CATHALOGUE

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CASE REPORT

Cracking the code: Effective approaches to no reflow management.

Iffat Aqeel & Muhammad Muneeb
Shalamar Institute of Health Sciences, Lahore-Pakistan.

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Corresponding Author Email:
iffataqeel32@gmail.com

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Abstract

Background: While the focus in ST-segment elevation myocardial infarction (STEMI) often centers on the epicardial coronary arteries, the microvasculature's role is frequently overlooked. The no-reflow phenomenon, characterized by inadequate myocardial perfusion despite successful reopening of the infarct-related artery, remains a significant challenge in STEMI management, impacting patient prognosis. Despite advancements in epicardial vessel reperfusion techniques, no-reflow continues to contribute to adverse outcomes due to microvascular involvement.

Case Presentation: We present the case of a 43-year-old male with a history of smoking and hypertension who presented with two days of chest pain indicative of inferior wall STEMI. He underwent primary percutaneous coronary intervention (PCI) for an occluded lesion in the right coronary artery. Despite successful revascularization, the patient experienced suboptimal coronary flow, leading to complete heart block and worsening chest pain secondary to ischemia. Additional stenting was necessary for symptom relief.

Management and Results: This case underscores the importance of understanding and effectively managing the no-reflow phenomenon in STEMI patients to minimize morbidity and mortality. Strategies to mitigate no-reflow-related mortality include judicious stent inflation, utilization of micro catheters for distal vasodilator delivery, and the administration of multiple vasodilator agents including nitrates, verapamil, epinephrine and glycoprotein IIb/IIIa inhibitors for refractory cases..

Conclusion: No-reflow phenomenon remains a significant contributor to mortality in STEMI patients undergoing percutaneous intervention. By implementing appropriate strategies during PCI, clinicians can mitigate the impact of no-reflow, thereby improving patient outcomes.

Keywords

STEMI, PCI, glycoprotein IIb IIIa inhibitors, intracoronary nitrates, epinephrine

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Introduction

The incidence rates of the no-reflow phenomenon mentioned in the text vary depending on the setting and patient population. In routine percutaneous coronary intervention (PCI), the incidence ranges from 1% to 5% as measured by the Thrombolysis in Myocardial Infarction (TIMI) grade. However, in the acute setting of myocardial infarction, the incidence can be notably higher, ranging from 2.3% to as high as 41%.

It's important to note that achieving a favorable TIMI grade following PCI doesn't necessarily guarantee optimal myocardial perfusion. Even when the arterial patency is restored, myocardial perfusion may remain suboptimal in a significant proportion of cases, with 15% to 40% exhibiting TIMI myocardial perfusion grade (TMPG) 0 to 1. Achieving TMPG grade 3 is crucial to ensure adequate and effective myocardial perfusion.

TIMI (Thrombolysis in Myocardial Infarction) and TMPG (TIMI myocardial perfusion grade) are scoring systems used to assess coronary blood flow and myocardial perfusion after PCI. TIMI grade evaluates the flow in the epicardial coronary artery, while TMPG assesses myocardial perfusion. TIMI grade ranges from 0 (no perfusion) to 3 (normal perfusion), while TMPG also ranges from 0 (no perfusion) to 3 (normal perfusion).

In the context of the no-reflow phenomenon, distal embolization, vasospasm, platelet activation, and inflammatory cell infiltration within the microvasculature can lead to compromised coronary flow despite successful restoration of arterial patency. Early identification and risk assessment of no-reflow in patients undergoing PCI are crucial for guiding treatment strategies and optimizing patient outcomes. Factors such as TIMI flow, thrombus burden, and the duration of coronary occlusion are significant predictors of the likelihood of developing no-reflow, emphasizing the importance of comprehensive pre- and intra-operative evaluations to assess the risk and initiate appropriate interventions promptly. treatment strategies aimed at minimizing its occurrence and optimizing patient outcomes.

Case Presentation

43-year-old male with a five-year history of hypertension and a smoking history of 5 pack-years, arrived at the emergency department of a tertiary care hospital complaining of chest pain for the past two days, with worsening symptoms over the last three hours. The chest pain was described as pressure-like, radiating to the left arm, and associated with diaphoresis. He denied any recent history of trauma, fever, or similar episodes in the past. His medical history was notable for hypertension, for which he was prescribed medication but reported irregular compliance. He had no known allergies and denied any family history of premature coronary artery disease.

On presentation, his vital signs were recorded as follows: a heart rate of 76 beats per minute, blood pressure of 180/90 mmHg, respiratory rate of 14 breaths per minute, and oxygen saturation of 97% on room air. Physical examination revealed no significant abnormalities except for mild distress due to ongoing chest pain. His cardiac auscultation was unremarkable, with no murmurs, rubs, or gallops appreciated. Pulmonary and abdominal examinations were within normal limits.

Laboratory investigations revealed a hemoglobin level of 14 g/dL, a total leukocyte count (TLC) of 10,500/μL, liver function tests (ALT and AST) within normal limits, urea of 50 mg/dL, creatinine of 1.0 mg/dL, sodium of 135 mmol/L, potassium of 4.3 mmol/L, and chloride of 102 mmol/L. An electrocardiogram (ECG) showed ST-segment elevation in leads II, III, and aVF, indicative of inferior wall myocardial infarction, without evidence of right ventricular involvement.

Given the high suspicion for acute coronary syndrome (ACS), the patient was promptly started on antiplatelet therapy, including aspirin and clopidogrel, and intravenous nitroglycerin for chest pain relief. He was then transferred urgently to the catheterization laboratory for primary percutaneous coronary intervention (PCI).

In the catheterization laboratory, left heart catheterization revealed moderate disease in the mid segments of the left anterior descending artery (LAD) and left circumflex artery (LCx). The right coronary artery (RCA) demonstrated significant plaque rupture and thrombotic stenosis in the mid-segment, with TIMI II distal flow. Initial attempts at direct stenting in the RCA lesion were unsuccessful due to severe calcification and tortuosity, necessitating pre-dilatation with a semi-non-compliant balloon (2.5x15 mm at 10 ATM) followed by deployment of a drug-eluting stent (DES) (3.5x33 mm at 12 ATM). However, post-procedure angiography revealed persistent TIMI grade 1 flow and TIMI myocardial perfusion grade (TMPG) 0, suggestive of the no-reflow phenomenon.

Subsequently, the patient developed complete heart block with worsening chest pain. Intracoronary nitroglycerin (200 μg) was administered to alleviate coronary artery spasm, and a bolus dose of intracoronary tirofiban (25 mg/kg) was given to inhibit platelet aggregation and promote coronary microvascular perfusion. Due to the contraindication of adenosine or verapamil in the setting of complete heart block, intracoronary epinephrine (100 μg in two divided doses) was administered to further augment myocardial perfusion.

A repeat angiogram revealed progression of thrombus burden in the proximal segment of the RCA, prompting the deployment of another DES (3.5x24 mm at 12 ATM). Post-intervention angiography demonstrated TIMI grade III flow and TMPG 1, with resolution of chest pain and complete heart block. The patient was then admitted to the coronary care unit for further monitoring. Over the next 72 hours, the patient remained hemodynamically stable with a heart rate of 65 beats per minute and blood pressure of 130/90 mmHg. He was managed With IV glycoprotein IIb/IIIa inhibitors infusion followed by transition to dual antiplatelet therapy (aspirin and clopidogrel), high-intensity statin therapy, and oral antihypertensive medication. Smoking cessation counseling was provided, and arrangements were made for outpatient cardiac rehabilitation and follow-up.

Diagnostic Assessment

Upon admission, a comprehensive diagnostic workup was initiated to evaluate the patient's cardiac status and ascertain the underlying etiology of his presenting symptoms. This assessment began with a detailed clinical evaluation, focusing on the characteristics of chest pain, associated symptoms, and cardiovascular risk factors such as hypertension and smoking history. Utilizing the Canadian Cardiovascular Society (CCS) angina classification system, the severity of chest pain was determined. Vital signs were measured, and a systemic examination was conducted to detect any signs of cardiac dysfunction. Laboratory investigations including hemoglobin, total leukocyte count, liver function tests, renal function tests, and electrolyte levels were performed to assess for anemia, inflammation, hepatic and renal function, and electrolyte disturbances, respectively.

Electrocardiography (ECG) was conducted to evaluate for evidence of myocardial ischemia or infarction, which in this case revealed inferior wall myocardial infarction without right ventricular involvement. Further imaging studies, particularly coronary angiography via left heart catheterization, visualized the coronary arteries and assessed for significant coronary artery disease. The angiogram revealed moderate disease in the mid-segments of the left anterior descending and left circumflex arteries, as well as significant plaque rupture and thrombotic stenosis in the mid-segment of the right coronary artery.

Based on the clinical presentation, ECG findings, and evidence of coronary artery disease on coronary angiography, a diagnosis of acute coronary syndrome (ACS) was established. Severity of coronary artery disease was assessed using the TIMI grading system, indicating compromised myocardial perfusion with TIMI II distal flow in the right coronary artery and TMPG 0. This comprehensive diagnostic assessment provided valuable insights into the patient's cardiac status, guiding subsequent therapeutic interventions

aimed at optimizing myocardial perfusion and reducing the risk of adverse cardiac events.

Therapeutic Intervention

The choice of pharmacological agents for adjunctive therapy during the procedure was based on several considerations. Intracoronary nitrate was administered to promote coronary artery vasodilation and improve myocardial perfusion. This was particularly important in response to the patient's elevated blood pressures, as vasodilation helps to reduce coronary resistance and enhance blood flow to the myocardium. Nitrate administration is a standard practice in PCI procedures to optimize coronary perfusion.

The administration of intracoronary tirofiban aimed to inhibit platelet aggregation and reduce thrombus burden, thereby promoting coronary flow and preventing further ischemic complications. Tirofiban is a glycoprotein IIb/IIIa inhibitor commonly used in PCI to prevent platelet aggregation and thrombus formation, especially in high-risk patients with ACS.

Intracoronary epinephrine was administered due to the presence of complete heart block and contraindications to adenosine or verapamil. Epinephrine helps to promote myocardial contractility and improve coronary perfusion. While adenosine and verapamil are also vasodilators commonly used in PCI procedures, they were contraindicated in this case, necessitating the use of epinephrine as an alternative.

Challenges encountered during the procedure included the unsuccessful attempts to directly stent the lesion in the right coronary artery due to calcified lesions. This necessitated pre-dilatation of the lesion using a semi-non-compliant balloon to facilitate stent placement and improve coronary blood flow. Additionally, progression of thrombus in the proximal segment of the right coronary artery required the deployment of another drug-eluting stent. These challenges were addressed by adapting the intervention strategy and selecting appropriate devices and pharmacological agents to optimize procedural outcomes and ensure adequate myocardial perfusion.

Following the interventions, the patient was closely monitored for signs of recurrent ischemia, arrhythmias, or procedural complications in the coronary care unit. Continuous monitoring of vital signs was performed to ensure hemodynamic stability and adequate tissue perfusion. Upon discharge, the patient was prescribed dual antiplatelet therapy, antihypertensive medication, and high-dose statins to optimize secondary prevention and reduce the risk of recurrent cardiovascular events. Smoking cessation counseling was also provided to mitigate further cardiovascular risk factors. These comprehensive therapeutic interventions underscore the importance of multidisciplinary collaboration and personalized care in ensuring optimal management of patients with ACS undergoing PCI.

Follow-U and Outcomes

Following the acute intervention and initial hospitalization, the patient underwent a structured follow-up plan to monitor his clinical progress and optimize long-term outcomes. In the coronary care unit (CCU), the patient remained under close observation for 72 hours post-procedure. Continuous telemetry was employed to assess vital signs, cardiac rhythm, and clinical status, ensuring prompt detection of any signs of recurrent ischemia, arrhythmias, or procedural complications. Throughout the CCU stay, the patient's hemodynamics remained stable, with a heart rate of 65 beats per minute and blood pressure maintained at 130/90 mmHg, indicative of successful management of the acute coronary syndrome and procedural complications.

Following the intervention, the patient reported resolution of chest pain and complete heart block, indicating successful restoration of coronary blood flow and myocardial perfusion. Post-intervention angiography revealed TIMI grade III flow in the right coronary artery and a TIMI myocardial perfusion grade of 1, confirming adequate coronary blood flow and myocardial tissue perfusion. The patient was discharged on a

regimen of dual antiplatelet therapy, including aspirin and a P2Y12 inhibitor, along with oral antihypertensive medication and high-dose statins to manage hypertension, optimize lipid levels, and reduce the risk of recurrent cardiovascular events.

Furthermore, smoking cessation counseling was provided to encourage the patient to quit smoking and adopt a heart-healthy lifestyle. Dietary recommendations and exercise counseling were also offered to promote cardiovascular health and prevent future cardiac events. Scheduled regular outpatient follow-up visits with the cardiologist were planned to monitor medication adherence, cardiovascular risk factors, and overall clinical progress. These appointments included clinical assessment, medication adjustment if necessary, and cardiovascular imaging studies as indicated. With appropriate medical therapy, lifestyle modifications, and close outpatient follow-up, the patient's long-term prognosis was expected to be favorable, with a reduced risk of recurrent cardiovascular events and improved overall quality of life.

Discussion

The no-reflow phenomenon, characterized by the inability to adequately perfuse previously ischemic tissue despite restoration of patency in the infarct-related artery, presents a significant challenge in the management of acute myocardial infarction. Studies conducted detailed histologic and electron microscopic analyses of myocardium exhibiting no reflow, revealing microvascular injury as a central mechanism underlying this phenomenon[6]. The study identified areas of localized endothelial swelling with formation of blebs, leading to obstruction of small vessels and capillaries[7]. Other observed microvascular damage included loss of pinocytotic vesicles, rupture of vessel walls with extravasation of erythrocytes, fibrin deposition, platelet clumping, and rouleaux formation of red blood cells. Edema within the endothelium and myocardium suggested initial flow into the region, subsequently ceasing due to microvascular damage or compression from swollen myocytes.

Resolution of ST-segment elevations on electrocardiography serves as a key marker of tissue-level reperfusion, but persistence of elevations and ongoing chest pain may indicate either epicardial artery occlusion or microvascular obstruction. The Thrombolysis in Myocardial Infarction (TIMI) flow grade and myocardial blush grade (TMPG) are established methods for assessing coronary flow and myocardial contrast density, respectively[8,9]. Clinical risk factors associated with no-reflow development include diabetes mellitus, advanced age, low ejection fraction, longer stent length, large thrombus burden, prolonged pain-to-balloon time, delayed reperfusion time, and initial TIMI 1 flow grade.

Preventive strategies for no-reflow should be integrated into pre-percutaneous coronary intervention (PCI) planning, particularly in patients with ST-segment elevation myocardial infarction (STEMI), delayed presentation, and extensive thrombus burden. During primary PCI, avoidance of high-pressure post-dilatation and consideration of embolic protection devices are recommended. Shorter burr runs and lower burr speeds during atherectomy can reduce the risk of no reflow secondary to debris embolization. Pharmacological therapies for no-reflow include vasodilators (e.g., adenosine, epinephrine, verapamil, nitroprusside) and antiplatelets (e.g., glycoprotein IIb/IIIa inhibitors). Mechanical thrombus aspiration before PCI has shown promise in high thrombus burden ACS patients, facilitating thrombus removal and restoring normal myocardial perfusion. Clinical trials such as the AMISTAD II trial and RESTORE trial have demonstrated the efficacy of certain pharmacological agents, while the CHEETAH Trial supports the use of mechanical thrombus aspiration in select patient populations[9-11].

Conclusion

The no-reflow phenomenon presents a significant challenge in acute myocardial infarction management, characterized by inadequate tissue perfusion despite restored artery patency. Microvascular injury plays a central role, emphasizing the need for precise clinical assessment and preventive strategies, including

pre-procedural planning and pharmacological interventions. Further research is warranted to refine treatment approaches and improve patient outcomes. By employing multidisciplinary approaches and emerging technologies, clinicians can better address the complexities of no-reflow, ultimately reducing associated morbidity and mortality.

Learning points

- **Recognition of Acute Coronary Syndrome (ACS):** Prompt recognition and diagnosis of ACS are essential for timely intervention and optimization of outcomes. Clinical assessment, including history-taking, physical examination, and electrocardiography, plays a crucial role in identifying patients at risk.
- **Importance of Invasive Coronary Angiography:** Invasive coronary angiography provides valuable information regarding the extent and severity of coronary artery disease, guiding treatment decisions and interventions. Assessment of coronary anatomy and identification of culprit lesions are crucial steps in the management of ACS.
- **Role of Primary Percutaneous Coronary Intervention (PCI):** Primary PCI is the preferred reperfusion strategy in patients with ST-segment elevation myocardial infarction (STEMI) and should be performed promptly to restore coronary blood flow and salvage myocardium. Adjunctive pharmacotherapy, including antiplatelet agents and glycoprotein IIb/IIIa inhibitors, is integral to optimizing outcomes and preventing stent thrombosis.
- **Management of No-Reflow Phenomenon:** No-reflow phenomenon, characterized by inadequate myocardial perfusion despite successful revascularization, poses a significant challenge in STEMI management. Strategies to mitigate no-reflow risk include intracoronary vasodilators, glycoprotein IIb/IIIa inhibitors, and mechanical measures to improve microvascular perfusion.
- **Multidisciplinary Approach to Care:** Optimal management of ACS requires a multidisciplinary approach involving cardiologists, interventionalists, critical care specialists, and nursing staff.
  Collaboration among team members facilitates timely decision-making, coordinated care delivery, and comprehensive patient management.
- **Long-Term Secondary Prevention:** Secondary prevention strategies, including dual antiplatelet therapy, statin therapy, blood pressure control, smoking cessation, and lifestyle modifications, are essential for reducing the risk of recurrent cardiovascular events. Regular outpatient follow-up and patient education are key components of long-term management, promoting medication adherence, lifestyle changes, and ongoing risk factor modification.
- **Patient-Centered Care:** Patient-centered care involves engaging patients in shared decision-making, addressing their concerns and preferences, and empowering them to actively participate in their own care.
- Education regarding the importance of medication adherence, lifestyle modifications, and regular follow-up promotes patient understanding and compliance, leading to improved outcomes and enhanced quality of life.

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Figure/Video

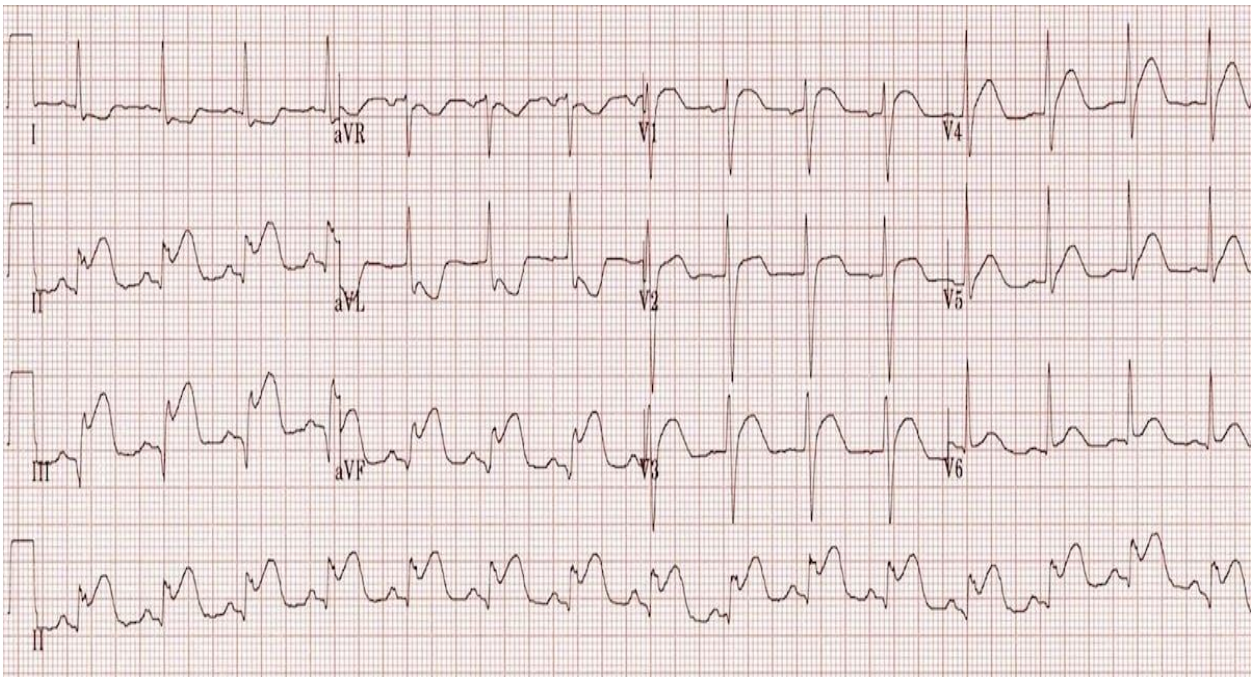

Figure 1: ECG showing Inferior Wall Myocardial Infarction

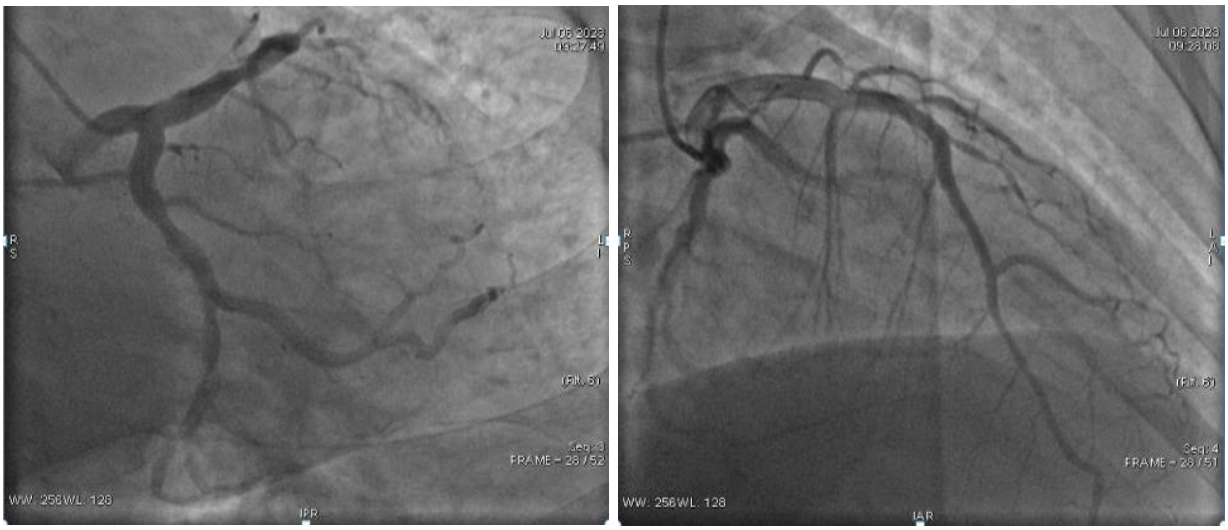

Figure 2A: Left Heart Catheterization - Moderate Disease in Mid Segment of Left Anterior Descending Artery

Figure 2B: Left Heart Catheterization - Moderate Disease in Mid Segment of Left Circumflex Artery

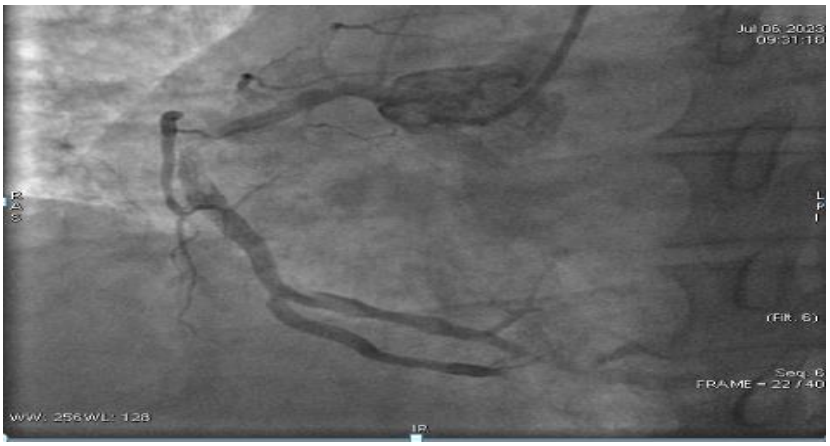

Figure 3: Left Heart Catheterization - Right Coronary Artery Dominant with Significant Plaque Rupture and Thrombotic Stenosis

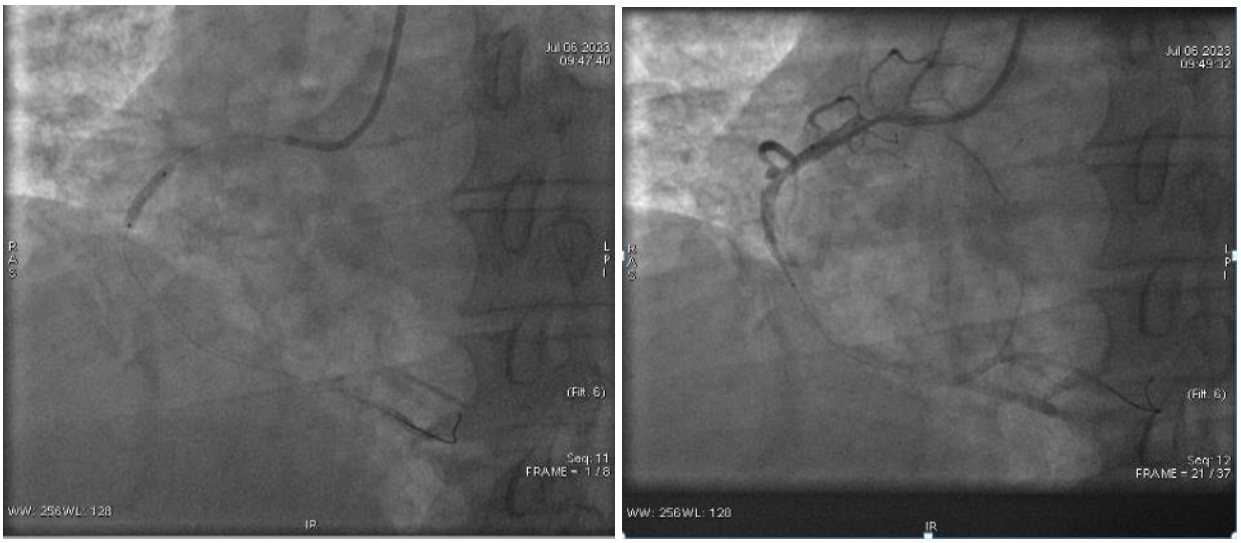

Figure 4A: Stent Placement in Right Coronary Artery - Pre-dilatation with Semi Non-Compliant Balloon

Figure 4B: Stent Placement in Right Coronary Artery - Lesion Stented with Drug Eluting Stent

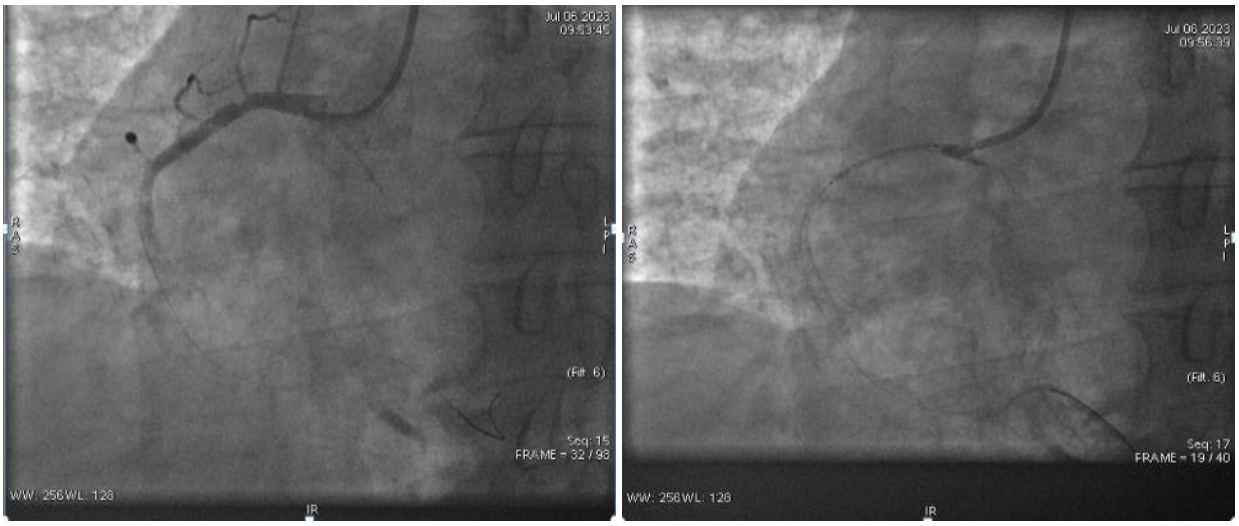

Figure 5A: Annexure G: Stent Placement in Right Coronary Artery - Check Injection Showing Distal Flow with TIMI Grade 1 and TMPG 0

Figure 5B: Additional Stent Placement in Right Coronary Artery - Resolution of Thrombus in Proximal Segment

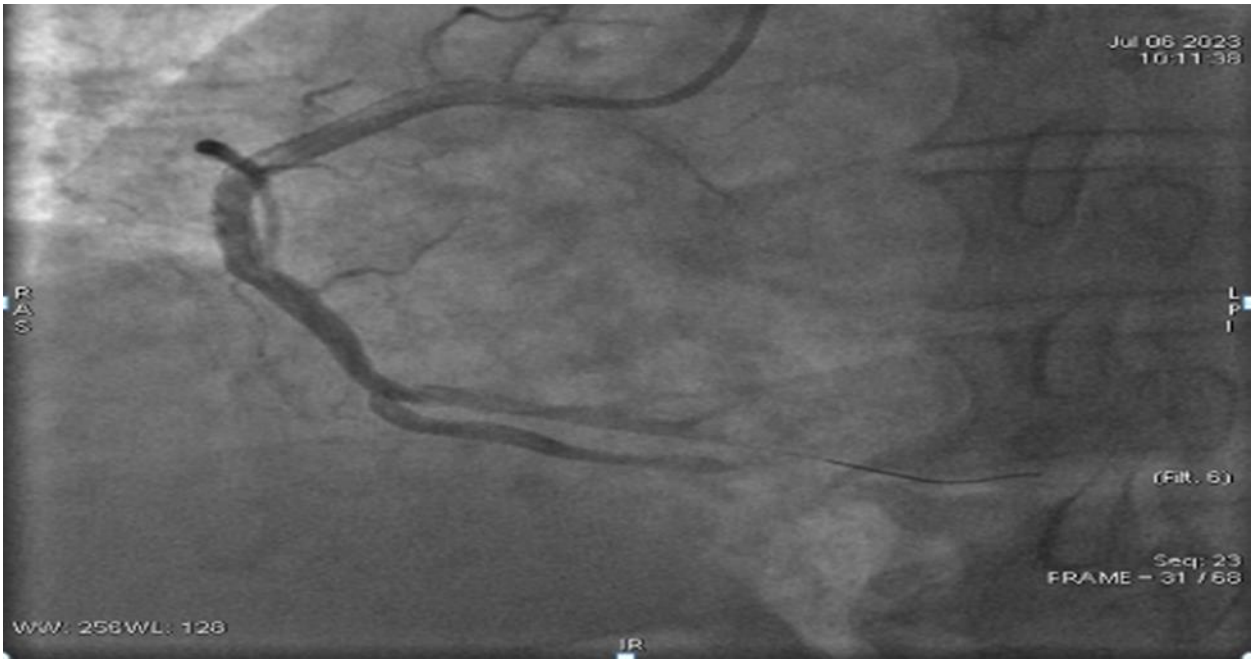

Figure 6: Additional Stent Placement in Right Coronary Artery - Check Injection Showing TIMI Grade III and TMPG 1