

Primary Percutaneous Coronary Intervention in Patients With ST-Segment–Elevation Myocardial Infarction and Concurrent Active Gastrointestinal Bleeding

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Reperfusion therapy via percutaneous coronary intervention (PCI) as the preferred method of treatment for an acute ST-segment–elevation myocardial infarction (STEMI) requires the use of potent antiplatelet agents (eg, aspirin, P2Y₁₂ inhibitors, and GPIIb/IIIa antagonists) and anticoagulant therapies, including heparin or bivalirudin,¹ both of which have potential risk of bleeding. An increased bleeding risk in some patients with STEMI makes the use of antiplatelet/anticoagulant agents a relative or absolute contraindication to PCI.

Acute gastrointestinal bleed (GIB) in the acute coronary syndrome setting is a particularly vexing situation requiring the balancing of risk/benefit for each condition and a resultant high-risk decision for the treatment of either condition. Clinically significant GIB may present concomitantly in an estimated 1.3% of cases of acute coronary syndrome, based on the Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) trial.² Guidance concerning optimal management and ensuing strategies in patients with STEMI and contraindications to antiplatelet/antithrombotic agents, specifically with respect to patients who present with parallel and active GIB from literature is scant at best.

In this report, we discuss the challenges of managing competing treatment strategies in a patient who presents with concurrent STEMI and acute active GIB.

Case Presentation

A 68-year-old woman presented to the emergency room with severe nausea and vomiting, accompanied by extreme fatigue, dizziness, and light headedness. The symptoms began 7 hours earlier and had been gradually increasing in severity. Vomitus was nonbilious, nonbloody, without coffee ground appearance. She denied chest pain or pressure, palpitations, orthopnea, and reported only mild dyspnea.

Two weeks before presentation, the patient described having melena. Her primary care physician documented hemoglobin of 5.1 g/dL. However, the patient refused a blood transfusion and preferred therapy with only iron infusion. An esophagogastroduodenoscopy revealed no abnormalities. Colonoscopic imaging was inconclusive because of inadequate gastrointestinal preparation.

In 2011, the patient had PCI with a drug-eluting stent to the mid left anterior descending (LAD) artery, 2 drug-eluting stents to the left circumflex artery, and received clopidogrel 75 mg/d and aspirin (81 mg/d). Hypertension, hypercholesterolemia, and insulin-dependent diabetes mellitus were treated in the standard fashion. There was no history of smoking, peripheral artery disease, or family history of atherosclerosis.

The patient was a thin short woman with a body mass index of 18.5. In the emergency room, the blood pressure was 88/49 mm Hg and the heart rate 54 bpm. She was drowsy with notable conjunctival pallor. The jugular venous pressure was estimated at 11 cm above the sternal angle. The heart rate was regular with normal S1 and S2, without murmurs, rubs, or gallops. The lungs were clear. The abdominal examination was benign with normal bowel sounds. There was no evidence of gross bleeding on rectal examination. The lower extremities were free of edema. The peripheral pulses were normal as was the neurological examination.

A chest radiograph was normal. The initial ECG demonstrated sinus bradycardia with inferior ST-segment–elevation with an accompanying right ventricle (RV) infarct pattern as depicted on the subsequent right-sided ECG (Figure 1). Cardiac troponin was elevated to 2.8 (ng/mL). Hemoglobin was 4.1 (g/dL) and hematocrit was 17%. A fecal occult blood test was positive.

The patient continued to be hypotensive with progressive bradycardia with intermittent Mobitz type II atrio-ventricular heart block. Although intravenous fluid resuscitation and aspirin (325 mg/PO) were administered, a dopamine drip was initiated and a temporary intravenous pacemaker was placed. With decreasing mental status, she was intubated and placed on mechanical ventilation.

Discussion

Dr Mohar: Should this patient proceed to the catheterization laboratory or should the GIB be addressed first?

Dr Seto: The decision of whether to bring any patient to the catheterization laboratory should be based on the operator's best judgment as to the risks of angiography and PCI, versus the risk of not performing PCI, considering the limited medical therapy that could be administered to this patient.

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Figure 1. ECG on presentation. **A**, 12-lead ECG. **B**, Right-sided 12-lead ECG.

Thrombolytics are obviously contraindicated with recent bleeding and have an unfavorable risk/benefit profile in this patient. Anticoagulation without PCI would likely be ineffective for STEMI treatment yet incur nearly the same bleeding risk as PCI. At the most basic level, opening a vessel with PCI should be the optimal strategy as catheters, wires, balloons, and aspiration devices by themselves carry a minimal risk of bleeding. It is the adjunctive pharmacotherapy of anticoagulation and antiplatelet agents that connotes a higher risk of further bleeding in the patient with GIB, and these can generally be managed with transfusion and supportive measures.

In several respects, the patient's presentation is helpful. Her history of several weeks of melena suggests a chronic rather than acute GIB. Her marked anemia in the absence of overt hematemesis, gross melena, or visible blood per rectum confirms a chronic GIB. The negative esophagogastroduodenoscopy definitively excluded a significant upper gastrointestinal source, but this could be inferred from her chronic presentation. In the absence of an esophagogastroduodenoscopy, a brief nasogastric tube saline lavage and rectal examination can be used to exclude acute GIB. A chronic GIB is most likely from small lower GIB source and we speculated less likely to become life threatening even with anticoagulation. In a patient with active bleeding, the risks would be significantly higher.

Deferring intervention might be reasonable if the patient had an active GIB. If the patient had an uncomplicated inferior STEMI, the prognosis is favorable (2%–9% mortality). However, the presence of RV infarction with cardiogenic shock, and severe heart block strongly suggests that the patient is unlikely to survive without intervention.

The Early Revascularization in Acute Myocardial Infarction Complicated by Cardiogenic Shock (SHOCK) trial clearly demonstrated the benefit of PCI in these high-risk patients.³ However, too often nonclinical factors affect clinical judgment in these situations, including risk selection, fear of litigation, public reporting, and even time and day of presentation. Recent data suggest that public reporting leads to reduced use of PCI in high-risk patients and increased in-hospital mortality among patients with acute MI.⁴ As professionals, cardiologists need to always focus on what gives their

patients the best hope of survival, while also advocating for systems of care that make that possible.

Dr Kern: Cardiogenic shock because of inferior MI with probable RV infarction requires immediate volume loading, inotropes, vasopressors, and perhaps RV mechanical support followed by reperfusion with PCI. The increased mortality of this presentation makes the decision to intervene with PCI more pressing than an uncomplicated inferior STEMI. Complicating such an approach, of course is the critical reduction in hemoglobin with decreased oxygen carrying capacity and the recent bleeding albeit from a chronic yet unknown source in the lower gastrointestinal tract. Reconciling the opposing treatment strategies is a true dilemma. Despite a discussion of nonmedical considerations, the least of which is the influence of public reporting, I favor stabilization with fluids and blood transfusion first to permit the vasopressors to be more effective, and after achieving a mean arterial pressure of at least 70 mm Hg, reevaluate degree of ST elevation. After transfusions, I think we could get by with immediate PCI, perhaps without a stent to minimize the post procedural need for intense anticoagulation accepting the fact that this would increase the risk of abrupt vessel closure.

Dr Mohar: The patient was referred for coronary angiography and possible PCI. Four units of packed red blood cells were ordered and transfusion began en route to catheterization suite. The transfusions continued through the periprocedural period.

Coronary angiography demonstrated focal distal left main stenosis (30%–40% diameter narrowed) and proximal LAD artery stenosis (50%–60%) with diffuse nonobstructive luminal irregularities throughout. The left circumflex artery had distal vessel stenosis (90%) proximal to the bifurcation of the 2nd obtuse marginal artery. Old stents in the LAD and left circumflex arteries were patent (Figure 2; Movies I–IV in the Data Supplement). Right coronary artery (RCA) angiography revealed a flush occlusion of the proximal vessel (Figure 3A; Movie V in the Data Supplement). Left ventriculography showed a left ventricular ejection fraction of 50% with moderate to severe hypokinesis of the basal, mid, and distal inferior wall (Movie VI in the Data Supplement).

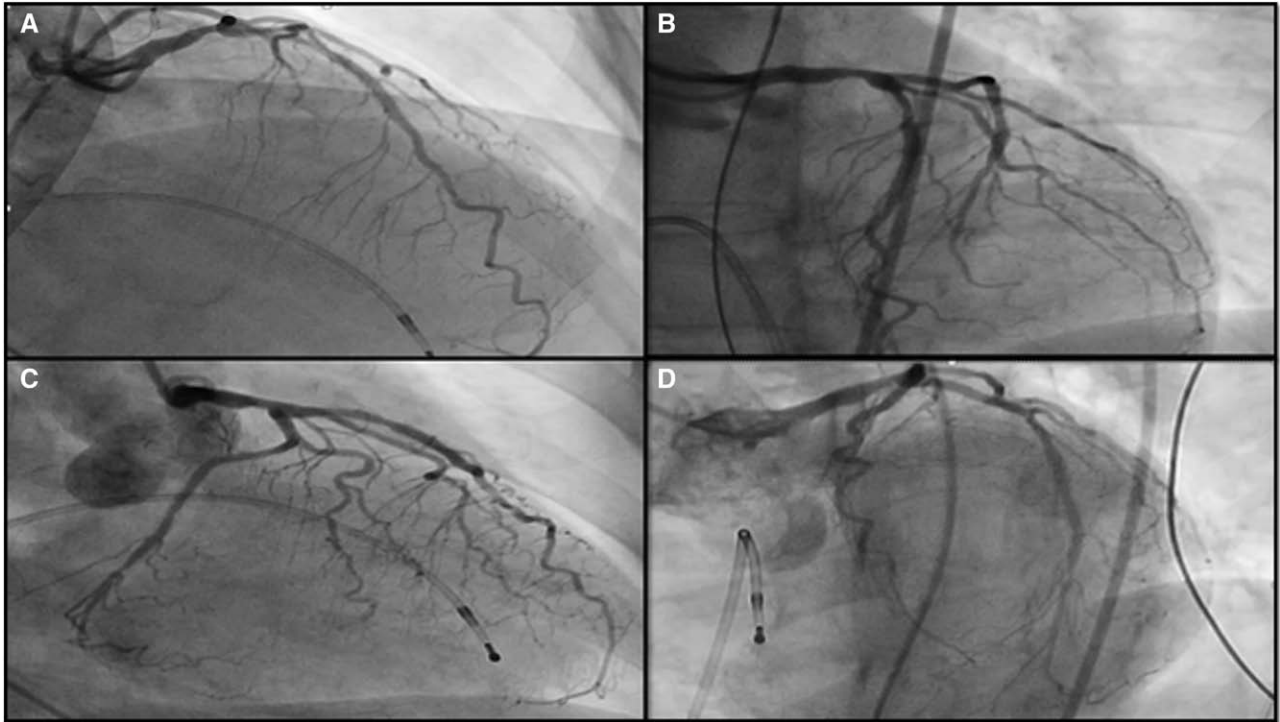


Figure 2. Left coronary artery angiogram. **A**, Right anterior oblique (RAO) view with cranial projection. **B**, Left anterior oblique (LAO) view with cranial projection. **C**, RAO view with caudal projection. **D**, LAO view with caudal projection.

Dr Mohar: Should we perform PCI or balloon angioplasty only, to temporize and avoid Dual antiplatelet therapy (DAPT)? What is the role of thrombus aspiration in this scenario with active GIB?

Dr Seto: On the basis of the history as discussed above, I think that the patient would most likely be able to tolerate DAPT, however, this is far from certain. Opening the vessel with either thrombus aspiration or balloon angioplasty would

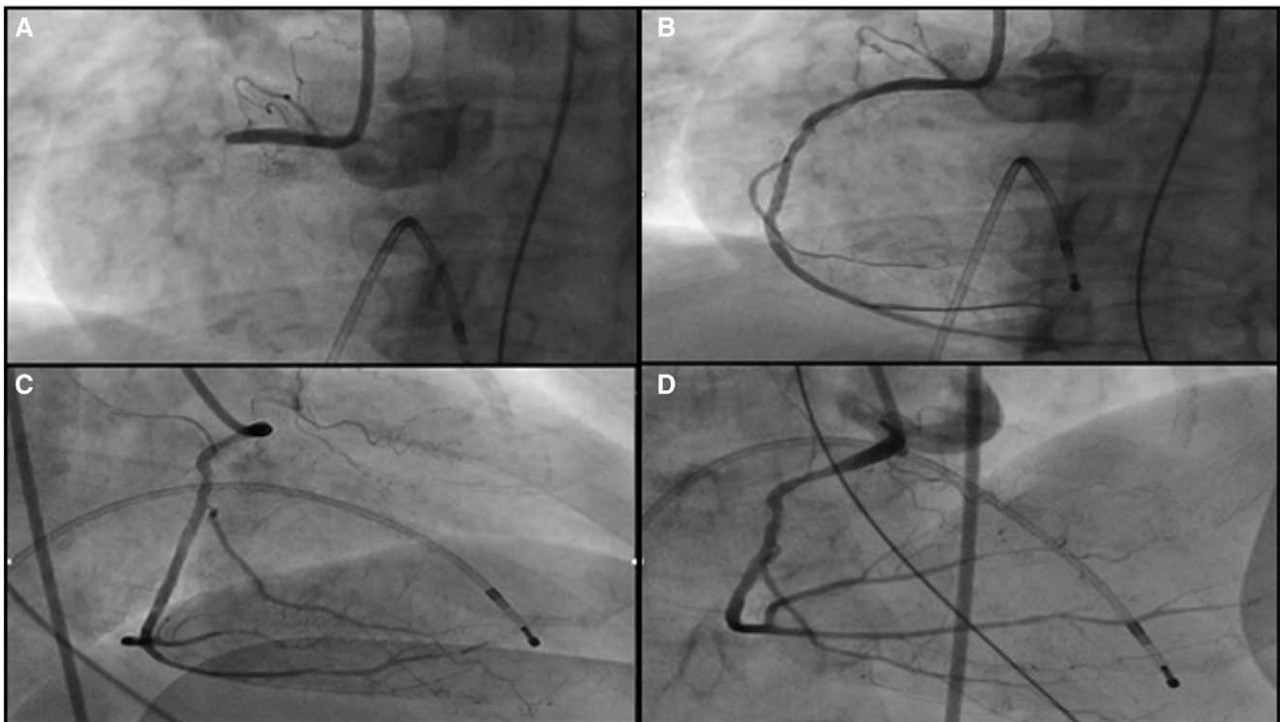


Figure 3. Right coronary artery angiography. **A**, Left anterior oblique (LAO) view. **B**, LAO view after percutaneous transluminal coronary angioplasty (PTCA). **C**, Right anterior oblique (RAO) view post PTCA. **D**, Anterior posterior view with cranial projection post PTCA.

be an appropriate first step. Deployment of a stent could be contingent on the degree of elastic recoil, residual thrombus, or Thrombolysis in Myocardial Infarction (TIMI) flow in the treated vessel. If one thinks that a stent has a higher risk of thrombosis, or a longer duration of such risk, compared with plain old balloon angioplasty, then reopening the vessel with angioplasty or thrombectomy alone could be a reasonable option. For the near term (several weeks), though, an uncovered ruptured plaque in a partially expanded vessel from angioplasty probably carries a similar risk of thrombosis as a stent, and would similarly benefit from DAPT.

The Thrombus Aspiration in ST-Elevation Myocardial Infarction in Scandinavia (TASTE) and A Randomized Trial of Routine Aspiration Thrombectomy With Percutaneous Coronary Intervention (PCI) Versus PCI Alone in Patients With ST-Elevation Myocardial Infarction Undergoing Primary PCI (TOTAL) trials have conclusively demonstrated no benefit of routine manual thrombus aspiration with PCI compared with PCI alone, although stenting was performed in the vast majority of patients.^{5,6} The small AngioJet Rheolytic Thrombectomy Before Direct Infarct Artery Stenting in Patients Undergoing Primary PCI for Acute Myocardial Infarction (JETSTENT) trial suggested a potential benefit of rheolytic thrombectomy with stenting.⁷ If the hope is to avoid stenting and minimize bleeding, I would recommend thrombus aspiration in this case to remove the large volume of thrombus present and maximize the angiographic result. Doing so could potentially minimize the risk of recurrent thrombosis and minimize the need for subsequent antithrombotics by removing any nidus for thrombus formation mechanically.

Dr Kern: Although the patient has 3-vessel coronary artery disease, the acute problem producing the shock-like state is the RCA thrombosis. The left main and LAD disease likely contribute to impaired septal function and hemodynamic compromise of the RV infarction. At this point, PCI of the RCA and other hemodynamically significant coronary lesions is indicated. One can consider using fractional flow reserve for intermediate lesions of noninfarct-related arteries as shown by the Primary PCI in Patients With ST-Elevation Myocardial Infarction and Multivessel Disease: Treatment of Culprit Lesion Only or Complete Revascularization (DANAMI3-PRIMULTI) Study.⁸ After the blood transfusion, I would proceed with the RCA with a small balloon inflation followed by thrombus aspiration based on the angiographic appearance. It would be unusual to have a thrombus-free active plaque afterward and the decision to defer placing a stent would require a near normal angiographic appearance.

After the RCA is treated, the consideration to staging of the PCI of the remaining vessel narrowings will be complex. Guidelines suggest that complete revascularization in patients in shock improves outcome over incomplete revascularization. In this setting, the bigger question is what is the intensity of the anticoagulant regimen for PCI and what agents would be best should GIB reactivate?

Dr Mohar: The RCA was treated using a JR4 guide catheter, a 0.014 mm guidewire and manual thrombus aspiration catheter, which yielded a moderate amount of red thrombus. As the first step, coronary balloon only angioplasty was performed (2.5×15 mm TREK balloon, Abbott Vascular). TIMI

3 flow was established. A long eccentric residual proximal to mid-RCA stenosis of 60% to 70% remained (Figures 3; Movies VII–IX).

Dr Mohar: What approach should be recommended next? Stent or a balloon only PCI? DAPT or not?

Dr Seto: Regardless of whether the patient received a stent or just balloon angioplasty for this STEMI, she would benefit from DAPT to reduce the risk of recurrent MI and thrombosis, typically with aspirin and an oral ADP antagonist. In this instance based on its rapid onset of action, reversible binding to the P2Y₁₂ receptor, and slightly faster offset compared with clopidogrel, I would suggest ticagrelor.

Although her bleeding seems to be chronic on presentation, if this assumption is incorrect, then the prolonged effect of the oral ADP antagonist may cause more severe bleeding. With the uncertainty of her bleeding risk, the ideal antiplatelet agent would be either short acting or reversible, so that it might be turned off in case of bleeding. To date, the only available intravenous antiplatelet agents were the glycoprotein inhibitors, which nearly completely inhibit platelet aggregation, have effects for several hours after discontinuation, and are not easily reversible. As a result, glycoprotein inhibitors would be inappropriate for this patient with recent bleeding. In contrast, the intravenous ADP antagonist cangrelor has a short duration of action (3-minute half-life), and arguably may cause less bleeding because of inhibition only of ADP-induced platelet aggregation rather than the downstream platelet glycoprotein IIb/IIIa receptor.⁹ With the recent US Food and Drug Administration approval of cangrelor, if the operator chooses not to administer oral DAPT, I would suggest substituting cangrelor for 24 to 48 hours as a test of whether oral DAPT could be tolerated, then administering oral ticagrelor. The empirical addition of a proton pump inhibitor to DAPT would be reasonable to reduce the risk of upper GIB, according to the Clopidogrel and the Optimization of Gastrointestinal Events (COGENT-1) study.¹⁰

The role of anticoagulation after PCI to prevent recurrent thrombosis in this patient is unclear. Historically, continuation of anticoagulation after successful percutaneous transluminal coronary angioplasty only increased vascular bleeding complications without providing ischemic benefits. Some operators use intravenous unfractionated heparin as a bridging agent when oral DAPT is high risk, but evidence supporting this approach is lacking.

Dr Kern: At this point, it is unknown whether heparin or bivalirudin might be the better intraprocedural anticoagulation. I would favor heparin because it can be quickly reversed in the event of massive bleeding. In addition, I would be leaning toward achieving an optimal balloon only result to avoid prolonged DAPT, until the cause of the chronic bleeding is determined. A short-acting P2Y₁₂ inhibitor-like ticagrelor seems the best choice. Certainly with more experience with IV cangrelor, we might select this agent during the first days after PCI.

Dr Mohar: After 4 U of packed red blood cells, the hemoglobin increased to 8.6 g/dL. A bolus of unfractionated heparin was given and heparin infusion periprocedurally was continued as serial hemoglobin and hematocrit measurements were monitored. Heparin was discontinued the following morning

after serial measurements revealed a stable hemoglobin and hematocrit. After a thorough discussion of risks and benefits using a multidisciplinary approach, which included gastrointestinal service consultation, DAPT with aspirin and clopidogrel was initiated and planned to continue for at least 30 days.

At 1-month follow-up after percutaneous transluminal coronary angioplasty, there were no episodes of melena or signs of GIB. A colonoscopy revealed a large circumferential mass located at the sigmoid colon. DAPT was held for 5 days before surgical resection. Pathology specimens demonstrated adenocarcinoma with favorable T2N0MX staging, which did not necessitate adjuvant chemotherapy. She resumed her DAPT in the postoperative period without subsequent episodes of GIB and has maintained an excellent exercise capacity without cardiac complaints.

Conclusions

STEMI, especially when complicated by cardiogenic shock (either from LAD or RCA with RV infarction) must be managed with immediate revascularization to increase likelihood of survival. In a patient with STEMI and GIB, managing the conflicting goals related to appropriate anticoagulation is a dilemma, which needs full assessment of risk and benefits of each condition individually. A successful PCI depends on maintaining an adequate blood pressure, which in the case of GIB also required fluids and blood transfusions and vasopressor support. Serious concern about the negative consequences of antiplatelet and antithrombin agents further complicates the technical approach. The fortunate stabilization of the patient with quiescent controlled subacute bleeding permitted use of needed antiplatelet and antithrombin agents for percutaneous transluminal coronary angioplasty. After recovery from surgery for adenocarcinoma of the bowel, the evaluation for remaining coronary artery disease can proceed in a routine fashion.

Disclosures

Dr Kern is consultant to St. Jude Medical Inc, Volcano Therapeutics Inc, ACIST Medical Inc, and Merit Medical Inc. Dr Seto is a consultant to Medicare International Inc and Acist Medical Inc in the past 12 months. The other author reports no conflicts.

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SUPPLEMENTAL MATERIAL

Videos Legend:

Video 1: Left Coronary Artery Angiogram; Left Anterior Oblique (LAO) view with caudal projection

Video 2: Left Coronary Artery Angiogram: LAO view with cranial projection

Video 3: Left Coronary Artery Angiogram; Right Anterior Oblique (RAO) view with cranial projection

Video 4: Left Coronary Artery Angiogram: Right Anterior Oblique (RAO) view with caudal projection

Video 5: Right Coronary Artery Angiogram; Left Anterior Oblique (LAO) view

Video 6: Left Ventriculogram

Video 7: Right Coronary Artery Angiogram; Left Anterior Oblique (LAO) view post Percutaneous

Transluminal Coronary Angioplasty (PTCA)

Video 8: Right Coronary Artery Angiogram; Right Anterior Oblique (RAO) view post PTCA.

Video 9: Right Coronary Artery Angiogram; Anterior Posterior (AP) view with cranial projection. Post PTCA.