREAM Trial showed that early fibrinolysis followed by early PCI showed similar outcomes to primary PCI, highlighting the significance of timely reperfusion [(14)].

A meta-analysis of recent studies revealed that regular early PCI following fibrinolysis has much

lower mortality and reinfarction rates than a more cautious ischaemia-guided strategy [(15)].

Study Limitations: Small sample size, short follow-up, use of streptokinase instead of tPA, and reliance on SPECT imaging. TIMI flow grade's subjective nature and the need for more objective measures.

Overall, early routine PCI within 24 hours after successful thrombolysis is beneficial, but achieving optimal TIMI flow remains crucial for better outcomes.

CONCLUSION

According to the findings of this study, which included 100 patients presenting by anterior STEMI treated with streptokinase to Ain Shams University hospitals and National Heart Institute in a selected period, we concluded that the best management for acute STEMI after thrombolytic therapy is early routine PCI. This method minimizes the frequency of unfavorable coronary events, improves LV outcomes, avoids re-occlusion, expedites risk classification, and decreases hospitalization. Time between symptom onset to thrombolytic therapy was the only independent predictor for MACCE during hospitalization and at 3 months.

No funding.

No conflict of interest.

REFERENCES

1. **Michels K, Yusuf S (1995):** Does PTCA in acute myocardial infarction affect mortality and reinfarction rates? A quantitative overview (meta-analysis) of the randomized clinical trials. Circulation, 91:476-485.
2. **Borgia F, Goodman S, Halvorsen S (2010):** Early routine percutaneous coronary intervention after fibrinolysis vs. standard therapy in ST-segment elevation myocardial infarction: a meta-analysis. Eur Heart J., 31: 2156-2169.
3. **Kushner F, Hand M, Smith S *et al.* (2009):** 2009 Focused Updates: ACC/AHA Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction (Updating the 2004 Guideline and 2007 Focused Update) and ACC/AHA/SCAI Guidelines on Percutaneous Coronary Intervention (Updating the 2005 Guideline and 2007 Focused Update): A Report of the American College of Cardiology. Circulation, 120: 2271-2306.
4. **Van de Werf F, Bax J, Betriu A *et al.* (2008):** Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation: the Task Force on the Management of ST- Segment Elevation Acute Myocardial Infarction of the European Society of Cardiology. Eur Heart J., 29:2909-2945.
5. **Boersma E, Primary Coronary Angioplasty vs. Thrombolysis Group (2006):** Does time matter? A pooled analysis of randomized clinical trials comparing primary percutaneous coronary intervention and in-hospital fibrinolysis in acute myocardial infarction patients. Eur Heart J., 2006; 27(7):779–788.
6. **Antman E, Hand M, Armstrong P *et al.* (2008):** 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, 117: 296-329.
7. **Eagle K, Nallamothu B, Mehta R *et al.* (2008):** Trends in acute reperfusion therapy for ST-segment elevation myocardial infarction from 1999 to 2006: we are getting better but we have got a long way to go. Eur Heart J., 29: 609-617.
8. **Widimsky P, Groch L, Widimský P *et al.* (2000):** Multicentre randomized trial comparing transport to primary angioplasty vs immediate thrombolysis vs combined strategy for patients with acute myocardial infarction presenting to a community hospital without a catheterization laboratory. The PRAGUE study. Eur Heart J., 21:823-831.
9. **Bates E, Jacobs A (2013):** Time to treatment in patients with STEMI. N Engl J Med., 369(10):889–892.
10. **Cantor W, Fitchett D, Borgundvaag B *et al.* (2009):** Routine early angioplasty after fibrinolysis for acute myocardial infarction. N Engl J Med., 360(26):2705–2718.
11. **Fernandez-Aviles F, Alonso J, Castro-Beiras A *et al.* (2004):** Routine invasive strategy within 24 hours of thrombolysis versus ischaemia-guided conservative approach for acute myocardial infarction with ST-segment elevation (GRACIA-1): a randomized controlled trial. Lancet; 364:1045-1053.
12. **Di Mario C, Dudek D, Piscione F *et al.* (2008):** Immediate angioplasty versus standard therapy with rescue angioplasty after thrombolysis in the Combined Abciximab REteplase Stent Study in Acute Myocardial Infarction (CARESS-in-AMI): an open, prospective, randomised, multicentre trial. Lancet, 371: 559–68.
13. **Kloner R, Rezkalla S (2002):** No-reflow phenomenon. Circulation, 105:656-662.
14. **Armstrong P, Gershlick A, Goldstein P *et al.* (2013):** Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. N Engl J Med., 368(15): 1379–1387.
15. **Wijeysundera H, You J, Nallamothu B *et al.* (2008):** An early invasive strategy versus ischaemia-guided management after fibrinolytic therapy for ST-segment elevation myocardial infarction: a meta-analysis of contemporary randomized controlled trials. Am Heart J., 156: 564-572.