A Case Report of Combining Procedural and Pharmacological Strategies to Reduce Bleeding Risk in a High Risk Patient Undergoing Percutaneous Coronary Intervention

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Case report
A 69-year-old male presented to the emergency department with substernal chest discomfort. His symptoms started four days prior to presentation with a stuttering pattern primarily related to exertion and relieved with rest. On the morning of presentation he developed chest pain at rest. His pain was described as a dull pressure with radiation to both arms. The discomfort was associated with mild dyspnea and diaphoresis, but no nausea, vomiting, or cough. Due to the progression of his discomfort, he called 911 and was brought to the hospital by ambulance. His review of systems was negative for other gastrointestinal or pulmonary symptoms. His history was significant for hypertension, hypercholesterolemia, and type 2 diabetes mellitus; there was no history of renal or pulmonary disease. His current medications included aspirin 81 mg daily, insulin, hydrochlorothiazide, benazapril, and simvastatin. The social history was significant for a 40-pack-year smoking history and occasional alcohol intake; there was no history of illicit drug use. The patient was married with three grown children and was a retired hospital administrator. He was a practicing Jehovah’s Witness.

On physical examination, he was an obese male in mild distress. His body mass index was 32 kg/m². His blood pressure was 168/74 in the right arm and 172/78 in the left arm; the pulse rate was 90 and regular, and the oxygenation saturation was 95% on 2L of supplemental oxygen delivered by nasal cannula. There was mild jugular venous distention, and his carotid artery pulses were normal without bruits. The chest examination revealed mild crackles at the bases that did not clear with coughing. The cardiac examination demonstrated a regular rate and rhythm, with normal S1 and S2, an S4, and a 1/VI systolic murmur along the left sternal border. There was no rub. The abdomen was benign and there was no edema of the extremities. His femoral pulses were 1+ with soft bilateral bruits.

En route to the hospital, the patient was treated with 325 mg of aspirin, sublingual nitroglycerin, and supplemental oxygen. On arrival to the emergency department, the patient’s chest discomfort had resolved. His 12-lead electrocardiogram showed normal sinus rhythm with a rate of 90 beats per minute, normal intervals, and 0.5 mm of ST-segment depression in leads I, II, and aVF. A portable chest radiograph showed cephalization of the pulmonary vessels. A point-of-care troponin assay was positive. Other laboratory values showed a hemoglobin value of 14 g/dl, a platelet count of 284,000, and a creatinine clearance of 50 ml/min. The creatine kinase was 260 mg/dl and the muscle-brain (MB) fraction was 25 mg/dl. The troponin T was 1.5 ng/ml. He was given an intravenous bolus of unfractionated heparin followed by an infusion, 300 mg of clopidogrel orally, two inches of topical nitroglycerin paste, and 40 mg of intravenous furosemide. He was then admitted to the coronary care unit (CCU) for further care.

In the CCU, the patient underwent transthoracic echocardiography that showed mild left ventricular hypertrophy, and an ejection fraction of 35% with mild anterior and inferior hypokinesis. There was mild mitral and tricuspid regurgitation. The patient was observed overnight and underwent cardiac catheterization the next day via the right femoral artery. This revealed a normal left main trunk, and an 80% lesion in the proximal left anterior descending (LAD) artery, a complex 80% lesion in the mid-LAD across the first and second diagonal branches (Figure 1), an 80% ulcerated lesion mid-left circumflex artery (Figure 2), a 60% lesion in the proximal right coronary artery, and a 70% lesion in the mid right coronary artery (Figure 3). The left ventricular end-diastolic pressure was 27 mmHg.
Given the severe three-vessel coronary artery disease involving the proximal LAD and the reduced ejection fraction, cardiothoracic surgery was consulted for coronary artery bypass grafting (CABG).

The patient was returned to the CCU and his femoral arterial sheath was removed. Hemostasis at the femoral arterial access site was achieved with manual compression. Five hours after sheath removal, the patient complained of nausea. His blood pressure was noted to be 85/65 and his heart rate was 110 beats per minute. The femoral access site had a 5 cm hematoma but no overt bleeding. He was treated with several 500 ml fluid boluses over the next three hours but his blood pressure remained low. Due to the clinical suspicion for a retroperitoneal hematoma, the patient underwent an abdominal CT scan that revealed a large retroperitoneal hematoma on the right side. His aspirin and clopidogrel were discontinued, and he was placed on intravenous dopamine to support his blood pressure. His hemoglobin was 9 mg/dl. Due to the patient's religious beliefs, he adamantly refused blood transfusion. Vascular surgery was consulted and they recommended observation, fluid repletion, and vasopressors as needed.

Over the next 24 hours, the patient's clinical condition stabilized and the dopamine was weaned off. His blood pressure was stable at 125/83. Over the next three days, his hemoglobin values were 9.1 mg/dl, 8.8 mg/dl, and 8.6 mg/dl. His aspirin and clopidogrel were restarted, as were other secondary prevention medications. On the fourth day after admission, he was transferred out of the CCU to the step-down unit where CT surgery agreed to proceed with CABG using a blood conservation protocol that was designed specifically for patients who refused transfusion. Given his anemia, it was recommended that the patient be discharged home on medical therapy and supplemental iron to raise his hemoglobin value prior to undergoing cardiac surgery.

On the fifth day after admission, the patient was ambulating in the hallway of the hospital ward when he developed acute substernal chest discomfort. An ECG obtained emergently demonstrated 1 mm of ST-segment depression in leads II, III, and aVF. His hemoglobin value that morning was 8.0 mg/dl; given this degree of anemia, systemic anticoagulation was not administered. Instead, both the cath lab and CT surgery were consulted to pursue revascularization. CT surgery was reluctant to proceed with CABG due to the patient's clinical instability and anemia, so the decision was made to perform high-risk emergent PCI.

The patient was taken to the cardiac catheterization laboratory where transradial PCI of the LAD, LCx, and RCA was performed successfully using drug-eluting stents with bivalirudin as the antithrombin agent (Figures 4–6). The patient recovered without incident and was to ambulate immediately after the procedure without angina. He was discharged on day 7 after admission with a prescription for aspirin along with clopidogrel indefinitely. His other secondary prevention medications were continued and oral iron supplements were added to his medication regimen. His hemoglobin value on the day of discharge was 8.3 mg/dl. Four weeks after admission he was seen in the outpatient clinic for follow-up. He was free of angina and his hemoglobin value was 11.6 mg/dl.

**Discussion**

This case highlights the importance of balancing ischemic and bleeding risk during the management of acute coronary syndromes (ACS). In patients with high-risk
features such as troponin elevation or evidence of heart failure, antiplatelet therapy, antithrombin therapy, and early invasive risk stratification are recommended.\(^1\) While this strategy is associated with improved outcomes,\(^2\) it carries a risk for bleeding. Several studies have found an association between bleeding complications and increased short- and intermediate-term mortality and morbidity.\(^3\) The mechanisms underlying these associations are likely related to decreased oxygenation in the presence of anemia and obstructive coronary artery disease, cessation of evidence-based medications, and blood transfusion. In the patient described above, brisk bleeding into the retroperitoneal space after diagnostic cardiac catheterization resulted in acute anemia that was responsible for post-infarction unstable angina. In addition, his antiplatelet therapy was discontinued, but it was reinstated once his bleeding event resolved and his clinical condition had stabilized. Ultimately, his underlying coronary artery disease was addressed using a combined pharmacological and procedural strategy that minimized the risk of any further bleeding and maximized ischemic benefit.

Bleeding complications have emerged as an important risk marker for adverse outcomes in patients with ACS and those undergoing PCI. Because of this, several risk scores have been developed to gauge the risk of bleeding in patients undergoing PCI\(^1\) and those with ACS.\(^4,5\) Characteristics consistently associated with an increased risk of bleeding include older age, female sex, chronic kidney disease, and anemia. In the PCI population, the most common site of bleeding is the vascular access site.\(^7\) Interestingly, the issue of whether procedure-related bleeding is clinically significant has been highlighted by an analysis by Mehran and colleagues.\(^6\) In 17,421 patients with ACS treated with early cardiac catheterization or primary PCI (the population included patients with both non-ST-segment elevation ACS as well as ST-segment elevation MI), isolated access site hematomas and CABG-related bleeding were not associated with increased 1-year mortality, while overt bleeding associated with significant hemoglobin decreases and/or blood transfusion was. On the other hand, procedural hemorrhagic complications that are more severe than superficial hematomas may have dire prognostic significance. In a study of 26,452 patients with ACS, Rao and colleagues found that GUSTO moderate (defined as bleeding that requires transfusion) and severe bleeding (defined as either intracranial hemorrhage or bleeding that is associated with hypotension) were independently associated with increased 30-day and 6-month mortality regardless of whether they occurred in the periprocedural setting or not.\(^6\) Similarly, Yatskar examined 6,656 patients undergoing PCI who were entered into the National Heart, Lung, and Blood Institute's Dynamic Registry and found that access site hematomas that require blood transfusion were associated with an increased risk for both in-hospital (adjusted hazard ratio 3.59, 95% CI 1.66–7.77) and 1-year mortality (adjusted hazard ratio 1.65, 95% CI 1.65–2.70). Moreover, retroperitoneal hematomas that can occur with femoral arterial access are highly associated with increased mortality.\(^7\) These data show that certain types of access site bleeding are clinically significant, particularly if they lead to transfusion\(^7\) and/or hypotension, or if they occur in the retroperitoneal space. Taken together, the available evidence suggests that major access-site and non-access site bleeding should be prevented to improve outcomes in patients undergoing PCI.
The “global” reduction of bleeding risk in the PCI population can be achieved through both pharmacological and procedural means. In this context, one strategy that has been consistently associated with a lower incidence of bleeding is the use of bivalirudin as the procedural antithrombin.11,12–14 This reduction in risk is consistent regardless of the bleeding definition used or the site of bleeding,11 and is associated with reduced short- and long-term mortality in patients undergoing primary PCI for STEMI.16 With respect to access-site complications such as hematomas or retroperitoneal bleeds, the transradial approach is consistently associated with reduced risk compared with the transfemoral approach,17 with similar rates of procedure success.17 Observational data also suggest an association between the transradial PCI and reduced 1-year mortality, primarily driven by a reduction in postprocedure blood transfusion.18

Achieving reduction in bleeding risk should not be accomplished by sacrificing efficacy. For example, the use of unfractionated heparin (UFH) alone is associated with a lower risk for hemorrhagic complications among patients undergoing elective PCI compared with the combination of UFH and glycoprotein IIb/IIIa inhibitors (GPI); however, the addition of GPI to UFH lowers the rate of periprocedural MI.19 This underscores the classic trade-off of bleeding risk versus ischemic risk. On the other hand, the use of bivalirudin in elective PCI, non-ST-segment ACS, and primary PCI for STEMI is associated with a 40% relative risk reduction in major bleeding compared with UFH (or enoxaparin) plus GPI without an increase in death, MI, or target vessel revascularization.12–14

In the patient described above, the presence of anemia, prior retroperitoneal hematoma after transfemoral cardiac catheterization, and refusal to accept blood products to treat his symptomatic anemia led to a decision to pursue PCI with a combination of transradial approach and bivalirudin. This combination resulted in excellent procedural outcomes in terms of both efficacy and safety.

References