

CLINICAL CASE UPDATE

Technical and Pharmacologic Advances in the Early, Invasive Treatment of STEMI and Hemodynamically Unstable NSTEMI

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Case 1

A 63-year-old woman with a history of spinocerebellar ataxia and depression presented to the emergency department with intermittent chest pain. She first noted the pain about 12 hours before presentation, while working on her computer. She was able to fall asleep, at which time her symptoms had resolved; however, when she awoke in the morning, she continued to have chest pain and decided to seek medical attention.

Upon arrival in the ED at 13:24, she was noted to be in no acute distress with a blood pressure of 89/52 mmHg, and a heart rate of 63 beats per minute (bpm). Her respiratory rate was 16 breaths per minute, and she was afebrile. Her first ECG was performed at 13:38; it demonstrated ST-segment elevation in the inferior leads. At this point, the STEMI team was activated. The patient received a chewable aspirin (325 mg), unfractionated heparin (5,000 units), and supplemental oxygen by nasal cannula (2 L per minute). Standard laboratory studies were sent.

She arrived in the cardiac catheterization laboratory at 13:46. Her right wrist and right groin were prepped and draped emergently. During the prep, right radial artery access was obtained with a 5 Fr vascular access sheath. Diagnostic angiography demonstrated only minimal angiographic abnormalities in the left coronary artery system while the right coronary artery (RCA) was occluded in the mid-segment. At this point, she received intravenous bivalirudin bolus (0.75 mg/kg) followed by an infusion (1.75 mg/kg/h).

After exchanging for a 6 Fr system, manual thrombectomy was performed, re-establishing antegrade blood flow at 14:12. Door-to-reperfusion time was 48 minutes. Given the thrombus burden and lack of familiarity with this patient, we opted to use a bare metal stent (3.5 x 18 mm) to treat her lesion. The stent was post-dilated to 4.0 mm. Optical coherence tomography (C7 Dragonfly catheter, St. Jude Medical, St.

Paul, MN) demonstrated optimal stent apposition and no evidence of stent-edge dissection (Figure 1).

The patient received clopidogrel (600 mg orally) at the end of the case. Bivalirudin infusion (1.75 mg/kg/h) was continued for 2 additional hours. The access sheath was removed in the catheterization laboratory, and a hemostatic compression device was applied for 2 hours.

The patient was admitted to the CCU for observation. Transthoracic echocardiogram demonstrated severe hypokinesis of the inferior and inferolateral walls with an estimated ejection fraction of 35%. Initial troponin level from the ED was 45 ng/mL, peaking at 137.62 ng/mL after the case. Similarly, CK-MB rose from an initial value of 291.7 IU/L to > 300 IU/L, the upper limit of the assay. Other laboratory results of interest included a hemoglobin of 13.8 g/dL, platelet count of $61^3 \times 10^3/\mu\text{L}$, creatinine 0.9 mg/dL and a low-density lipoprotein (LDL) of 128 mg/dL.

She was able to ambulate later that afternoon and was discharged on hospital day 3. There were no bleeding or vascular complications. At the time of discharge, she was prescribed aspirin, clopidogrel, atorvastatin, metoprolol, and lisinopril. The patient was seen in clinic 1 month later and remained chest pain-free. Her radial artery was patent; LDL is now 72 mg/dL.

Case 2

A 72-year-old woman with known coronary artery disease, chronic obstructive pulmonary disease, and hypertension — but no prior revascularization — was transferred to our institution for urgent cardiac catheterization. She had presented to the referring hospital with worsening dyspnea on exertion and chest pain at rest. The patient reported that pain had initially improved with baking soda and prayer. Upon presentation to the referring center's ED, her pain began increasing in intensity. In the ED, she received aspirin (81 mg orally), morphine, nitroglycerin (0.4 mg sublingual), clopidogrel (600 mg orally) and unfractionated heparin (UFH) (5000 units iv followed by a continuous infusion). With this therapy, the patient was chest-pain free. She was noted to have diffuse ST-segment depression on her initial ECG. While awaiting her transfer to our institution, an elevated troponin (1.6 ng/mL) was noted.

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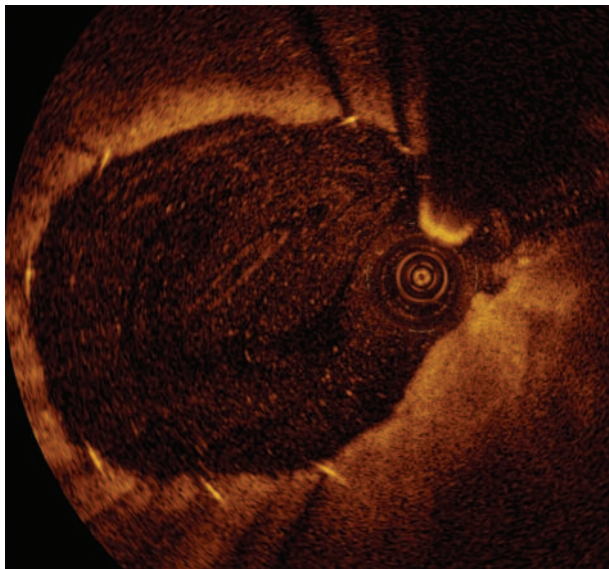


Figure 1. Optical coherence tomography image following stent implantation in the right coronary artery

Upon arrival at our institution, she was brought directly to the cardiac catheterization laboratory. She was in mild distress with a blood pressure of 98/65 mmHg, and heart rate of 124 bpm. Respiratory status was more tenuous: respiratory rate was 18 breaths per minute, oxygen saturation was 100% on a non-rebreather mask. Diagnostic angiography was performed using the right radial approach. The left main coronary artery had a severe, ostial lesion with evidence of thrombus; remaining vessels had only mild to moderate angiographic abnormalities.

Based on her anatomy and clinical presentation, we consulted cardiac surgery for emergent bypass surgery. Cardiac surgery determined the patient was too high-risk, and should be managed medically and be offered percutaneous revascularization once stabilized. At this point, a right heart catheterization was performed using a 4 Fr venous sheath in her right antecubital vein. Filling pressures were elevated (mean pulmonary capillary wedge pressure = 36 mmHg), and estimated Fick cardiac output was 2.5 L/minute. The patient began to deteriorate from a respiratory standpoint and was urgently intubated.

Given the hemodynamic and respiratory status, the decision was made to immediately proceed with PCI. An intra-aortic balloon pump was placed through the right femoral artery. A 6 Fr XBLAD 3.5 guiding catheter (Cordis Corporation, Miami, FL) was used for the PCI. It was inserted through the right radial sheath. Bivalirudin bolus (0.75 mg/kg) followed by infusion (1.75 mg/kg/h) was started.

After wiring the lesion, a bare-metal stent (4.0 x 8 mm) was deployed across the lesion. While there was a satisfactory angiographic result, intravascular ultrasound (IVUS) demonstrated incomplete apposition of

the stent and a residual, more proximal lesion. A second bare-metal stent was placed, overlapping the proximal edge of the initial stent. Both stents were post-dilated with a non-compliant balloon (5.0x8mm) at high pressure. Repeat IVUS demonstrated good stent expansion and complete coverage of the initial lesion. Bivalirudin infusion was discontinued at this time. The right radial sheath was removed with the use of a hemostasis band. The patient was then transferred to the cardiac ICU for further management.

Overnight, the patient became hemodynamically unstable despite the assistance of the IABP. Therefore, a dopamine infusion was initiated; blood pressure was stabilized. A transthoracic echocardiogram demonstrated severely depressed left ventricular systolic function with an estimated ejection fraction of less than 20%. Troponin peaked at 15 ng/mL, and hemoglobin remained stable. The patient underwent aggressive diuresis and heart failure management over the next 2 days. Respiratory and hemodynamic status improved steadily. On hospital day 3, the patient's IABP was removed without incident. She remained in the ICU until day 6, when she was transferred to the telemetry unit. The patient was ultimately discharged to home on hospital day 11.

Discussion

Both these cases illustrate the changing approach in the management of patients with acute coronary syndromes. In particular, this clinical update will highlight strategies to minimize bleeding risk while preserving ischemic outcomes. Routine application of multiple bleeding-avoidance strategies in high-risk patients will become increasingly important, particularly as society develops less tolerance for reimbursing potentially preventable complications such as bleeding.

Bleeding-avoidance strategies

There has been awareness of the link between post-PCI bleeding and short and long term mortality.¹⁻³ In the past, the focus has been towards a minimization of ischemic complications. Now, there is a similar interest in reducing post-PCI complications, primarily bleeding. Marso et al demonstrated the impact of targeted therapies to decrease bleeding. They studied the utility of specific bleeding-avoidance strategies (BAS), in particular vascular-closure devices and the direct thrombin inhibitor bivalirudin. The investigators noted reduced bleeding events with either strategy and an additive effect when both were used.⁴ In a related study, the same investigators included bivalirudin and radial access as the BAS. Both radial access and bivalirudin decreased bleeding risk in patients undergoing PCI.⁵ They observed a higher absolute reduction in bleeding among patients who were at the highest risk of bleeding.

The prior studies give scientific merit to a common practice in clinical decision-making. Clinicians either explicitly or implicitly estimate a patient's risk

of complications before any type of intervention.⁶⁻⁸ Several patient-specific risk factors are associated with increased risk of vascular and bleeding complications post-PCI, including female gender, advanced age, low body-mass index, and renal failure.⁶ Clinical context also impacts risk of bleeding. Patients experiencing an acute coronary syndrome have a higher bleeding risk than patients undergoing elective PCI. These cases illustrated common clinical scenarios where multiple risk factors for post-PCI bleeding were present. A combined approach of pharmacology and radial access were used to mitigate bleeding risk using proven BAS.

In the first case, the synergistic role of bivalirudin and transradial access was used in the management of ST-segment elevation myocardial infarction (STEMI). The HORIZONS-AMI trial demonstrated the utility of bivalirudin for the management of patients with STEMI who were treated with primary PCI within 12 hours of presentation.⁹ At 30 days, patients receiving bivalirudin had less bleeding events (6.8% versus 10.8%, $P < 0.001$) and a lower overall death rate than the patients in the heparin plus glycoprotein inhibitor group. At 1 year, patients who received bivalirudin continued to demonstrate less net adverse clinical events (composite of major bleeding, death, myocardial infarction, target vessel revascularization, or stroke) and a lower mortality rate than patients receiving UFH plus a glycoprotein inhibitor (GPI).¹⁰

Patients suffering from acute coronary syndromes are at an increased risk of bleeding complications.^{6,11} Some of the commonly cited reasons for this observation include that these patients are not always known to the operators, the procedures are often emergent, and many of these patients may require multiple concomitant anticoagulants. Transradial access is uniquely positioned to address many of the issues that lead to increased bleeding in this patient population. A recent meta-analysis of clinical trials of access site in patients with STEMI demonstrated significantly less bleeding (0.77% versus 2.61%, OR 0.30 [95% CI 0.16–0.55], $P = .0001$) and lower mortality (2.04% versus 3.06%, OR 0.54 [95% CI 0.33–0.86], $P = .01$) among patients undergoing transradial (TR) access compared to transfemoral (TF) access (Figure 2).¹²

In the recently published radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL) trial, over 7,000 patients with acute coronary syndromes including STEMI were randomized to TR versus TF access.¹³ In a *post hoc* analysis of STEMI patients, there was a benefit with radial access for the composite of death, myocardial infarction, and stroke ($P = 0.011$), and

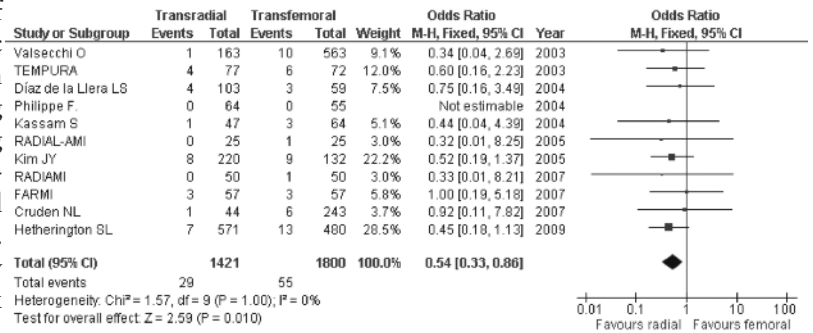


Figure 2. Risk of Death - Meta-analysis of clinical trials comparing transradial to transfemoral access for treatment of acute myocardial infarction (Reproduced with permission from Vorobcsuk, et al. *Am Heart J* 2009;158:814-21.)

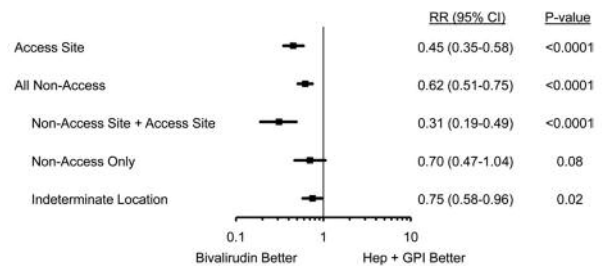


Figure 3. Relative risk of location-specific TIMI (major and minor) bleeding by anticoagulation regimen. (Reproduced with permission from Verheugt et al, *J Am Coll Cardiol Intv* 2011;4:191-7)

death alone ($P = 0.001$). This trial included physicians who perform a high volume of PCI procedures (median = 300), with 40% of cases using the TR approach.

Non-access-site bleeding

TR access does not eliminate all sources of bleeding. Patients who undergo TR access will still experience bleeding complications. Although bleeding at the access site is rarely of clinical significance, bleeding can occur at sites other than the arm. In fact, non-access-site bleeding has been shown to be more common than bleeding at the access site^{13,14} and portends a much worse prognosis.¹⁴ Gastrointestinal and pulmonary bleeding are the most common sources of non-access-site bleeding. It is clear that access-site choice alone will not impact non-access-site bleeding. In the retrospective analysis by Verheugt and colleagues, use of bivalirudin led to lower rates of access-site and non-access-site bleeding when compared to UFH + GPI (Figure 3).¹⁴

Time to reperfusion

While time to reperfusion was not collected in RIVAL, prior studies have demonstrated that TR access prolongs reperfusion time by a few minutes.¹⁵ However, it is unclear if such a delay outweighs the benefit of reduced bleeding and vascular complications with this approach. Focusing on improved system-wide efficiency and in-lab practices will almost certainly close the gap. Obtaining access as the staff is completing their

prep, and using left radial access¹⁶ are a few examples of time saving practices with this approach. In a meta-analysis of prospective, clinical trials of acute MI patients by access site, there was no difference in reperfusion times.¹²

Time to reperfusion is an important quality marker that is publicly reported in the United States. Consequently, physicians and medical centers are particularly interested in maintaining these times below the currently prescribed threshold. This has led many to question the wisdom of selecting TR access for STEMI cases for fear of missing the target. Performing PCI for patients with STEMI using TR access requires a certain level of proficiency with the approach. While it is clear that the interventionalist must have sufficient experience, the nursing and technical staff must also be familiar with rapid preparation of the patient and stocking the appropriate supplies.

At the University of Illinois-Chicago and the Jesse Brown VA Medical Center, we began utilizing the TR approach for treating STEMI patients after completing approximately 100 diagnostic cases and 50 PCI procedures. To this day, we continue to prep a femoral artery access site in the rare instance we need to change access or, more commonly, to place a hemodynamic support system. Setting a time limit for achieving access and engaging the coronary ostia can also help limit significant delays in reperfusion. For example, if we are unable to begin diagnostic angiography within 10 minutes, we will switch to the other arm or leg. In contrast to our diagnostic cases, we use a default 6 Fr system for all TR-STEMI cases. Choice of catheters is left to the individual operator.

Conclusion

These cases demonstrate the evolving landscape of PCI therapies. While device development continues to evolve in incremental steps, operators are searching for strategies to minimize complications. Several BAS have shown clinical efficacy in the published literature. Oftentimes, multiple strategies can be applied to incrementally improve outcomes. While its antithrombotic effects are well known, bivalirudin is also a superior anticoagulant in terms of reducing both access-site and non-access-site bleeding. In experienced centers, TR access allows for rapid reperfusion and decreased vascular and bleeding complications. TR access and bivalirudin are synergistic therapies that can improve outcomes for patients at highest risk of bleeding.

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