https://doi.org/10.29309/TPMJ/2026.33.02.9954 www.theprofesional.com

ORIGINAL ARTICLE

The relationship of patent infarct-related artery with time to thrombolysis in patients with ST-Segment Elevation Myocardial Infarction.

Zia Ullah Khan[1], Rukhshanda Afsar[2], Mohammad Imran Khan[3], Saad Shams[4], Aftab Ahmed[5], Matiullah Khan[6]

ABSTRACT… Objective: To find out the spectrum of TIMI flow in the infarct-related artery amongst the patients who are thrombolysed in different time zones from pain to thrombolysis. **Study Design:** Prospective, Comparative study. **Setting:** Department of Cardiology, Ayub Medical Teaching Institute. **Period:** August 2022 to January 2023. **Methods:** A total of 122 consecutive patients with their first STEMI thrombolysed within 12 hours of pain were included in the study. Data on demographics, medical history, and physical examination findings were collected using a specially designed proforma. Patients were assessed for the success or failure of thrombolysis according to our prespecified criteria. All patients underwent coronary angiography as per our institutional protocol. TIMI flow in the infarct-related artery was documented. Results were analyzed using SPSS statistical software version 21.0. **Results:** 77% were male, 43% were hypertensives, one-third of patients were smokers, and 26% were diabetic. Anterior STEMI was seen in 38% of patients, while 57% had inferior STEMI. 46% of patients were thrombolysed within 3 hours, 33% within 3 to 6 hours, 10% between 6 to 9 hours, and 11% between 9 to 12 hours. The rate of TIMI III flow was the highest (89%) in patients thrombolysed within 3 hours, 85% in patients thrombolysed between 3 to 6 hours, 83% in patients thrombolysed between 6 to 9 hours, and 78% in patients thrombolysed between 9 to 12 hours. There were significantly more patients with ≥70% resolution of ST-segment elevation amongst those thrombolysed within 3 hours since the onset of pain, compared to those thrombolysed after 9 hours since the onset of pain. **Conclusion:** The highest frequency of TIMI III flow was seen when patients were thrombolysed within 3 hours. The rate of TIMI III flow decreased as the time to thrombolysis increased from less than 3 hours to 12 hours. However, the differences in TIMI III flow were not statistically significant. There was a statistically significant relationship between the degree of ST-segment resolution and time since pain to thrombolysis.

Key words: Infarct-related Artery, STEMI, Thrombolysis, TIMI III Flow, Time Since Pain-to-thrombolysis.

Article Citation: Khan Z, Afsar R, Khan MI, Shams S, Ahmed A, Khan M. The relationship of patent infarct-related artery with time to thrombolysis in patients with ST-Segment Elevation Myocardial Infarction. Professional Med J 2026; 33(02):231-236. https://doi.org/10.29309/TPMJ/2026.33.02.9954

INTRODUCTION

The primary goal of thrombolytic therapy is rapid, complete, and sustained restoration of TIMI III flow in the occluded infarct-related artery. Studies have shown that early thrombolysis results in smaller infarct size after STEMI.[1] Occluded infarct-related artery at 90 minutes was associated with 8.9% mortality at 30 days compared to only 4% mortality with normal TIMI III (Thrombolysis in Myocardial Infarction grade III) flow.[2]

Streptokinase is a leading Thrombolytic agent used for thrombolysis in STEMI patients across Pakistan. There is some evidence that non-fibrin specific agents may lose their fibrinolytic efficacy as the time from the onset of symptoms to the start of treatment increases.[3] An angiographic study to assess the efficacy of Streptokinase has never been done in our institution. For emerging centers that are in their developing phases and who cannot offer primary PCI to all patients, such a study would be useful to select patients for primary PCI rather than thrombolysis if a certain threshold of time since pain is established, beyond which Streptokinase would start losing its ability to establish TIMI III flow. We therefore wanted to find out how the hours since pain to thrombolysis influence the rate of TIMI III flow in patients with STEMI who are eligible for and treated with timely thrombolysis.

METHODS

122 consecutive patients presenting with STEMI were prospectively included in the study between August 2022 and January 2023.

1. MBBS, Post Graduate Fellow in Cardiology, Ayub Medical Teaching Institute.
2. MBBS, Post Graduate Fellow in Cardiology, Ayub Medical Teaching Institute.
3. MBBS, FCPS, MRCP (UK), MRCP (Ire), MMSc (Ire), CHPE (Pak), Chairman Medicine, Ayub Medical Teaching Institute.
4. MBBS, Post Graduate Fellow in Cardiology, Ayub Medical Teaching Institute.
5. MBBS, Post Graduate Fellow in Cardiology, Ayub Medical Teaching Institute.
6. MBBS, FCPS, Associate Professor Cardiology, Ayub Medical Teaching Institute.
Correspondence Address:
Dr. Mohammad Imran Khan
Department of Medicine
Ayub Medical Teaching Institute.
sidharat1@gmail.com

Article received on:
07/07/2025
Date of revision:
23/08/2025
Accepted for publication:
15/09/2025

The study was conducted in the Department of Cardiology Ayub Medical Teaching Institute, Abbottabad. Informed consent was taken from all patients. Data was collected using a specially designed proforma, which included demographics like age, gender, time from the onset of pain, contraindications to thrombolysis, co-morbidities, and complete physical examination findings. Categorical values were summarized as percentages, and numerical values were summarized as means. Data was analyzed using SPSS statistical software version 21.0. The chi-square test was used to test the significance of the difference in TIMI flow across different time zones from pain to thrombolysis. A p-value of 0.05 was considered significant. The study was approved by the institutional ethical review committee (RC-2022/EA-01/116).

Inclusion Criteria

1) Age 20 to 75 years
2) Patients with first STEMI as per the operational definition
3) Those who received thrombolytic therapy within 12 hours of the onset of chest pain.

Exclusion Criteria

1) All patients who did not receive thrombolytic therapy.
2) Patients who did not consent for the study.
3) All patients who did not undergo angiographic studies.
4) Patients who died before thrombolytic therapy and/or angiography
5) Patients with prior CABG or STEMI
6) Patients with Cardiogenic shock
7) Patients with valvular heart diseases
8) Patients with left bundle branch block.

All patients with STEMI presenting within 12 hours of the onset of chest pain and fulfilling our inclusion criteria who consented to the study were included. Patients received Streptokinase uninterrupted within one hour. Anterior STEMI was defined as ST elevation of ≥0.2 mV at the J point in V1, V2, or more anterior leads. Lateral STEMI was defined as ≥0.1 mV ST elevation in AVL and Lead I. Inferior STEMI was defined as ≥0.1 mV ST elevation in Leads II, III, AVF. Successful thrombolysis or otherwise was assessed based on pain relief and ECG criteria 90 minutes after finishing Streptokinase infusion by an experienced postgraduate cardiology fellow as follows:

1. Categorical verbal rating scale as described by T Bendinger and N Plunkett (Measurement in pain medicine. BJA Education, Vol16. Issue 9, Sept 2016. Pages 310-315.) was used to assess the severity and relief of pain. The magnitude of pain was categorized as none, mild, moderate, or severe.

Significant pain relief was defined as follows:

i. Significant pain relief in patients with severe pain was defined as no to mild residual pain.
ii. Significant pain relief in patients with moderate pain was defined as no to mild residual pain.
iii. Significant pain relief in patients with mild pain was defined as no residual pain.

2. Successful thrombolysis was defined as ≥70% resolution in ST segment measured in mm, at 90 minutes after stopping Streptokinase infusion in the lead showing the highest ST elevation and significant pain relief.
3. Unsuccessful thrombolysis was defined as persistent pain and/or <70% resolution in ST segment measured in mm, at 90 minutes after stopping Streptokinase infusion in the lead showing the highest ST segment elevation.
4. Patent-Infarct-Related Artery was defined as TIMI III flow in the artery most likely to be the culprit artery.

Streptokinase was administered at a dose of 1.5 MU over 1 hour. All patients received a loading dose of Aspirin 300 mg, Clopidogrel 300mg, and high-dose Statins. Baseline pulse rate, blood pressure, and oxygen saturation by pulse oximetry were recorded. The vertical height of ST segment elevation in the lead with the maximum ST segment elevation, before and at 90 minutes after finishing thrombolysis, was measured in mm, 80 ms from the J point. ECG interpretation of successful or failed thrombolysis was performed by a single observer who was not involved in performing angiographies of these patients. All patients underwent coronary angiography by experienced operators. All angiographies were analyzed by a single expert who classified coronary flow as per the TIMI

criteria. According to our protocol, angiography was performed in patients who underwent successful thrombolysis within 72 hours after discharge. The patients who did not fulfil the criteria of successful thrombolysis underwent angiography as inpatients.

RESULTS

Table 1 displays the baseline characteristics of the patient population and information about the types of Myocardial Infarction and a summary of angiographic findings. The majority of the patients were males, predominantly between the ages of 41 years to 70. 43% of patients had hypertension, 35% were smokers, and about 26% of the patients were diagnosed with diabetes. Of the total population, 47 (38%) patients had Anterior STEMI and 70 (57%) patients had Inferior STEMI. All patients underwent angiography. 40% of patients had single-vessel coronary artery disease, 30% had double disease, while 24% had multi-vessel coronary artery disease. A small number had left main disease and a nonobstructive recanalized artery on angiography.

Overall, 46% of patients were thrombolysed within 3 hours, and another 33% were thrombolysed within 3 to 6 hours. The rest of the patients were thrombolysed within 6 to 9 hours and 9 to 12 hours. (Table-II)

All patients were thrombolysed within 12 hours. There was a significantly higher percentage of patients achieving ≥70% ST-segment resolution in patients thrombolysed within 3 hours compared to those who were thrombolysed between 9 to 12 hours. There was a statistically significant relationship between the time since pain to thrombolysis and the degree of ST-segment resolution ($p = 0.0075$).

Table-IV shows the results of a logistic regression analysis of ≥70% ST-segment resolution and time since pain to thrombolysis with < 3 hours as a reference group.

The 3 to 6 hour and 6 to 9 hour groups did not differ significantly from the less than 3 hour group in the odds to achieving ≥70% ST-Segment resolution. Patients thrombolysed between 9 to 12 hours had 88% less odds of achieving ≥70% ST-Segment resolution than those thrombolysed less than 3 hours since pain.(OR=0.12, P=0.002)

TABLE-I

Baseline characteristics and summary of Angiographic findings.

Serial No.	Parameter	Number	Percentage
1	Age 30 to 40 years	1	0.8
2	Age 41 to 50 years	29	24
3	Age 51 to 60 years	40	33
4	Age 61 to 70 years	41	33
5	Age 71 to 80 years	12	10
6	Males	94	77
7	Diabetes Mellitus	32	26
8	Hypertension	53	43
9	Smokers	43	35
10	Anterior Wall MI	48	39
11	Inferior Wall MI	70	57
12	High Lateral Wall MI	4	3
13	Postero-lateral Wall MI	1	0.8
14	Single Vessel disease	49	40
15	Double Vessel disease	37	30
16	Multi-Vessel Disease	29	24
17	Left Main Disease	2	1.6
18	Recanalized non-obstructive plaque	3	2.4

TABLE-II

Summary of Time since pain to thrombolysis.

Pain To Needle Time	Number of Patients	Percentage
< 3 Hours	56	46
3 to 6 Hours	40	33
6 to 9 Hours	13	10
9 to 12	14	11

Over all 86% of patients had TIMI III flow in their infarct-related arteries. 10% had TIMI 0 flow.

TABLE-III

ST-Segment resolution among time to thrombolysis groups

Time Since Pain To Thrombolysis	Number of Patients	>70% St-Segment Resolution	<70% St-Segment Resolution
< 3 HOURS	56	50	6
3 TO 6 HOURS	40	33	7
6 TO 9 HOURS	13	12	1
9 TO 12 HOURS	14	7	7
Total	123	102	21

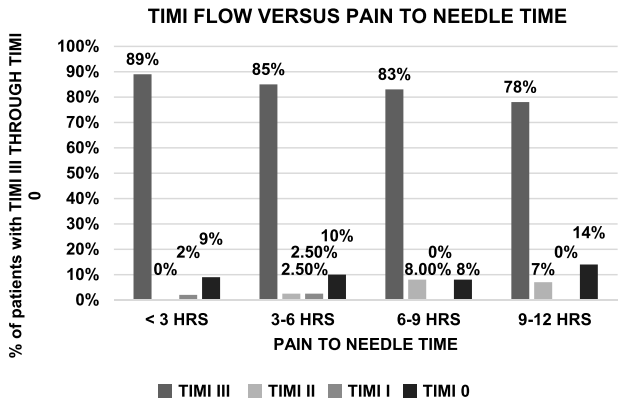
TABLE-IV

Time groups compared to < 3 hour group.

Time Group vs < 3 h	Odds Ratio	95% CI	P-Value
3-6 hours	0.50	0.16-1.56	0.23
6-9 hours	1.44	0.16-13.1	0.75
9-12 hours	0.12	0.03-0.46	0.002

FIGURE-1

Variable TIMI III flow in patients with different times to thrombolysis since pain.

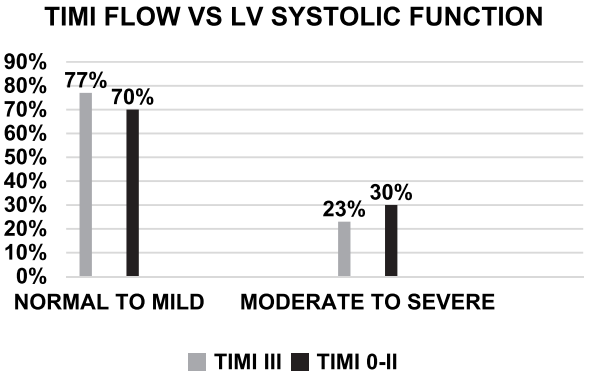


The differences in TIMI flow grades across the pain-to-needle categories were not statistically significant (p=0.79). Similarly, there was no significant difference among the pain-to-needle time groups in the proportion of patients achieving TIMI III flow (p=0.74). However, the power to detect any significant differences was low since the later pain-to-needle groups had only 13 and 14 patients.

There were equal proportions of patients with normal to mildly impaired left ventricles in patients with TIMI III flow and TIMI II to 0. There were equal proportions of patients with moderate to severely impaired Left ventricles in patients with TIMI III and TIMI II to 0 flows in their infarct related arteries. (Figure-2).

FIGURE-2

TIMI flow and Left Ventricular Function



DISCUSSION

Since 1994 when Schroeder et al showed in their retrospective analysis of ISAM study, more than 70% resolution of ST segment in post thrombolytic ECG has been considered a sign of good short and long term prognosis.[4] Around the same time other researchers[5] correlated the resolution of ST segment with the presence of TIMI III flow in infarct related arteries.

Our study adds to the existing body of literature by showing that the rate of TIMI III flow declines with time. There was a nonsignificant trend of declining rate of TIMI III flow from 89% to 78% as the time since pain to thrombolysis increased from less than 3 hours to 12 hours. When the patients were categorized according to hours since pain to thrombolysis, from less than 3 hours through 3-6 hours, 6-9 hours, and 9-12 hours, the percentage of patients achieving ≥70% decreased significantly.

In a study by P.Gabriel Steg et al, the 90-minute patency of the infarct-related artery reduced from 81.7% when Streptokinase was given in less than three hours compared to 53.6% when Streptokinase was given after 3 hours.[3] In a similar study, U Zeymer et al studied TIMI flow in patients treated with either fibrin-specific or non-fibrin-specific thrombolytic agents within 3 hours or beyond 3 hours of symptom onset. It was observed that front-loaded Alteplase and Reteplase were equally effective within 3 hours

and beyond 3 hours. But the ability to achieve TIMI III flow at 90 minutes beyond 3 hours was reduced significantly for Streptokinase, Urokinase, and Anisoylated plasminogen streptokinase activator complex.[6] This difference in the thrombolytic ability to achieve TIMI III flow at 90 minutes is reflected also in ultimate sizes of the infarcts[7] and also in mortality differences between Fibrin specific and non-fibrin specific agents.[8] Previous research has also shown the importance of TIMI rather than just Infarct related artery patency, with higher ejection fractions in patients with not only patent infarct related arteries but also effective (TIMI III) compared to those with patent arteries but ineffective (TIMI II or less) flow. This difference was seen in patients with similar times from symptom onset to thrombolysis.[9]

Streptokinase is a bacterial protein that combines with Plasminogen to generate plasmin that has proteolytic activity.[10] The trial that comprehensively proved its efficacy after its intravenous use for ST-segment elevation Myocardial infarction was the GISSI[11] published in the Lancet. This trial also showed the declining efficacy of Streptokinase as the time from pain to Thrombolysis increased, with the highly significant 23% mortality reduction when patients were treated within 3 hours and falling to a nonsignificant benefit when patients were treated after 6 hours.

Our study is consistent with the results of the previous trials that the efficacy of Streptokinase in achieving TIMI III flow reduces in a time-dependent fashion, with the highest likelihood of achieving TIMI III flow when the patients are treated within 3 hours of pain and the least likelihood of TIMI III flow when patients are treated after 9 to 12 hours. ST-segment resolution dropped in a time-dependent fashion as the time to thrombolysis since pain increased. The highest proportion of ≥70% appeared amongst those thrombolysed within 3 hours and declined thereafter. This finding is also consistent with the previous studies of ST-segment resolution analysis, both in the settings of Thrombolysis and Mechanical reperfusion.[12,13]

We were not able to show any association of time to treatment with left ventricular function nor was there any association with achievement of TIMI III flow or otherwise with better left ventricular systolic function or otherwise. It is possible, as shown in previous studies of acute vs convalescent left ventricular function studies, that the left ventricular function does not improve acutely due to the fact that it might be stunned and recovers only over a passage of time.[14,15]

CONCLUSION

We conclude that the highest likelihood of achieving TIMI III flow post-streptokinase is when the lytic agent is administered within 3 hours and up to 9 hours since the onset of pain. After 9 hours, the likelihood of achieving TIMI III flow reduces to 78%. The likelihood of achieving TIMI III was 89% when thrombolysis was administered within 3 hours, reducing to 85% and 83% respectively, with thrombolysis administered between 3 to 6 hours and 6 to 9 hours. There was therefore a trend towards reduction in TIMI flow in the infarct-related artery, as the time to thrombolysis window increases. This reduction in TIMI III flow did not reach statistical significance. A larger study is required to confirm or otherwise the efficacy of Streptokinase to achieve TIMI III flow in patients who are thrombolysed after 9 hours of the onset of pain.

LIMITATIONS

Patients in the 6 to 9 hours and 9 to 12 hours categories were small, which reduced the power of the study to detect any significant differences in the efficacy of Streptokinase to achieve TIMI III flow across all time zones.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

SOURCE OF FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

REFERENCES

1. Simoons ML, Serruys PW, van den Brand M, Verheugt FW, Krauss XH, Remme WJ, et al. **Early thrombolysis in acute myocardial infarction: limitation of infarct size and improved survival.** Journal of the American College of Cardiology. 1986 Apr 1; 7(4):717-28.

2. GUSTO Angiographic Investigators. **The effects of Tissue Plasminogen Activator, Streptokinase or both on coronary artery patency, ventricular function and survival after acute myocardial infarction.** NEJM Med. 1993; 329:1615-22.
3. Steg PG, Laperche T, Golmard JL, Juliard JM, Benamer H, Himbert D, et al. PERM Study Group 1. **Efficacy of streptokinase, but not tissue-type plasminogen activator, in achieving 90-minute patency after thrombolysis for acute myocardial infarction decreases with time to treatment.** Journal of the American College of Cardiology. 1998 Mar 15; 31(4):776-9.
4. Schröder R, Dissmann R, Brüggemann T, Wegscheider K, Linderer T, Tebbe U, et al. **Extent of early ST segment elevation resolution: A simple but strong predictor of outcome in patients with acute myocardial infarction.** Journal of the American College of Cardiology. 1994 Aug 1; 24(2):384-91.
5. Shah PK, Cercek B, Lew AS, Ganz W. **Angiographic validation of bedside markers of reperfusion.** J Am Coll Cardiol. 1993; 21:55-61.
6. U Zeymer, U Tebbe, R v Essen, W Haarmann, K L Neuhaus. **Influence of time to treatment on early infarct-related artery patency after different thrombolytic regimens.** ALKK-Study Group. Am Heart J. 1999 Jan; 137(1):34-8.
7. Baardman T, Hermens WT, Lenderink T, Molhoek GP, Grollier G, Pfisterer M, et al. **Differential effects of tissue plasminogen activator and streptokinase on infarct size and on rate of enzyme release: Influence of early infarct related artery patency.** The GUSTO Enzyme Substudy. Eur Heart J. 1996 Feb; 17(2):237-46.
8. GUSTO Angiographic Investigators. **The effects of tissue plasminogen activator, streptokinase, or both on coronary-artery patency, ventricular function, and survival after acute myocardial infarction.** N Engl J Med. 1993 Nov 25; 329(22):1615-22.
9. Belenkie I, Thompson CR, Manyari DE, Knudtson ML, Duff HJ, Poon MC, et al. **Importance of effective, early and sustained reperfusion during acute myocardial infarction.** The American Journal of Cardiology. 1989 Apr 15; 63(13):912-16.
10. Cristian Capitanescu, Anca Monica Macovei Oprescu, Dan Ionita, Gabi Valeriu Dinca, Claudiu Turculet, Gheorghe Manole, et al. **Molecular processes in the streptokinase thrombolytic therapy.** Journal of Enzyme Inhibition and Medicinal Chemistry. 2016; 31(6):1411-14.
11. Gruppo IP, Miocardico SN. **The effectiveness of intravenous thrombolytic treatment in acute myocardial infarction.** Lancet. 1986; 1:397-402.
12. Fu Y, Goodman S, Chang WC, Van de Werf F, Granger CB, Armstrong PW. **Time to treatment influences the impact of ST-segment resolution on one-year prognosis: Insights from the assessment of the safety and efficacy of a new thrombolytic (ASSENT-2) trial.** Circulation. 2001 Nov 27; 104(22):2653-9.
13. De Luca G, Van't Hof AW, de Boer MJ, Ottervanger JP, Hoorntje JC, Gosselink AM, et al. **Time-to-treatment significantly affects the extent of ST-segment resolution and myocardial blush in patients with acute myocardial infarction treated by primary angioplasty.** European Heart Journal. 2004 Jun 1; 25(12):1009-13.
14. Charuzi Y, Beeder C, Marshall LA, Sasaki H, Pack NB, Geft I, et al. **Improvement in regional and global left ventricular function after intracoronary thrombolysis: Assessment with two-dimensional echocardiography.** The American Journal of Cardiology. 1984 Mar 1; 53(6):662-5.
15. Reduto LA, Smalling RW, Freund GC, Gould KL. **Intracoronary infusion of streptokinase in patients with acute myocardial infarction: Effects of reperfusion on left ventricular performance.** Am J Cardiol 1981; 48:403-9.

AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Zia Ullah Khan:** Results compilation.
2	**Rukhshanda Afsar:** Data collection.
3	**Mohammad Imran Khan:** Conception, writing of paper.
4	**Saad Shams:** Proof reading.
5	**Aftab Ahmed:** Data collection.
6	**Matiullah Khan:** Data entry.