Original Article

Bleeding Outcomes of Ticagrelor Loading in STEMI Thrombolysis with Streptokinase and Tenecteplase: A Single-Centre Retrospective Study in a Malaysian Population

Hock Peng Koh[1], Jivanraj R Nagarajah[1], Sin Nan Lai[2]

[1]Pharmacy Department, Hospital Kuala Lumpur, Ministry of Health Malaysia, Jalan Pahang, 50586 Kuala Lumpur, Malaysia
[2]Emergency and Trauma Department, Hospital Kuala Lumpur, Ministry of Health Malaysia, Jalan Pahang, 50586 Kuala Lumpur, Malaysia

Abstract

Background: Ticagrelor loading in ST-elevation myocardial infarction (STEMI) thrombolysis is not uncommon, particularly in cases initially planned for primary percutaneous coronary intervention but later cancelled and diverted to thrombolytic therapy. However, data on bleeding outcomes with ticagrelor loading, rather than clopidogrel loading, in thrombolytic therapy among Asian STEMI patients are limited. This study aimed to assess bleeding outcomes among STEMI patients who received a loading dose of ticagrelor for STEMI thrombolysis. **Methods:** This single-centre retrospective study collected data from STEMI patients who presented between January 2021 and March 2024 and received a 180 mg loading dose of ticagrelor (alongside acetylsalicylic acid and fondaparinux) in the Emergency Department (ED) for thrombolytic therapy. Consecutive patient enrolment was performed. Any bleeding event, classified according to thrombolysis in myocardial infarction (TIMI) bleeding criteria, was the primary endpoint. **Results:** A total of 117 patients were included in the final analyses. Their mean age was 57.2±12.4 years, and they were predominantly male (n=105, 89.7%). Most patients had MI with anterior involvement STEMI (n=67, 57.3%) and received tenecteplase as thrombolytic therapy (n=84, 71.8%). The in-hospital mortality rate was 15.4% (n=18). No major or minor bleeding was observed within 24 hours after the administration of the ticagrelor loading agent or thrombolytic agent. Eight (6.8%) minimal bleeding events (7 cases of gum bleeding and 1 case of epistaxis) occurred in the ED; all gum bleeding cases were treated with a tranexamic acid gargle. **Conclusion:** This study suggests acceptable short-term bleeding outcomes with ticagrelor loading for STEMI thrombolysis among our Asian population. However, more extensive studies with a control group are needed to confirm these findings further.

Keywords: *ticagrelor; STEMI; thrombolysis; bleeding; Asian population*

BACKGROUND

Pharmacological thrombolysis remains the primary reperfusion strategy for ST-elevation myocardial infarction (STEMI) management in many Asian and developing countries, including Malaysian public hospitals, due to the limited availability of percutaneous coronary intervention (PCI)-capable centres.[1] In patients with STEMI, occlusive thrombus formation involves platelet adhesion and aggregation, and high platelet reactivity following STEMI thrombolysis is a concern.[2] Thus, treatment with dual antiplatelet therapy (DAPT) with acetylsalicylic acid and a P2Y12 receptor inhibitor is recommended once the STEMI diagnosis is established.[3]

The chosen reperfusion strategy partly determines the selection of a P2Y12 receptor inhibitor. For patients receiving primary PCI, guidelines recommend ticagrelor or prasugrel over clopidogrel; for patients planning for pharmacological thrombolysis, clopidogrel is the only recommended option.[3,4] Current guidelines do not recommend ticagrelor in DAPT loading for STEMI thrombolysis because of the possible increased risk of bleeding and lack of evidence.[3–5] However, in routine clinical practice, ticagrelor loading in STEMI thrombolysis is not uncommon, especially when patients are initially planned to transfer to a PCI-capable centre but are cancelled for some reason.

Compared with clopidogrel, ticagrelor is a more potent antiplatelet agent that has demonstrated better efficacy and reduced mortality in acute coronary syndrome (ACS). However, these benefits are associated with an increased risk of bleeding.[6,7] The evidence for the use of ticagrelor loading in STEMI thrombolysis is limited, with only two studies published on the outcomes of this approach.[8,9] The MIRTOS trial was the first to compare ticagrelor and clopidogrel in STEMI thrombolysis, using alteplase, tenecteplase, and reteplase, with anticoagulants such as unfractionated heparin, bivalirudin or low-molecular-weight heparin (LMWH).[8] The MIRTOS trial reported similar rates of major bleeding between the two drugs, but the ticagrelor arm had a higher rate of minor bleeding.[8] Another retrospective study in Turkey with 150 STEMI patients treated with tenecteplase or alteplase concomitantly with ticagrelor reported a 6% rate of major bleeding.[9]

However, research gaps exist where no data are available for ticagrelor loading in STEMI thrombolysis using streptokinase and fondaparinux. Current studies on ticagrelor loading have been conducted only in Greece and Turkey, where different thrombolytic agents and anticoagulants have been employed. Streptokinase is still widely used in Asian regions due to its significantly lower cost and comparable efficacy to tenecteplase for the local population.[10] Locally, fondaparinux is the preferred anticoagulant in STEMI management. LMWH will be used if the patient's creatinine clearance is expected to be less than 30 mL/min.[10] Additionally, studies have reported a greater risk of bleeding in Asians than in Caucasians with ACS.[11,12] The data collected from other regions may not be generalisable to our population, given the diversity and physical differences among people. Thus, this study aimed to assess bleeding outcomes among STEMI patients who received a loading dose of ticagrelor for STEMI thrombolysis.

MATERIALS AND METHODS

Study design

This single-centre, retrospective observational study was conducted at Hospital Kuala Lumpur, the largest tertiary care public hospital in Malaysia, under the Ministry of Health, Malaysia. Hospital Kuala Lumpur is a non-PCI-capable hospital. This study was approved by the Medical Research and Ethics Committee, Ministry of Health Malaysia (NMRR ID-24-01247-JIO). Informed consent was waived because of the retrospective nature of the study. The study conformed to the principles outlined in the Declaration of Helsinki.

Study setting and population

At our centre, all patients diagnosed with STEMI and deemed eligible for reperfusion therapy are consented and referred to the National Heart Institute for primary PCI. Patient consent is crucial, as transfer is contingent upon the patient's willingness, ability to cover treatment costs, or insurance coverage.

This study included adult patients aged ≥ 18 years who were diagnosed with STEMI upon admission to the Emergency and Trauma Department from 1 January 2021 to 15 March 2024 and who received a ticagrelor loading dose in conjunction with thrombolytic therapy. All the STEMI patients who were given a ticagrelor loading dose initially provided consent and were referred to the National Heart Institute, but aborted for reasons such as patient or family refusal for PCI after providing initial consent, being hemodynamically unstable for transfer, and experiencing cardiac arrest before transfer.

The exclusion criteria for this study were incomplete administration of thrombolytic therapy, receiving a lower than the recommended dose of thrombolytic treatment, not receiving standard concurrent antiplatelet and anticoagulant therapy, receiving thrombolytic therapy despite the presence of absolute contraindications, and incomplete data from the patient's medical record.

Thrombolysis protocol

The selection of the thrombolytic agent is based on an in-house protocol, where tenecteplase will be selected if the patient with STEMI is contraindicated for streptokinase, hemodynamically unstable, and has extensive MI. The dose of streptokinase was 1.5 million units, which was diluted in 100 mL of normal saline and given over one hour. Tenecteplase was administered according to the patient's body weight, as specified in the metalyse product insert, and given as a rapid bolus. All STEMI patients who received the thrombolytic agent were given DAPT, i.e., 180 mg of ticagrelor plus 300 mg of acetylsalicylic acid and 2.5 mg of fondaparinux as part of acute management. Enoxaparin was used only in patients with a creatinine clearance rate of less than 30 mL/min.

Data collection

Consecutive patient enrolment was performed, including all eligible patients during the study period. The list of all STEMI patients who received a ticagrelor loading dose in conjunction with thrombolytic therapy was retrieved from the Thrombolysis Registry in the

Emergency and Trauma Department. All medical records were retrieved from the Records Office and screened according to the eligibility criteria. The pertinent data obtained from the patients' medical records included (A) patients' sociodemographic, (B) comorbidities, (C) STEMI diagnosis, (D) thrombolytic therapy, (E) bleeding outcomes, and (F) all-cause mortality.

Primary outcome

In this study, the primary outcome was the incidence of bleeding events that occurred within 24 hours of the index event following the administration of 180 mg of ticagrelor loaded with thrombolytic therapy. The duration was limited to 24 hours, as the antiplatelets were converted to clopidogrel for maintenance. All bleeding events were classified according to the Thrombolysis in Myocardial Infarction (TIMI) bleeding classification.[13]

Data analysis

Data analysis was performed via the Statistical Package for the Social Sciences (SPSS) for Windows, version 26 (IBM Corp., Armonk, NY, USA). The Kolmogorov–Smirnov test was used to assess normality for all continuous variables. Normally distributed data are reported as the means ± standard deviations (SDs). Nonparametric data are reported as medians with interquartile ranges (IQRs). Categorical variables are reported as numbers and percentages. The chi-square test or Fisher's exact test was used to determine the associations between two relevant dichotomous variables. All the statistical tests with a p-value of <0.05 were considered statistically significant.

RESULTS

Subjects' demographics

One hundred seventeen STEMI patients who received ticagrelor loading with thrombolytic therapy were included in the final analyses. No patients were excluded, as none met the exclusion criteria. The majority of patients were male (n=105, 89.7%) and current smokers (n=63, 53.8%), with a mean age of 57.2±12.4 years. Hypertension (n = 70, 59.8%) and diabetes mellitus (n = 51, 43.6%) were the most common preexisting underlying comorbidities. Most STEMI cases involved the anterior location (n = 67, 57.3%), and the majority of patients presented with a Killip class of II or higher (n = 77, 65.8%). Most STEMI patients received tenecteplase for thrombolysis (n = 84, 71.8%) (Table 1).

Table 1. Baseline demographics and clinical characteristics of STEMI patients (N=117)

Parameters	Frequency, n (%)
Age	
Mean (±SD)	57.2 (±12.4)
Range	30 – 90
≥ 75	10 (8.5)
Male	105 (89.7)
Race	
Malay	60 (51.3)
Chinese	22 (18.8)
Indian	25 (21.4)
Others	10 (8.5)
Current smoker	63 (53.8)
Family history of IHD	
Yes	6 (5.1)
No	37 (31.6)
Unknown	74 (63.2)
Comorbidities	
Hypertension	70 (59.8)
Diabetes mellitus	51 (43.6)
Dyslipidemia	31 (26.5)
Ischemic heart disease	35 (29.9)
Heart failure	3 (2.6)
History of ischemic stroke	2 (1.7)
Anterior involvement STEMI	67 (57.3)
The thrombolytic agent used	
Tenecteplase	84 (71.8)
Streptokinase	33 (28.2)
Killip class on arrival ≥ 2	77 (65.8%)
Door-to-needle (DNT) time ≤ 30 minutes	51 (43.6)
Time from symptom onset to needle time	
0 – 2 hours	14 (12.0)
>2 – 4 hours	21 (17.9)
> 4 hours	28 (23.9)
Not documented	53 (45.3)
Systolic blood pressure ≥ 160 mmHg at presentation	14 (12.0)
Heart rate ≥ 100 bpm at presentation	20 (17.1)

Primary outcome

Table 2 shows the outcomes following thrombolysis. No major or minor bleeding occurred within 24 hours after ticagrelor loading and thrombolysis. There were 8 (6.8%) cases of minimal bleeding that occurred within 24 hours following thrombolysis, comprising 7 cases of spontaneous gum bleeding and 1 case of epistaxis. The incidence of minimal bleeding was numerically greater in the streptokinase arm than in the tenecteplase arm (Table 3). There was 1 case of minor bleeding (lower gastrointestinal bleeding from the rectal tumour) that occurred after 24 hours of thrombolysis with an antiplatelet agent that was switched to clopidogrel.

Table 2. Outcomes following thrombolysis

Parameters	Frequency, n (%)	95% CI
Bleeding events		
Major	0 (0.0)	0.0 – 3.1
Minor	0 (0.0)	0.0 – 3.1
Minimal	8 (6.8)	3.0 – 13.0
In-hospital all-cause mortality	18 (15.4)	9.4 – 23.2
Cardiac events		
Hypotension	13 (11.1)	6.1 – 18.3
Bradycardia	3 (2.6)	0.5 – 7.3
Reinfarction	1 (0.9)	0.0 – 4.7
Congestive heart failure	1 (0.9)	0.0 – 4.7
Cardiogenic shock	1 (0.9)	0.0 – 4.7
Asystole	9 (7.7)	3.6 – 14.1
VF/Pvt	9 (7.7)	3.6 – 14.1

VF/pVT ventricular fibrillation/pulseless ventricular tachycardia, *CI* confidence interval

Table 3. Comparison of minimal bleeding events between STEMI patients who received tenecteplase and those who received streptokinase (N=117)

Outcomes	Tenecteplase (n=84)	Streptokinase (n=33)	P value
Minimal bleeding	4 (4.8)	4 (12.1)	0.156[a]
Gum bleeding	3	4	-
Epistaxis	1	0	-

[a] Fisher's exact test

DISCUSSION

Bleeding outcomes are crucial primary safety endpoints in studies involving thrombolytic agents. Currently, no STEMI guidelines recommend the use of ticagrelor loading in STEMI thrombolysis. It is crucial to monitor the safety outcomes of medications used off-label to ensure patient safety when there are deviations from standard guidelines. The use of ticagrelor loading in STEMI thrombolysis is a concern because of its potential increased risk of bleeding, especially in the Asian population, which has a greater bleeding risk with ACS treatment.[11,12] Additionally, the selection of thrombolytic agents and injectable anticoagulants for STEMI thrombolysis varies across regions and healthcare systems. This study further narrows the research gaps concerning the bleeding outcomes of ticagrelor loading in STEMI thrombolysis, which includes novel findings on streptokinase and fondaparinux.

Our STEMI cohort was generally younger than that reported in the Greek and Turkish studies on ticagrelor loading, with a high prevalence of hypertension and diabetes mellitus.[1,8,9] These comorbidities, along with the predominance of anterior STEMI, reflect the higher cardiovascular risk profile of our population and provide important content when interpreting the bleeding outcomes observed. Compared with a local study on STEMI thrombolysis, our cohort had a greater incidence of hypertension, diabetes, and ischemic heart disease, with a similar proportion of anterior MI but a higher incidence of Killip class ≥2 on arrival.[14]

Surprisingly, when the primary outcome was examined, we found that no major or minor bleeding occurred within 24 hours following ticagrelor loading for STEMI thrombolysis in our local Asian population. Our findings contrast with the 1.2–6.0% of major bleeding events observed in the Greek and Turkish studies on ticagrelor loading, which reported cumulative bleeding events during the hospitalisation period.[8,9] However, it was unknown whether the bleeding events reported in the previous studies were due to the concurrent administration of the ticagrelor loading dose with thrombolytic therapy or due to the effect of ticagrelor with the injectable anticoagulant, as the onset of bleeding was not documented. Thus, the bleeding outcomes in this study are more specific, which can be attributed to the concurrent use of thrombolytic therapy with antiplatelet and anticoagulant agents. It is essential to consider the thrombolytic effect for up to 24 hours, as fibrinogen depletion can persist for up to 24 hours, especially with streptokinase, a non-fibrin-specific thrombolytic agent.[15]

The observed incidence of minimal bleeding appears acceptable, particularly since all patients were managed conservatively without the need for blood transfusions or procedural interventions. This rate is also lower than the 14.0% minimal bleeding reported in a local study using clopidogrel loading, which additionally documented rates of 0.8% and 1.8% for major and minor bleeding, respectively. Taken together, these findings suggest that compared with the published clopidogrel regimen, ticagrelor loading in STEMI thrombolysis does not result in excess clinically significant bleeding in our local Asian population.

Fondaparinux is the preferred injectable anticoagulant for STEMI in our local setting because of its

comparable efficacy with LMWH, convenient once-daily dosing, and minimal risk of heparin-induced thrombocytopenia (HIT).[16,17] Compared with unfractionated heparin, it also does not require routine monitoring. We postulated that the more favourable bleeding outcome observed with ticagrelor loading and thrombolytic therapy in this study may be related, in part, to the widespread use of fondaparinux, in contrast to the unfractionated heparin, LMWH, and bivalirudin used in the Greek and Turkish studies.[8,9] However, causation cannot be established, and other factors beyond anticoagulant choice may also have contributed. Notably, the better safety profile of fondaparinux than LMWH was demonstrated in the OASIS-5 (The Fifth Organisation to Assess Strategies in Acute Ischemic Syndromes) trial.[16] Additionally, a 5-year analysis in a Malaysian study on STEMI thrombolysis with concomitant clopidogrel, acetylsalicylic acid, and fondaparinux reported low major bleeding events and comparable minor bleeding to landmark trials on STEMI thrombolysis. [14]

Streptokinase, tenecteplase, alteplase, and reteplase are the four thrombolytic agents currently approved for STEMI thrombolysis [5]. Streptokinase is the only non-fibrin-specific thrombolytic agent that remains relevant in our region due to its significantly lower cost and comparable efficacy to tenecteplase for the local population.[10] However, it is associated with a greater risk of adverse events such as hypotension and allergic reactions.[10] Previous studies on ticagrelor loading in STEMI thrombolysis involved only fibrin-specific agents, i.e., tenecteplase, alteplase, and reteplase. In this study, we report novel findings concerning the bleeding outcomes of ticagrelor loaded with streptokinase.

While the streptokinase arm presented numerically higher bleeding rates than the tenecteplase arm, this difference was not statistically significant, and the study was underpowered to detect meaningful differences between the thrombolytic agents. Nevertheless, the observed trend is plausible. Non-fibrin-specific streptokinase carries a greater bleeding risk, as it activates plasminogen to plasmin throughout the circulatory system, which breaks down fibrin clots and affects circulating fibrinogen and other clotting factors.[18] In contrast, fibrin-specific tenecteplase selectively activates plasminogen bound to fibrin within the clot, leading to localised clot breakdown while sparing systemic fibrinogen.[18]

The use of ticagrelor in STEMI patients receiving pharmacological thrombolysis is limited. This study provides a baseline bleeding assessment of the risk of ticagrelor loading in patients with thrombosis in an Asian population, which will guide further research on the use of ticagrelor in acute STEMI patients receiving pharmacological thrombolysis in the future. Nevertheless, research gaps still exist in the Asian population regarding the use of ticagrelor loaded with alteplase and other injectable anticoagulants (UFH and LMWH). Alteplase is not the preferred thrombolytic agent in our local setting due to its significantly higher cost, prolonged infusion time, and limited data in the Asian population.

In the emergency setting, ticagrelor loading in STEMI patients who subsequently receive thrombolysis is sometimes unavoidable. Our findings provide preliminary evidence that this approach is associated with an acceptable bleeding profile, suggesting that thrombolysis can be safely performed in patients already loaded with ticagrelor, particularly when PCI access is delayed or cancelled. Nevertheless, caution is warranted, and emergency physicians should remain vigilant for potential bleeding events given the study's limitations.

We acknowledge several limitations in this study. First, the retrospective observational nature of this study may affect the data quality, including potential detection bias in the assessment and documentation of bleeding events. Nevertheless, missing data were likely to be minimal, as the reporting of STEMI cases is one of the key performance indicators for the Emergency and Trauma Department, and our Cardiology Unit is a primary source for the Malaysian National Cardiovascular Disease Registry. Second, this was a single-centre study with a relatively small sample size conducted in a tertiary urban hospital. The patient cohort may not fully represent the broader Malaysian population and may not be generalisable to the whole population in Malaysia, a multiethnic country. Selection bias is also possible, as this study recruited only patients who initially agreed and were referred for primary PCI. Third, we did not compare our group with a control group receiving clopidogrel loading, which limits direct comparison with the current standard of care. Finally, although these limitations restrict definitive conclusions, this study provides important real-world data on ticagrelor loading in conjunction with thrombolysis.

Future studies should include prospective randomised controlled trials directly comparing ticagrelor versus clopidogrel loading in the setting of STEMI thrombolysis. Multicentre collaboration across different regions would improve generalisability beyond a single-centre experience. More extended follow-up periods are needed to capture delayed bleeding events that may not be evident within the first

24 hours. In addition, cost-effectiveness analyses would be valuable in resource-limited or heavily subsidised healthcare settings, where affordability and accessibility influence antiplatelet selection.

CONCLUSION

This single-centre study suggests acceptable short-term bleeding outcomes with ticagrelor loading in STEMI thrombolysis in our Malaysian population, with no major/minor bleeding events and minimal manageable bleeding events. However, the small sample size, short follow-up period, and lack of a control group limit the ability to draw definitive conclusions about comparative safety. These preliminary findings should not alter current guideline recommendations, which favour the use of clopidogrel for STEMI thrombolysis. Larger prospective controlled studies are needed to establish comparative safety and efficacy.

ACKNOWLEDGEMENT

We would like to thank the Director-General of Health Malaysia for his permission to publish this article.

AUTHORS' CONTRIBUTIONS

HPK contributed to the idea and study design. All the authors contributed to the data collection and interpretation of the results and critically reviewed the final manuscript. HPK wrote the first manuscript and performed all the statistical analyses. All the authors contributed to the manuscript review and approved the manuscript for publication.

FUNDING

This study was self-funded.

AVAILABILITY OF DATA AND MATERIALS

The raw data are not attached.

CONFLICT OF INTEREST DECLARATION

The authors declare that they have no conflicts of interest.

CONSENT TO PARTICIPATE

Informed consent was waived by the Medical Research and Ethics Committee, Ministry of Health Malaysia, owing to the retrospective nature of the study.

CONSENT TO PUBLICATION

Approval for publication was obtained from the Director-General of Health, Malaysia.

DATA AVAILABILITY

The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

CONFERENCE PRESENTATION AND ABSTRACT PUBLICATION

The findings of this study were presented as an oral presentation at the 6th Emergency Medicine Annual Symposium (EMAS) 2024. The abstract of the presentation was published in the Malaysian Journal of Emergency Medicine, Vol. 6 No. 3 (2024): 2024 EMAS Supplementary.

CORRESPONDENCE

Koh Hock Peng
Pharmacy Department, Hospital Kuala Lumpur, Jalan Pahang, 50586 Kuala Lumpur, Malaysia
ORCID ID: 0000-0003-2676-7755
Email: wilsonkoh821@gmail.com

REFERENCES

1. Tern PJW, Ho AKH, Sultana R, et al. Comparative overview of ST-elevation myocardial infarction epidemiology, demographics, management, and outcomes in five Asia-Pacific countries: a meta-analysis. Eur Heart J Qual Care Clin Outcomes. 2021;7(1):6-17.
2. Sabatine MS, Cannon CP, Gibson CM, et al. Addition of clopidogrel to aspirin and fibrinolytic therapy for myocardial infarction with ST-segment elevation. N Engl J Med. 2005;352(12):1179-89.
3. Ministry of Health Malaysia. Clinical practice guidelines: management of acute ST-segment elevation myocardial infarction (STEMI). Putrajaya: MOH Malaysia; 2019.
4. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction. J Am Coll Cardiol. 2013;61(4):e78-e140.
5. Ibanez B, James S, Agewall S, et al. 2017 ESC guidelines for the management of acute myocardial infarction in patients presenting

6. with ST-segment elevation. Eur Heart J. 2018;39(2):119-77. doi:10.1093/eurheartj/ehx393.
7. Wallentin L, Becker RC, Budaj A, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. N Engl J Med. 2009;361(11):1045-57.
8. Bonaca MP, Bhatt DL, Cohen M, et al. Long-term use of ticagrelor in patients with prior myocardial infarction. N Engl J Med. 2015;372(19):1791-800.
9. Hamilos M, Kanakakis J, Anastasiou I, et al. Ticagrelor versus clopidogrel in patients with STEMI treated with thrombolysis: the MIRTOS trial. EuroIntervention. 2021;16(15):1163-9.
10. Günlü S, Demir M. Comparison of tenecteplase versus alteplase in STEMI patients treated with ticagrelor: a cross-sectional study. Am J Emerg Med. 2022;58:52-6.
11. Koh HP, Md Redzuan A, Mohd Saffian S, et al. The outcomes of reperfusion therapy with streptokinase versus tenecteplase in ST-elevation myocardial infarction (STEMI): a propensity-matched retrospective analysis in an Asian population. Int J Clin Pharm. 2022;44(3):641-50.
12. Misumida N, Ogunbayo GO, Kim SM, et al. Higher risk of bleeding in Asians presenting with ST-segment elevation myocardial infarction: analysis of the National Inpatient Sample database. Angiology. 2018;69(6):548-54.
13. Lam S, Lee SW, Chan K, et al. A 10-year review of thrombolytic therapy in patients with ST-segment elevation myocardial infarction in a university hospital in Hong Kong: intracranial bleeding and other outcomes. J Am Coll Cardiol. 2012;59(13 Suppl):E461.
14. Chesebro JH, Knatterud G, Roberts R, et al. Thrombolysis in myocardial infarction (TIMI) trial, phase I: a comparison between intravenous tissue plasminogen activator and intravenous streptokinase. Circulation. 1987;76(1):142-54.
15. Koh HP, Md Redzuan A, Mohd Saffian S, et al. Mortality outcomes and predictors of failed thrombolysis following STEMI thrombolysis in a non-PCI capable tertiary hospital: a 5-year analysis. Intern Emerg Med. 2023;18(6):1169-80.
16. Dauerman HL, Gogo JB Jr, Sobel BE. Reperfusion therapies for acute ST elevation myocardial infarction. In: Brown DL, editor. Cardiac intensive care. 3rd ed. Philadelphia: Elsevier; 2019. p. 103-16.
17. Yusuf S, Mehta SR, Chrolavicius S, et al. Comparison of fondaparinux and enoxaparin in acute coronary syndromes. N Engl J Med. 2006;354(14):1464-76.
18. Chen LY, Khan N, Lindenbauer A, et al. When will fondaparinux induce thrombocytopenia? Bioconjug Chem. 2022;33(7):1574-80.
19. Adivitiya, Khasa YP. The evolution of recombinant thrombolytics: current status and future directions. Bioengineered. 2017;8(4):331-58.