

The role of intracoronary thrombolysis in thrombus-laden coronary artery: a case report

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Introduction: Large intracoronary thrombus in patients presenting with ST elevation myocardial infarction (STEMI) can cause distal embolization, the no-reflow phenomenon, and stent thrombosis. Approximately 10% of patients undergoing primary percutaneous coronary intervention (PCI) have distal embolization of thrombus, causing coronary microvascular obstruction and reduced myocardial tissue perfusion. This can lead to ongoing ischemia, a larger infarct size, and a significant increase in 30-day mortality, regardless of successful PCI with normal epicardial vessel flow.

Case Presentation: A 51-year-old Asian male presented with STEMI. Coronary angiography revealed a large thrombus totally occluding the proximal portion of the right coronary artery (RCA). Catheter-directed intracoronary thrombolysis with streptokinase was performed after multiple attempts at manual aspiration thrombectomy (MAT) and balloon angioplasty had failed to achieve coronary blood flow recovery. After successful stenting, a diffuse residual thrombus remained in the RCA. Evaluation angiography of the RCA performed four days later showed complete thrombus dissolution with thrombolysis in myocardial infarction (TIMI) grade 3 flow.

Discussion: While there is no gold-standard therapy to deal with intracoronary thrombus, there are combinations of both pharmacological and mechanical therapies that can be utilized. MAT should not be used routinely in STEMI, but may be helpful in selected cases. Catheter-directed intracoronary thrombolysis can be a safe and effective alternative reperfusion strategy when MAT alone fails to achieve sufficient coronary blood flow in the thrombotic infarct-related artery (IRA).

Conclusion: The management of intracoronary thrombus during PCI remains a therapeutic challenge, and an aggressive, case-by-case, tailored approach can lead to improved outcomes.

Key words: intracoronary streptokinase, manual aspiration thrombectomy (MAT), intracoronary thrombus, primary percutaneous coronary intervention (PCI), ST-elevation myocardial infarction (STEMI).

Role intrakoronární trombolýzy v případě trombotizované koronární tepny: kazuistika

Úvod: Velké intrakoronární tromby u pacientů s infarktem myokardu s elevací úseku ST (STEMI) mohou způsobit distální embolizaci, fenomén „no-reflow“ a trombózu stentu. Přibližně u 10 % pacientů podstupujících primární perkutánní koronární intervenci (PCI) dochází k distální embolizaci trombu, což způsobuje mikrovaskulární obstrukci koronárních tepen a snížení perfuze myokardiální tkáně. To může mít za

DECLARATIONS:

Declaration of originality:

The manuscript is original and has not been published or submitted elsewhere.

Ethical principles compliance:

The authors attest that their study was approved by the local Ethical Committee and is in compliance with human studies and animal welfare regulations of the authors' institutions as well as with the World Medical Association Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects adopted by the 18th WMA General Assembly in Helsinki, Finland, in June 1964, with subsequent amendments, as well as with the ICMJE Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals, updated in December 2018, including patient consent where appropriate.

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následek přetrvávající ischemii, větší velikost infarktu a významné zvýšení 30denní mortality, a to bez ohledu na úspěšnou PCI s normálním průtokem epikardiálními cévami.

Kazuistika: Jedenapadesátiletý muž asijského původu byl přijat s diagnózou STEMI. Koronarografie prokázala velký trombus obturující proximální část levé koronární tepny (ACS). Poté, co opakované pokusy o manuální aspirační trombektomii (MAT) a balonkovou angioplastiku nevedly k obnovení průtoku krve koronárními tepnami, byla provedena katetrizační intrakoronární trombolýza s aplikací streptokinázy. Po úspěšném zavedení stentu zůstal v ACS difúzní reziduální trombus. Angiografické zhodnocení ACS provedené o čtyři dny později prokázalo úplné rozpuštění trombu s průtokem infarktovou tepnou TIMI 3.

Diskuze: I když v oblasti léčby intrakoronárního trombu neexistuje zlatý standard, je možné využít kombinace farmakologické a mechanické léčby. MAT by v případě STEMI neměla být používána rutinně, nicméně ve vybraných případech může být užitečná. Katetrizační intrakoronární trombolýza může být bezpečnou a účinnou alternativou reperfuze strategie, pokud MAT samotnou nedosáhneme dostatečného průtoku krve infarktovou tepnou (IRA).

Závěr: Řešení intrakoronárního trombu během PCI je i nadále terapeutickou výzvou, přičemž lepších výsledků lze dosáhnout pomocí agresivního, individuálního přístupu šitého na míru.

Klíčová slova: intrakoronární streptokináza, manuální aspirační trombektomie (MAT), intrakoronární trombus, primární perkutánní koronární intervence (PCI), infarkt myokardu s elevací úseku ST (STEMI).

Introduction

Intracoronary thrombus remains one of the main enemies of the interventional cardiologist. Approximately 10% of patients undergoing primary PCI experience distal embolization of the thrombus, resulting in coronary microvascular obstruction and decreased myocardial tissue perfusion. This could result in continued ischemia, more extensive infarct size, and a significantly increased 30-day mortality (hazard ratio [HR] 3.0, 95% confidence interval [CI] 1.19–7.58; $P = 0.02$), despite a successful PCI with normal epicardial vascular flow (1). The MAT procedure is often performed as a first-line measure to reduce these side effects, although its beneficial effect during PCI is still debated (2). When MAT fails to achieve adequate coronary blood flow, intracoronary thrombolysis using a catheter may be a safe and effective alternative reperfusion strategy for IRA complicated by a large thrombus (3). We report a case of coronary reperfusion via a combination of MAT, balloon angioplasty, and intracoronary catheter thrombolysis in a STEMI-induced thrombotic occlusion in the RCA.

Case Presentation

A 51-year-old Asian man presents to the emergency room with sudden chest pain that has lasted for 11 hours, accompanied by cold sweat and nausea. The patient is a two-pack daily smoker with high blood pressure without any history of medication use. The patient also consumes coffee and energy

drinks every day as a public transport driver. At the first medical contact, the patient appeared fully conscious, GCS 4/5/6, blood pressure of 140/90 mmHg, a heart rate of 100 bpm, and a respiratory rate of 24 breaths/min, with the remainder of physical examination within normal limits. The ECG showed a sinus rhythm of 100 beats/min with ST segment elevation in leads II, III, AVF, and V3R–V6R (Fig. 1). Serum creatinine was 1.1 mg/dL, serum troponin-I was 3.0 ng/mL, random blood glucose was 211 mg/dL, and hepatitis B was reactive. In this antiplatelet-naïve patient, a loading dose

of 300 mg aspirin and 180 mg ticagrelor was administered, followed by primary PCI.

Coronary angiography showed normal appearance of the left main coronary artery (LMCA), left anterior descending (LAD), and left circumflex (LCx) (Fig. 2a), whereas the RCA was completely occluded by thrombus proximally (Fig. 2b). The PCI procedure was followed by an intravenous (IV) bolus of 100 u/kg BW unfractionated heparin (7,000 units), without the addition of GP IIb/IIIa inhibitor therapy (not available at the time of the procedure). Wire crossing was performed using

Fig 1. Electrocardiogram at admission

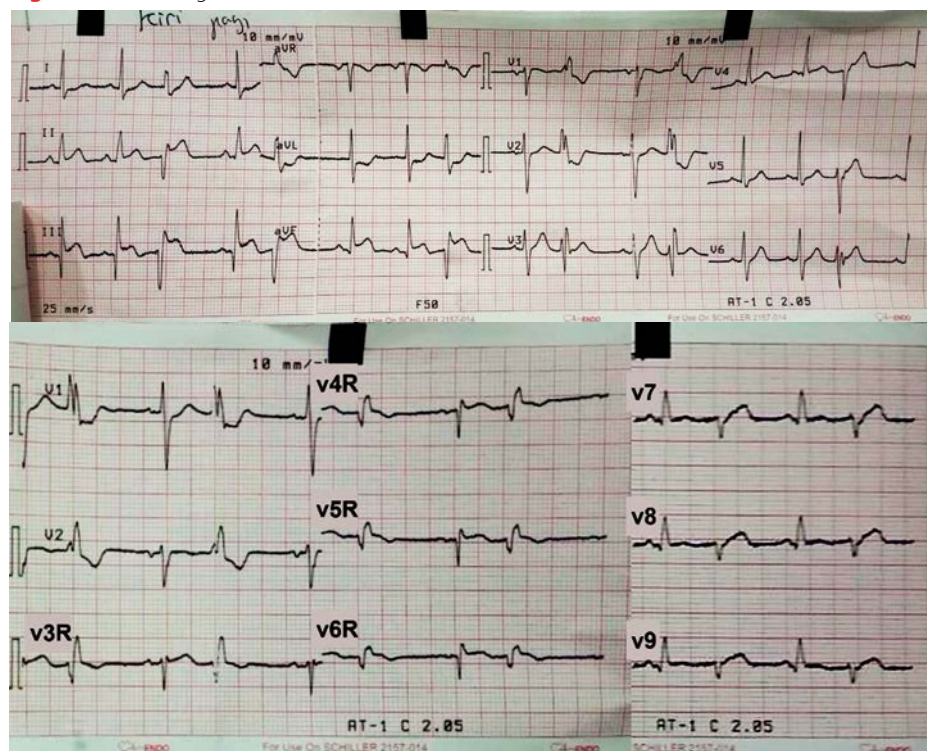
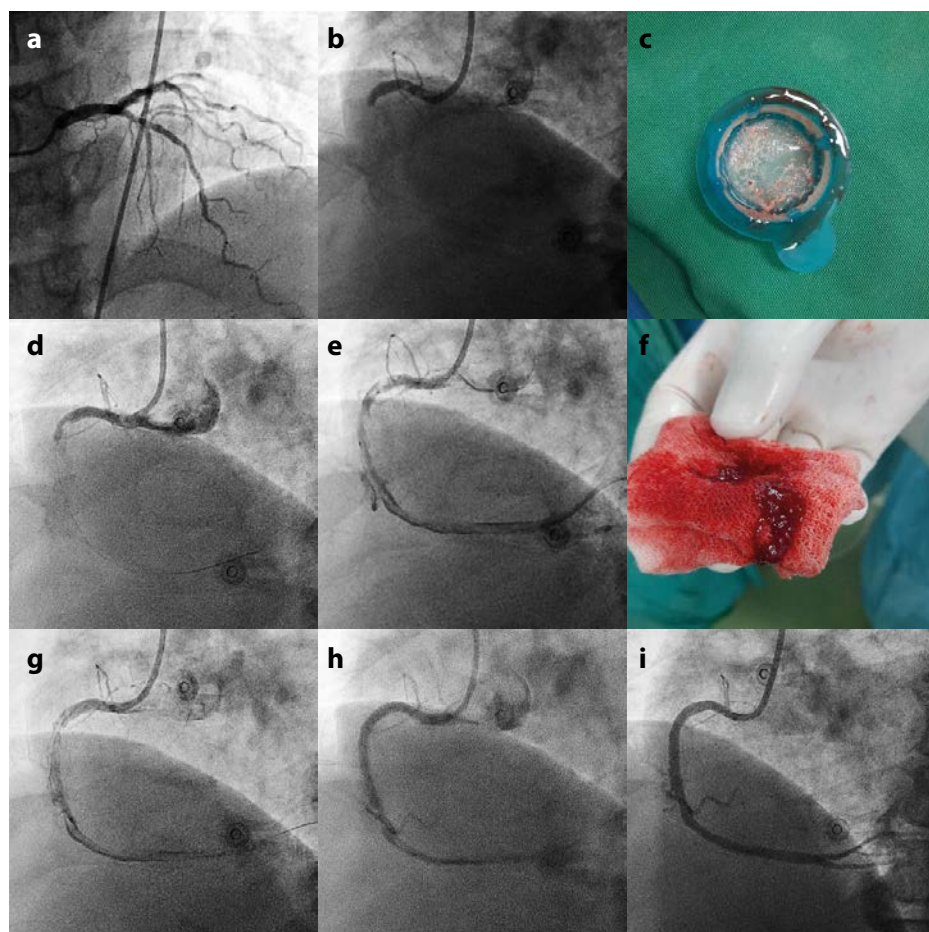


Fig 2. Coronary Angiography. (a) LMCA, LAD, and LCx appear normal. (b) Total occlusion of the proximal part of the RCA with TIMI flow grade 0. (c) MAT succeeded in obtaining a red and white thrombus. (d) Evaluation after the first MAT. (e) Evaluation after the first balloon angioplasty. (f) There is a clot blocking the aspiration catheter after the second MAT. (g) Evaluation after intracoronary thrombolysis and balloon angioplasty. (h) Post-stent evaluation proximal to mid-RCA. (i) Angiography evaluation 4 days after primary PCI



a 0.014" high-torque hydrophilic guidewire (Whisper MS, Abbot, Minneapolis, USA) and successfully penetrated the lesion distal to the RCA; however, antegrade flow was obtained on angiography, with grade 0 TIMI flow and grade 5 TIMI thrombus quantification.

MAT was performed using a 6-Fr aspiration catheter (Capturer, iVascular, Barcelona, Italy), and a red and white thrombus was obtained (Fig. 2c); however, there was no antegrade flow from the proximal RCA (Fig. 2d). To compress the lesion, a 1.5 × 15 mm semi-compliant balloon (Sapphire II, OrbusNeich, Netherlands) was inflated to 16 atmospheres (atm) proximal to distal to the RCA, followed by administration of 0.5 mg atropine sulfate as the patient developed bradycardia and hypotension. The procedure was continued by dilating the lesion using a 2.25 × 12 mm semi-compliant balloon (Sapphire II, OrbusNeich, Netherlands) to 15 atm midway to the pro-

ximal RCA. Angiography after balloon angioplasty showed an increase in coronary blood flow from TIMI flow grade 0 to 2 with a diffuse thrombus along the RCA (Fig. 2e). A second MAT was performed in an attempt to remove the remaining thrombus, only to find the aspiration catheter blocked by a clot (Fig. 2f).

Due to a diffuse thrombus in the RCA, we decided to perform intracoronary thrombolysis. Streptokinase 250,000 units (Fibrin, Lyocontract, Lisenburg, Germany) diluted in 16.7 mL normal saline was administered slowly over 5 minutes using a 4.0 6-Fr Judkin Right guiding catheter (Launcher, Medtronic, Minneapolis, USA), followed by dilatation with a 3.0 × 20 mm semi-compliant balloon (Sapphire II, OrbusNeich, Hoevelaken, Netherlands) up to 15 atm for manipulating the partially lysed thrombus; however, angiography showed disappointing results. We decided to continue intracoronary thrombolysis

using the same amount of streptokinase, but there was almost no difference in antegrade flow in the distal portion of the RCA. After repeated intracoronary thrombolysis five times with a total of 1,500,000 units of streptokinase over 30 minutes, an antegrade flow improvement to TIMI flow grade 3 was seen with the thrombus still in place (Fig. 2g). The proximal to the middle of the RCA was then stented using a 3.5 × 36 mm sirolimus drug-eluting stent (DES) (X-limus, Cardionovum, Bonn, Germany) developed to 16 atm (Fig. 2h). After undergoing the procedure, there were no complaints of chest pain anymore, but the patient began to experience hypotension; therefore, he was given dopamine (5 mcg/kg/min) and norepinephrine (0.1 mcg/kg/min) with a target systolic blood pressure of > 140 mmHg.

With a residual thrombus after stent placement, the risk of stent thrombosis is very high. After considering the low bleeding risk (PRECISE-DAPT score = 10), the patient was given triple therapy: aspirin 100 mg every 24 hours and ticagrelor 90 mg every 12 hours, followed by warfarin 2 mg every 24 hours one day after PCI. During the three days of intensive care after primary PCI, there were no complaints of chest pain or signs of bleeding; this may be related to the absence of an increase in the INR value in the lab results. On evaluation angiography performed four days after primary PCI, complete dissolution of the thrombus was seen with TIMI flow grade 3 on the RCA. Subsequently, the patient was discharged six days post-primary PCI with dual antiplatelet therapy (aspirin and ticagrelor) for more than 12 months. There were no complaints of chest pain or bleeding during the patient's follow-up visits on days 3 and 30 after being discharged from hospital.

Discussion

Intracoronary Thrombus

The pathophysiology underlying the development of intracoronary thrombus is Virchow's triad, triggered by rupture or erosion of an atherosclerotic plaque resulting in thrombus formation in the epicardial coronary arteries. In approximately 70% of cases, acute thrombus formation occurs after atherosclero-

tic plaque rupture, and in the remaining 30%, there is plaque erosion (4). Disruption of the atherosclerotic plaque results in the sub-endothelial thrombogenic matrix being exposed to circulating platelets, leading to platelet adhesion, aggregation, and white thrombus formation. The concomitant release of tissue factor from the site of arterial injury activates the extrinsic coagulation cascade, resulting in the formation of thrombin, which then converts fibrinogen to fibrin. This process culminates in the formation of a red thrombus composed of more densely packed platelets, erythrocytes, inflammatory cells, and fibrin, which over time becomes progressively more robust (5).

Massive intracoronary thrombi are associated with reperfusion failure and more unfavorable clinical outcomes (6–9). If not treated thoroughly, intracoronary thrombus can cause distal and microvascular obstruction, which is known as the no-reflow phenomenon. The no-reflow phenomenon can occur in 50% of cases of acute coronary syndrome (ACS) with a high thrombus load, resulting in reduced myocardial perfusion at the microvascular level, increased infarct size, and higher mortality (10, 11).

Intracoronary thrombus is defined as a filling defect with decreased contrast density. Quantification of intracoronary thrombus can be performed by angiography using the TIMI thrombus grade. The TIMI thrombus scale relies on relative estimates of the size of the thrombus and affected vessels, using a scaled score of 0 (no thrombus) to 5 (total occlusion by thrombus) (12). The TIMI thrombus scale can be simplified into a low thrombus load (grades 1–3) and a high thrombus load (grades 4–5) (13).

Current guidelines recommend primary PCI as the treatment of choice for STEMI patients. Primary PCI with stent implantation can restore patency in the IRA, resulting in a smaller infarct area and a lower number of acute and long-term events, including recurrent infarction and death (2). However, until now, there has been no gold-standard therapy for lesions with a high thrombus burden. Several mechanical and pharmacological approaches have been proposed to reduce the thrombus burden and post-PCI complications.

Platelet Inhibition

Early administration of dual antiplatelet therapy (DAPT) can reduce the thrombus burden and improve clinical outcomes. Aspirin can be given orally by chewing or intravenously at an initial dose of 150–300 mg to inhibit thromboxane A₂-mediated platelet activation (Class I; LOE B). The onset of action of aspirin occurs within 30–60 minutes and persists for the lifetime of the platelets. Potent P2Y₁₂ inhibitors such as prasugrel 60 mg or ticagrelor 180 mg can be selected if available, or clopidogrel 600 mg if more aggressive treatment is contraindicated (Class I; LOE A). Prasugrel and ticagrelor have a more rapid onset of action, stronger potency, and are superior to clopidogrel in clinical outcomes. Intravenous P2Y₁₂ agents (cangrelor) may also be considered in patients who have never taken an oral P2Y₁₂ receptor inhibitor at the time of PCI or in those who are intubated and unable to take oral agents (Class IIb; LOE A) (2).

Glycoprotein IIb/IIIa (GPI) inhibitors are angiographically proven effective agents for dissolving a thrombus and are capable of restoring TIMI flow by inhibiting the final pathway of platelet aggregation through competition for binding of GP IIb/IIIa receptors with von Willebrand factor and fibrinogen. GPIs inhibit platelet response to all agonists, resulting in rapid and almost complete inhibition of platelet aggregation, making them more potent antiplatelet agents than P2Y₁₂ inhibitors (14). Despite the proven efficacy of GPI in primary PCI settings, high bleeding rates remain a concern. In a meta-analysis of 10,123 patients undergoing primary PCI, Winchester et al. (15) reported that using GPI reduced non-fatal myocardial infarction (MI) at 30 days (5.1% vs. 8.3%; $p < 0.001$) with a significant increase in cost and risk of minor bleeding (3% vs. 1.7%; $p < 0.001$). Based on available data, current guidelines state that the routine use of upstream GPIs in STEMI cases is not recommended, but should be considered for bailout if there is evidence of the no-reflow phenomenon or thrombotic complications (Class IIa; LOE C) (2). Our patient did not receive GPI therapy due to its unavailability at the time of PCI. Nevertheless, we used several strategies, namely MAT, balloon angioplasty, and intracoronary thrombolysis, during PCI to obtain good results.

Anticoagulation

Effective anticoagulation must be maintained during primary PCI to inhibit the coagulation cascade and thrombus formation. Unfractionated heparin (UFH) is the most widely used anticoagulant of choice for primary PCI, besides enoxaparin and bivalirudin. Heparin binds to antithrombin, which causes surface changes and deactivates thrombin. Antithrombin binding blocks two major factors of the coagulation cascade: thrombin (Factor IIa) and Factor Xa, blocking the conversion of fibrinogen to fibrin, thereby preventing clot formation (15). Although there are no randomized, placebo-controlled studies evaluating UFH in primary PCI, there is considerable experience with this agent. Therefore, the routine use of UFH in primary PCI remains a class I (LOE A) recommendation (2).

In the ATOLL study involving 910 STEMI patients, enoxaparin 0.5 mg/kg IV bolus compared to UFH did not significantly reduce the primary composite endpoint of 30-day death, recurrent MI, procedural failure, or major bleeding, but there was a decrease in the secondary endpoint of death, recurrent MI, or urgent revascularization (16). In contrast, a meta-analysis of 23 PCI studies (30,966 patients, 33% primary PCI) reported the superiority of enoxaparin over UFH in reducing mortality and bleeding outcomes in the context of primary PCI (17). Based on these data, the routine use of IV enoxaparin should be considered during primary PCI (Class IIa; LOE A) (2).

The use of bivalirudin in PCI has shown no advantage over UFH, but data have shown a reduced risk of major bleeding in a recent meta-analysis of five trials (10,350 patients), although this was offset by an increased risk of acute stent thrombosis (18). Based on these data, the use of bivalirudin as an anticoagulant during primary PCI procedures is recommended for class IIa (LOE A) in patients with a high risk of bleeding or class I recommendations (LOE C) for patients with heparin-induced thrombocytopenia (2).

PCI Strategy

ACS differs from stable coronary artery disease in which the thrombus burden is higher. Compression or displacement of a thrombus by a balloon or strut stent can result in distal embolization and microvascular dysfunction.

Tab. 1. TIMI Flow Grade (39)

| | |
|----------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Grade 0 (No Perfusion) | There is no antegrade flow beyond the point of occlusion. |
| Grade 1 (Penetration Without Perfusion) | Contrast material crosses the area of obstruction but fails to opacify the entire artery distal to the obstruction during cinema-angiography. |
| Grade 2 (Partial Perfusion) | contrast material crosses the obstruction and opacifies the arteries in the area distal to the obstruction. However, the rate of filling of the contrast material into the artery distal to the obstruction or the rate of clearance distally (or both) appears to be slower than that of filling or clearance in comparable areas. |
| Grade 3 (Complete Perfusion) | Antegrade flow to the area distal to the obstruction occurs as quickly as antegrade flow to the proximal portion of the obstruction, and clearance of the contrast material in the involved area is as fast as that of the uninvolved area in the same or opposing arteries. |

Tab. 2. TIMI Thrombus Grade (12)

| | |
|-------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Grade 0 | There are no cinematic-angiographic characteristics of the thrombus. |
| Grade 1 (Flurry, Possible Thrombus) | Angiography shows characteristics such as decreased contrast density, haziness, an irregular contour of the lesion, or a fine convex "meniscus" at the site of total occlusion that is suggestive but not diagnostic of a thrombus. |
| Grade 2 (Small Size) | A definitive thrombus with the greatest linear dimension less than or equal to 1/2 the vessel diameter |
| Grade 3 (Medium Size) | Definitive thrombus with greatest linear dimension greater than 1/2 but less than 2x the vessel diameter |
| Grade 4 (Large Size) | A definitive thrombus with the greatest linear dimension greater than 2x the vessel diameter |
| Grade 5 (Total Thrombotic Occlusion) | May involve some collateralization but usually does not involve extensive collateralization. It tends to have a "beak" shape with blurred edges or a distinctive thrombus appearance. |

In the long term, resolution of an abluminal thrombus can lead to stent malposition, which leads to an increased risk of stent thrombosis. Delaying stent placement for primary PCI has been investigated as an option to reduce this complication. However, the DANAMI 3-DEFER trial reported that delayed stenting had no effect on composite all-cause mortality, non-fatal MI, or ischemia-driven revascularization in non-IRA lesions. Based on these findings, delaying routine stenting is not recommended (Class III; LOE B) (2).

In a meta-analysis of five small single-center studies with 754 patients, direct stenting appeared to improve reperfusion, as evidenced by a significant increase in ST segment resolution and a decrease in in-hospital cardiac death. In this study, there was no single use of contemporary DES or adjunctive medical treatment (19). Saad et al. also reported a significant reduction in infarct size and a lower incidence of heart failure hospitalization and death in the case of direct stent insertion without a pre-dilated balloon strategy. However, the major limitation of direct stent placement in this study was the presence of a thrombus, which limited the choice of stent. Other limitations of

direct stent insertion include underestimated arterial size, failure to penetrate a tortuous or calcified lesion, inadequate stent expansion, and late stent malposition, which can increase the risk of stent re-stenosis or thrombosis (20). These data suggest that direct stenting with or without balloon angioplasty and/or thrombus aspiration can be applied safely (Class I; LOE A) (2), particularly in certain ACS patients with low TIMI thrombus levels (1–3). To date, there has been no single strategic recommendation in the guidelines that would fit our case scenario. The large thrombus burden (TIMI thrombus grade > 3) and slow blood flow (TIMI flow grade 0) require a special management approach. In fact, we perform several strategies, namely MAT, balloon angioplasty, and intracoronary thrombolysis, during PCI.

Aspiration Thrombectomy

MAT is one of the most frequently used thrombectomy methods for primary PCI because the procedure is simple and has a low risk of vascular injury and distal embolism. Several small-scale or single-center studies and one meta-analysis of 11 small trials suggest that there may be an advantage to MAT

in primary PCI (21). However, data from several studies to date still report inconsistent results in terms of the benefit in primary PCI.

The TASTE (n > 7,000) and TOTAL (n > 10,000) randomized controlled trials showed no benefit of MAT on mortality, re-hospitalization, stent thrombosis, or overall clinical outcome, while the TOTAL study also reported an increased rate of stroke incidence (1, 22–25). However, 1–5% of randomized patients in these studies switched from PCI alone to MAT (1, 22). In the subgroup with high thrombus burden (TIMI thrombus grade ≥ 3), MAT was associated with lower cardiovascular mortality (2.5% vs. 3.1%; HR 0.80, 95% CI 0.65–0.98; P = 0.03) and a higher incidence of stroke or transient ischemic attack (0.9% vs. 0.5%; odds ratio [OR] 1.56, 95% CI 1.02–2.42, P = 0.03) (26). These results may be related to thrombus aspiration and inadequate restoration of coronary blood flow in cases of massive intracoronary thrombosis.

Randomized controlled trials have reported that rheolytic thrombectomy is more effective than MAT in thrombus removal and myocardial reperfusion in patients with STEMI (27, 28). The AngioJet rheolytic thrombectomy (RT) catheter uses a high-velocity saline jet, creating a strong suction of about 600 mmHg at the catheter tip and producing a venturi effect that leads to dissolution and suction of the thrombus. However, study reports failed to show differences in infarct size or adverse cardiac events after PCI between RT and MAT (29, 30).

Based on recent data and meta-analyses, routine thrombus aspiration is not recommended (Class III; LOE A), but can be considered when a high thrombus load is encountered after penetrating the lesion with a guidewire or balloon (2). Safe and feasible alternative strategies are needed when MAT fails during primary PCI.

Balloon Angioplasty

Balloon angioplasty remains an integral part of PCI for pre-dilating lesions, helping to traverse the lesion easily without complications and being useful for estimating coronary size, stent placement, insertion, and further development of stents (2). Simple balloon angioplasty can also be used to expand the lumen by stretching, compressing, and redistributing the thrombus along the longitudinal axis of the arterial wall to

some extent; however, this method can increase the likelihood of plaque detachment and fragmentation of the remaining thrombus, leading to distal embolization (5, 20). Furthermore, in our case, the use of balloon angioplasty along with intracoronary thrombolysis was aimed at manipulating a partially lysed thrombus.

Intracoronary Thrombolysis

Before coronary stents became widely used, intracoronary thrombolysis using plasminogen activator was used in almost all patients with various types of coronary artery disease (31). The principle of thrombolytic therapy is that the use of streptokinase, alteplase, or tenecteplase increases the conversion of plasminogen to active plasmin, resulting in a cascade that culminates in fibrin lysis. However, as primary PCI with stent implantation has become routine, followed by studies with disappointing results regarding excess bleeding rates, intracoronary thrombolysis has been used less and less in clinical practice (32, 33). In recent years, intracoronary thrombolysis has regained popularity as an adjunctive therapy for primary PCI, as studies using different thrombolytic agents and better antiplatelet regimens have proven this method to be safe and effective. In a pilot study by Sezer et al., 41 patients undergoing primary PCI were randomized to receive intracoronary streptokinase (250,000 units) or placebo. An evaluation two days later showed a significant increase in coronary flow reserve and a decrease in TIMI frame count when compared with placebo (34). Subsequently, 54 patients were added to the cohort to allow long-term assessment. After six months, there was a smaller infarct size on SPECT evaluation (22.7% vs. 32.9%, $p = 0.003$) and a higher LVEF (57.2% vs. 51.8%, $p = 0.018$) in the streptokinase group compared with placebo, with marked reductions in end-diastolic and systolic volumes on echocardiography (3).

In a small study involving 34 ACS patients with the no-reflow phenomenon, distal embolization, or intracoronary thrombus findings at PCI, Kelly et al. reported that the addition of intracoronary tenecteplase adjuvant therapy (mean dose = 10.2 ± 5.2 mg) proved safe and effective for thrombus dissolution and/or improving flow in 91% of patients. Seventy-six percent of patients in this study received GPI therapy, with major and minor bleeding events

found in one and three cases, respectively (35). Boscarelli et al. also reported that in cases of STEMI with a high thrombus burden that were unsuccessful on MAT, low-dose intracoronary adjuvant alteplase therapy (5 mg, 5-min intervals, maximum 30 mg) significantly reduced the TIMI thrombus grade and increased coronary epicardial outflow. In this study, although alteplase was given with GPI in half of the patients, there were no reports of major bleeding events, demonstrating the safety of this strategy (36).

Bleeding and Ischemic Risk

In contrast to elective procedures, primary PCI is associated with higher bleeding rates because of the need for potent antithrombotic and antiplatelet agents. GPIs, in combination with thrombolytic agents, can significantly increase the risk of bleeding events. However, the doses of thrombolytic agents administered by the intracoronary route are usually much lower than those used by the intravenous route. Kelly et al. reported only one case of major bleeding (2.9%) among 34 patients receiving intracoronary tenecteplase, which did not differ from the rate of major bleeding events in ACS cases in the GRACE data (3.9%) (35, 37). In fact, our patient did not receive GPI therapy.

Ischemic risk management must be considered after undergoing a PCI procedure. Thrombus manipulation and evidence of residual thrombus after stent implantation in our patients carry a high risk for microvascular obstruction or even acute stent thrombosis (20). To address this issue, the 2018 ESC/EACTS guidelines on myocardial revascularization recommend triple therapy for 1–6 months in patients at ischemic risk due to ACS or other anatomic or procedural characteristics that are higher than the risk of bleeding (Class IIa; LOE A) (38). With a low bleeding risk (PRECISE-DAPT score = 10), warfarin was added to DAPT therapy using aspirin and ticagrelor and was discontinued immediately on the fourth day after the results of angiographic evaluation showed no residual thrombus with grade 3 TIMI flow.

Conclusion

Intracoronary thrombi in cases of STEMI may result in a poorer clinical outcome, apart from successful PCI with normal epicardial vascular flow. Although there is no gold-standard

therapy for intracoronary thrombus, combined pharmacological and mechanical treatment options are being explored. MAT is not recommended to be performed routinely in STEMI cases, but may be helpful in certain cases at the discretion of the operator and intervention team. Intracoronary thrombolysis can be a safe and effective alternative reperfusion strategy when the MAT procedure alone fails to achieve adequate coronary blood flow in an IRA with a high thrombus load. The management of intracoronary thrombus in STEMI cases continues to be a challenge in interventional cardiology, so a case-by-case approach is needed in order to obtain better results.

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Ethics Committee approval

Our institution exempted ethical approval.

Informed Consent

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Author contribution

IGDS and RZ conceived the idea and mainly designed the report. RZ was involved in patient management of this case and was a major contributor to writing the manuscript. RZ and FT edited the manuscript for publication. IGDS and FT contributed to artwork editing and grammar correction. IGDS reviewed the article before submission. All authors have read and approved the final manuscript.

Availability of data and materials

The datasets used are available from the corresponding author on reasonable request.

Registration of research studies

Not applicable.

Conflict of interest

The authors declare that there is no conflict of interest. Acknowledgment not applicable.

REFERENCES

- Jolly SS, Cairns JA, Yusuf S, et al; TOTAL Investigators. Randomized trial of primary PCI with or without routine manual thrombectomy. *N Engl J Med*. 2015 Apr 9;372(15):1389-98. doi: 10.1056/NEJMoa1415098. Epub 2015 Mar 16. PMID: 25853743; PMCID: PMC4995102.
- Ibanez B, James S, Agewall S, et al; ESC Scientific Document Group. 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). *Eur Heart J*. 2018 Jan 7;39(2):119-177. doi: 10.1093/eurheartj/ehx393. PMID: 28886621.
- Sezer M, Cimen A, Aslanger E, et al. Effect of intracoronary streptokinase administered immediately after primary percutaneous coronary intervention on long-term left ventricular infarct size, volumes, and function. *J Am Coll Cardiol*. 2009 Sep 15;54(12):1065-71. doi: 10.1016/j.jacc.2009.04.083. PMID: 19744615.
- Kumar V, Sharma AK, Kumar T, et al. Large intracoronary thrombus and its management during primary PCI. *Indian Heart J*. 2020 Nov-Dec;72(6):508-516. doi: 10.1016/j.ihj.2020.11.009. Epub 2020 Nov 19. PMID: 33357638; PMCID: PMC7772595.
- Braunwald E, Zipes DP, Libby P, et al. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine, Eleventh Edition. 11th ed. Philadelphia: Elsevier Inc.; 2019. 1944 p.
- Ndrepepa G, Tiroch K, Fusaro M, et al. 5-year prognostic value of no-reflow phenomenon after percutaneous coronary intervention in patients with acute myocardial infarction. *J Am Coll Cardiol*. 2010 May 25;55(21):2383-9. doi: 10.1016/j.jacc.2009.12.054. PMID: 20488311.
- Sianos G, Papafakis MI, Daemen J, et al. Angiographic stent thrombosis after routine use of drug-eluting stents in ST-segment elevation myocardial infarction: the importance of thrombus burden. *J Am Coll Cardiol*. 2007 Aug 14;50(7):573-83. doi: 10.1016/j.jacc.2007.04.059. Epub 2007 Jul 30. PMID: 17692740.
- Kushner FG, Hand M, Smith SC Jr, et al; American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 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 Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2009 Dec 1;120(22):2271-306. doi: 10.1161/CIRCULATIONAHA.109.192663. Epub 2009 Nov 18. Erratum in: *Circulation*. 2010 Mar 30;121(12):e257. Dosage error in article text. PMID: 19923169.
- Napodano M, Dario G, Al Mamary AH, et al. Thrombus burden and myocardial damage during primary percutaneous coronary intervention. *Am J Cardiol*. 2014 May 1;113(9):1449-56. doi: 10.1016/j.amjcard.2014.01.423. Epub 2014 Feb 12. PMID: 24630783.
- Jaffe R, Dick A, Strauss BH. Prevention and treatment of microvascular obstruction-related myocardial injury and coronary no-reflow following percutaneous coronary intervention: a systematic approach. *JACC Cardiovasc Interv*. 2010 Jul;3(7):695-704. doi: 10.1016/j.jcin.2010.05.004. PMID: 20650430.
- Rezkalla SH, Stankowski RV, Hanna J, et al. Management of No-Reflow Phenomenon in the Catheterization Laboratory. *JACC Cardiovasc Interv*. 2017 Feb 13;10(3):215-223. doi: 10.1016/j.jcin.2016.11.059. Erratum in: *JACC Cardiovasc Interv*. 2017 Jun 26;10(12):1282. PMID: 28183461.
- Gibson CM, de Lemos JA, Murphy SA, et al; TIMI Study Group. Combination therapy with abciximab reduces angiographically evident thrombus in acute myocardial infarction: a TIMI 14 substudy. *Circulation*. 2001 May 29;103(21):2550-4. doi: 10.1161/01.cir.103.21.2550. PMID: 11382722.
- Topaz O, Topaz A, Owen K. Thrombus grading for coronary interventions: the role of contemporary classifications. *Interv Cardiol*. 2011 Dec;3(6):705-12. Available from: <http://www.futuremedicine.com/doi/abs/10.2217/ica.11.76>.
- De Luca G, Savonitto S, van't Hof AW, et al. Platelet GP IIb/IIIa Receptor Antagonists in Primary Angioplasty: Back to the Future. *Drugs*. 2015 Jul;75(11):1229-53. doi: 10.1007/s40265-015-0425-7. PMID: 26177890.
- Winchester DE, Wen X, Brearley WD, et al. Efficacy and safety of glycoprotein IIb/IIIa inhibitors during elective coronary revascularization: a meta-analysis of randomized trials performed in the era of stents and thienopyridines. *J Am Coll Cardiol*. 2011 Mar 8;57(10):1190-9. doi: 10.1016/j.jacc.2010.10.030. PMID: 21371635.
- Montalescot G, Zeymer U, Silvain J, et al; ATOLL Investigators. Intravenous enoxaparin or unfractionated heparin in primary percutaneous coronary intervention for ST-elevation myocardial infarction: the international randomised open-label ATOLL trial. *Lancet*. 2011 Aug 20;378(9792):693-703. doi: 10.1016/S0140-6736(11)60876-3. PMID: 21856483.
- Silvain J, Beygui F, Barthélémy O, et al. Efficacy and safety of enoxaparin versus unfractionated heparin during percutaneous coronary intervention: systematic review and meta-analysis. *BMJ*. 2012 Feb 3;344:e553. doi: 10.1136/bmj.e553. PMID: 22306479; PMCID: PMC3271999.
- Capodanno D, Gargiulo G, Capranzano P, et al. Bivalirudin versus heparin with or without glycoprotein IIb/IIIa inhibitors in patients with STEMI undergoing primary PCI: An updated meta-analysis of 10,350 patients from five randomized clinical trials. *Eur Heart J Acute Cardiovasc Care*. 2016 Jun;5(3):253-62. doi: 10.1177/2048872615572599. Epub 2015 Mar 6. PMID: 25746943.
- Alak A, Lugomirski P, Aleksova N, et al. A Meta-Analysis of Randomized Controlled Trials of Conventional Stenting Versus Direct Stenting in Patients With Acute Myocardial Infarction. *The Journal of Invasive Cardiology*. 2015 Sep;27(9):405-409. PMID: 26121706.
- Saad M, Stiermaier T, Fuernau G, et al. Impact of direct stenting on myocardial injury assessed by cardiac magnetic resonance imaging and prognosis in ST-elevation myocardial infarction. *Int J Cardiol*. 2019 May 15;283:88-92. doi: 10.1016/j.ijcard.2018.11.141. Epub 2018 Dec 3. PMID: 30573280.
- Burzotta F, De Vita M, Gu YL, et al. Clinical impact of thrombectomy in acute ST-elevation myocardial infarction: an individual patient-data pooled analysis of 11 trials. *Eur Heart J*. 2009 Sep;30(18):2193-203. doi: 10.1093/eurheartj/ehp348. Epub 2009 Sep 2. PMID: 19726437.
- Fröbert O, Lagerqvist B, Olivecrona GK, et al; TASTE Trial. Thrombus aspiration during ST-segment elevation myocardial infarction. *N Engl J Med*. 2013 Oct 24;369(17):1587-97. doi: 10.1056/NEJMoa1308789. Epub 2013 Aug 31. Erratum in: *N Engl J Med*. 2014 Aug 21;371(8):786. PMID: 23991656.
- Lagerqvist B, Fröbert O, Olivecrona GK, et al. Outcomes 1 year after thrombus aspiration for myocardial infarction. *N Engl J Med*. 2014 Sep 18;371(12):1111-20. doi: 10.1056/NEJMoa1405707. Epub 2014 Sep 1. PMID: 25176395.
- Jolly SS, Cairns JA, Yusuf S, et al. Stroke in the TOTAL trial: a randomized trial of routine thrombectomy vs. percutaneous coronary intervention alone in ST elevation myocardial infarction. *Eur Heart J*. 2015 Sep 14;36(35):2364-72. Available from: <https://academic.oup.com/eurheartj/article-lookup/doi/10.1093/eurheartj/ehv296>.
- Jolly SS, Cairns JA, Yusuf S, et al; TOTAL Investigators. Outcomes after thrombus aspiration for ST elevation myocardial infarction: 1-year follow-up of the prospective randomised TOTAL trial. *Lancet*. 2016 Jan 9;387(10014):127-35. doi: 10.1016/S0140-6736(15)00448-1. Epub 2015 Oct 22. PMID: 26474811; PMCID: PMC5007127.
- Jolly SS, James S, Džavík V, et al. Thrombus Aspiration in ST-Segment-Elevation Myocardial Infarction: An Individual Patient Meta-Analysis: Thrombectomy Trialists Collaboration. *Circulation*. 2017 Jan 10;135(2):143-152. doi: 10.1161/CIRCULATIONAHA.116.025371. Epub 2016 Dec 9. PMID: 27941066.
- Ali A, Cox D, Dib N, et al; AIMI Investigators. Rheolytic thrombectomy with percutaneous coronary intervention for infarct size reduction in acute myocardial infarction: 30-day results from a multicenter randomized study. *J Am Coll Cardiol*. 2006 Jul 18;48(2):244-52. doi: 10.1016/j.jacc.2006.03.044. Epub 2006 Jun 23. PMID: 16843170.
- Migliorini A, Stabile A, Rodriguez AE, et al; JETSTENT Trial Investigators. Comparison of AngioJet rheolytic thrombectomy before direct infarct artery stenting with direct stenting alone in patients with acute myocardial infarction. The JETSTENT trial. *J Am Coll Cardiol*. 2010 Oct 12;56(16):1298-306. doi: 10.1016/j.jacc.2010.06.011. Epub 2010 Aug 5. PMID: 20691553.
- Carrabba N, Parodi G, Maehara A, et al. Rheolytic thrombectomy in acute myocardial infarction: Effect on microvascular obstruction, infarct size, and left ventricular remodeling. *Catheter Cardiovasc Interv*. 2016 Jan 1;87(1):E1-8. doi: 10.1002/ccd.25961. Epub 2015 Jun 24. PMID: 26108162.
- Vergara R, Valenti R, Migliorini A, et al. Rheolytic Thrombectomy for Acute Myocardial Infarction Complicated by Cardiogenic Shock. *J Invasive Cardiol*. 2016 Dec;28(12):E193-E197. Epub 2016 May 15. PMID: 27187985.
- Goudreau E, DiSciascio G, Vetrovec GW, et al. Intracoronary urokinase as an adjunct to percutaneous transluminal coronary angioplasty in patients with complex coronary narrowings or angioplasty-induced complications. *Am J Cardiol*. 1992 Jan 1;69(1):57-62. doi: 10.1016/0002-9149(92)90676-p. PMID: 1729868.
- Keeley EC, Boura JA, Grines CL. Comparison of primary and facilitated percutaneous coronary interventions for ST-elevation myocardial infarction: quantitative review of randomised trials. *Lancet*. 2006 Feb 18;367(9510):579-88. doi: 10.1016/S0140-6736(06)68148-8. Erratum in: *Lancet*. 2006 May 20;367(9523):1656. PMID: 16488801.
- Assessment of the Safety and Efficacy of a New Treatment Strategy with Percutaneous Coronary Intervention (ASSENT-4 PCI) investigators. Primary versus tenecteplase-facilitated percutaneous coronary intervention in patients with ST-segment elevation acute myocardial infarction (ASSENT-4 PCI): randomised trial. *Lancet (London, England)*. 2006 Feb 18;367(9510):569-78. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0140673606681476>.
- Sezer M, Ofiaz H, Gören T, et al. Intracoronary streptokinase after primary percutaneous coronary intervention. *N Engl J Med*. 2007 May 3;356(18):1823-34. doi: 10.1056/NEJMoa054374. PMID: 17476008.
- Kelly RV, Crouch E, Krumnacher H, et al. Safety of adjunctive intracoronary thrombolytic therapy during complex percutaneous coronary intervention: initial experience with intracoronary tenecteplase. *Catheter Cardiovasc Interv*. 2005 Nov;66(3):327-32. doi: 10.1002/ccd.20521. PMID: 16208711.
- Boscarelli D, Vaquerizo B, Miranda-Guardiola F, et al. Intracoronary thrombolysis in patients with ST-segment elevation myocardial infarction presenting with massive intraluminal thrombus and failed aspiration. *Eur Heart J Acute Cardiovasc Care*. 2014 Sep;3(3):229-36. doi: 10.1177/2048872614527008. Epub 2014 Mar 17. PMID: 24637066.
- Moscucci M, Fox KA, Cannon CP, Klein W, López-Sendón J, Montalescot G, White K, Goldberg RJ. Predictors of major bleeding in acute coronary syndromes: the Global Registry of Acute Coronary Events (GRACE). *Eur Heart J*. 2003 Oct;24(20):1815-23. doi: 10.1016/s0195-668x(03)00485-8. PMID: 14563340.
- Neumann FJ, Sousa-Uva M, Ahlsson A, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. *Eur Heart J*. 2019;40(2):87-165.
- TIMI Study Group. The Thrombolysis in Myocardial Infarction (TIMI) trial. Phase I findings. *N Engl J Med*. 1985 Apr 4;312(14):932-6. doi: 10.1056/NEJM198504043121437. PMID: 4038784.