

# CLINICAL CASE UPDATE

## Individualized Approach to High Risk Patients Undergoing Percutaneous Coronary Intervention

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### Case Report

A 75-year-old male presented to his cardiologist's office with a 1-month history of progressive substernal chest pain. The symptoms were worse with exertion and associated with some mild dyspnea. The patient reported that, before the symptoms started, he had been going to the gym five times a week, performing isometrics and aerobic exercises. He denied any prior history of myocardial infarction (MI) or congestive heart failure. Cardiac risk factors included age, hypertension, dyslipidemia, and a 10-pack-a-year history of smoking he had quit 50 years prior.

Additional medical history was remarkable for benign prostatic hypertrophy. His medical regimen included aspirin, metoprolol, lisinopril, and rosuvastatin. Physical examination revealed a heart rate of 60 beats/minute and a blood pressure of 136/74 mmHg. The patient appeared comfortable. There was no jugular venous distension, carotid bruits, or thyromegaly. Heart examination revealed a regular rate, normal first and second heart sounds, and no murmurs or gallops. The lungs were clear and the abdomen unremarkable. Femoral and distal pulses were intact bilaterally, and the Allen's test was negative bilaterally.

Laboratory studies showed WBC 6.4 K/uL, hemoglobin 12.4 g/dL, platelet count of 189,000, BUN 16 mg/dL, creatinine 1.6 mg/dL, fasting glucose 100 mg/dL, cholesterol 163 mg/dL, triglycerides 213 mg/dL, HDL 40 mg/dL, and a LDL 80 mg/dL. An initial EKG revealed normal sinus rhythm with a right bundle branch block and non-specific ST- and T-wave changes in the inferior leads. Cardiac CT was performed the next day and revealed the following: a total occlusion of an anomalous right coronary artery (RCA), a 70% proximal left anterior descending (LAD) bifurcation lesion involving the diagonal 1 artery, an overall calcium score of 330, and a normal ejection fraction of 58%. The patient's symptoms persisted despite up-titration of his medications and he was

referred for cardiac catheterization.

A short 6 Fr sheath was inserted into the right common femoral artery, then exchanged for a long 6 Fr sheath due to significant right iliac artery tortuosity. Diagnostic coronary angiography revealed an anomalous dominant RCA from the left coronary cusp, a chronic total occlusion (CTO) of the proximal RCA with the distal vessel filled by LAD collaterals, and an 80% proximal LAD bifurcation lesion. The decision was made to intervene on the proximal LAD lesion.

Bivalirudin was administered per protocol. A 6 Fr JL 4.0 guide was used engage the left main coronary artery and percutaneous transluminal coronary angioplasty. Drug-eluting stent placement was performed on the proximal LAD lesion with a 3.5 mm by 18 mm stent, post-dilated to high pressures with a 4.0 mm by 15 mm non-compliant balloon. Repeat angiography revealed moderate residual ostial diagonal 1 artery stenosis, originating through the stent with TIMI-3 flow.

Right groin hemostasis was achieved via manual compression. His course was complicated by a drop in hematocrit 11.1 g/dL and a large right femoral pseudoaneurysm requiring ultrasound-guided thrombin injection. The patient remained in the hospital for 4 days post-procedure and was discharged home on aspirin 325 mg and clopidogrel 75 mg daily.

One week after procedure, he presented to our institution with continued exertional chest pain at a similar exercise burden, despite complying with his medications. Nitrates and ranolazine were added to his medical regimen. An exercise stress test was performed with the patient walking for 6:01 minutes of Bruce protocol, developing 1 mm inferolateral ST depressions, and demonstrating a large, severe inferior and inferolateral reversible defect.

Repeat cardiac catheterization was performed via the right radial artery using a 6 Fr hydrophilic sheath. Selective coronary angiography using a Jacky catheter revealed a patent proximal LAD stent and unchanged remainder of the coronary anatomy (Figures 1 and 2). The decision was made to intervene on the RCA total occlusion.

Bivalirudin was administered per the same proto-

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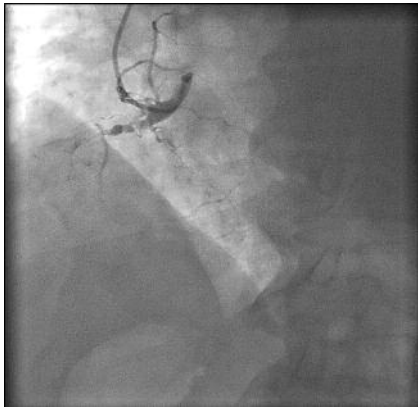


Figure 1. Right coronary angiogram demonstrating an anomalous origin of the right coronary artery from the left coronary cusp and a chronic total proximal occlusion.

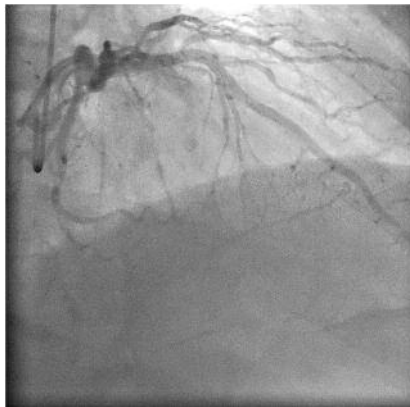


Figure 2. Left coronary angiogram demonstrating a patent proximal left anterior descending artery stent with moderate ostial diagonal 1 artery stenosis originating through the stent. Faint collaterals filling the distal right coronary artery territory from the left coronary system are noted.

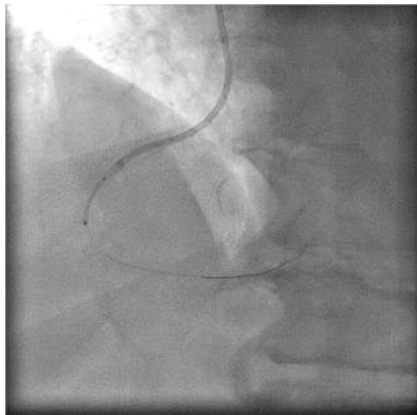


Figure 3. For the intervention, a 6 Fr Amplatz Left 1 guide was used to engage the right coronary artery. Buddy wires were placed for improved device delivery and support.

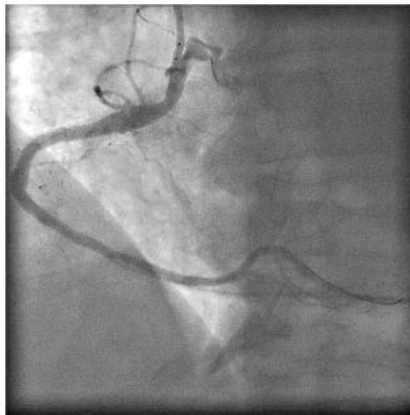


Figure 4. Post-intervention right coronary angiogram demonstrating successful stenting of the right coronary artery chronic total occlusion.

col. A 6 Fr Amplatz Left 1 guide was used to engage the RCA. The proximal total occlusion was crossed using a CTO guidewire with the support of an over-the-wire (OTW) balloon. Pre-dilation was performed with the 2.5 mm compliant OTW balloon, re-establishing flow to a large RCA system. A second guidewire was placed for buddy-wire support, and the vessel was stented with 4.0 mm by 28 mm and 4.0 mm by 15 mm drug-eluting stents (Figure 3). The stents were post-dilated to high pressures with a 4.5 mm non-compliant balloon (Figure 4). Hemostasis was achieved using a radial compression device.

The patient was sitting in a chair immediately after the procedure and was discharged home the next day. Within 1 month of his intervention, he returned to his gym and, in a recent 6-month follow-up, was doing well.

## Discussion

**Association of bleeding and worse outcomes.** Bleeding is a common occurrence among patient who have acute coronary syndrome (ACS) and has emerged

as a powerful independent predictor of early and late mortality with increasing bleeding severity. Even mild bleeding portends a significant clinical risk.<sup>1,2</sup> The exact mechanism connecting bleeding and adverse outcomes is unclear but may be explained in part by decreased tissue oxygenation, cessation of evidence-based medications, and blood transfusions.<sup>3,4</sup>

Multiple risk scores have been developed to assess the bleeding risk in patients with ACS and in those undergoing percutaneous coronary intervention (PCI).<sup>5,6</sup> Risk factors for bleeding include many patient-related, procedural-related, and treatment-related factors. Patient-related factors include older age (>75 years), female gender, obesity, anemia, and renal failure. It is the non-patient-related factors — including procedural factors such as puncture site (femoral versus radial approach) — and treatment-related factors such as the type of anticoagulation or antithrombin therapies used that can be altered to potentially reduce bleeding and adverse outcomes. A risk score applied to our patient places him at a bleeding risk of nearly 8% and, given his prior bleeding event, there was an elevated concern for recurrence.

**Procedural-related factors: Access site.** Vascular access via the radial artery, a superficial and compressible vessel, has been suggested to result in less bleeding than access through the femoral artery. A meta-analysis of 4500 patients revealed that radial access reduced major bleeding by 73% with a trend for reductions in the composite of death, MI, or stroke (2.5% versus 3.8%  $P = 0.06$ ).<sup>7</sup> The Radial versus Femoral (RIVAL) trial was the first randomized trial comparing radial to femoral artery access,  $n = 3500$ .<sup>8</sup> There was a significant reduction in a composite of death, MI, stroke, and non-CABG-related major bleeding at 30 days for patients undergoing radial access compared to femoral access, with similar rates of success between the 2 groups. This benefit was, however, noted only in the subgroup of patients performed at the highest tertile volume radial centers (hazard ratio 0.49) and in patients with ST-elevation myocardial infarction (hazard ratio 0.6).

Furthermore, there is concern that the transradial approach may be technically more difficult for treatment of complex lesions or in elderly patients. An age >

75 years is a predictor of transradial PCI failure, possible as a consequence of arterial tortuosity's complicating catheter passage.<sup>9,10</sup> Despite this concern, published series suggest transradial catheterization can be performed in the elderly with a high technical success rate and minimal transfemoral crossover (< 10%), while preserving its major advantage of decreased adverse events.<sup>9,11,12</sup> Complex lesions including anomalous coronary arteries and chronic total occlusion, as described in our case, as well as left main disease have been successfully treated in high-risk patients.<sup>13-15</sup>

**Treatment-related factors.** Access-site bleeding accounts for only a portion of the bleeding events and has a lower associated mortality than non-access-site bleeding. Non-access-site bleeding, on the other hand, is more common after PCI, accounting for approximately two-thirds of all bleeding events, and is associated with a fourfold increase in mortality at 1 year.<sup>16</sup> Antithrombotic agents — including enoxaparin, fondaparinux, and bivalirudin — in different clinical scenarios have been shown to significantly reduce major bleeding while effectively reducing ischemic complications.<sup>17-21</sup> The use of bivalirudin rather than heparin +/- glycoprotein IIb/IIIa inhibitor (GP IIb/IIIa) significantly decreases both access- and non-access-site bleeding events by nearly 40%.

**Combining the transradial approach and bivalirudin.** When combining the transradial approach and bivalirudin in moderate- to high-risk ACS patients, the benefit of reducing bleeding rates is still maintained. In a substudy of the Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) trial comparing femoral access to radial access (n = 798), bivalirudin compared to heparin +/- GP IIb/IIIa significantly reduced access-site major bleeding with femoral but not radial artery access.<sup>22</sup> However, non-access site bleeding was reduced to a similar extent for both, 4.1% versus 7.4% for the femoral and 4.9% versus 7.2% for the radial approaches. Overall there was no significant difference in composite ischemia between the radial and femoral approaches at 30 days, with fewer overall major bleeding complications with radial cases (3.0% versus 4.8%).

In more than 95,000 patients analyzed from the National Cardiovascular Data Registry database, the combination of transradial approach and bivalirudin provided the fewest overall bleeding events in patients with the highest bleeding risk, > 3% (femoral/manual 6.2%, bivalirudin 4.0%, radial 3.0%, and bivalirudin/radial 1.6%).<sup>23</sup>

In an ACS population similar to RIVAL and ACUITY trial patients, only one-third of major bleeds arise from the access site. On the other hand, in the elective-PCI population, nearly two-thirds of non-CABG major bleeding arises from the access site. Additionally, the use of a vascular closure devices (VCD) and bivalirudin with the femoral approach has been shown to signifi-

cantly reduce major access-site bleeding to 0.7%.<sup>24</sup> Given that intraprocedural use of bivalirudin was only 3% in the RIVAL trial, and that only 6% of the cases in the ACUITY trial were performed radially, the literature is limited. It is yet to be determined whether the benefit of combination therapy would be maintained or even more pronounced in patients undergoing elective PCI or when compared to patients undergoing PCI transfemorally with a VCD and bivalirudin.

**Economic and patient-comfort considerations.** Cost and quality of life are additional important factors to consider in cardiac catheterization. Total procedural costs including access, catheters, contrast, VCD, and recovery costs have been shown to be significantly lower in diagnostic catheterization for the radial approach compared to the femoral approach. There is an average cost savings of \$77 and \$184 per case for a radial diagnostic procedure versus a femoral procedure, with and without a closure device respectively.<sup>25</sup> In a recent Clinical Case Update by Mathias, he showed that, in his own series of ACS patients undergoing intervention, there was nearly a \$5000 variable cost savings per case for transradial compared to transfemoral procedures.<sup>26</sup>

In the Randomized Evaluation in PCI Linking Angiomax to Reduced Clinical Events (REPLACE-2) and ACUITY trials, bivalirudin monotherapy when compared with heparin + GP IIb/IIIa was associated with similar 30-day ischemic outcomes, with significantly reduced rates of major bleeding.<sup>17,18</sup> These differences are consistent in both stable or low-risk ACS patients, as well as moderate- and high-risk ACS patients. In the economic substudy of REPLACE-2, which included more than 4600 patients, economic outcomes favored the bivalirudin + provisional GP IIb/IIIa arm with a cost savings of approximately \$400 per patient during the index hospitalization and at 30 days.<sup>27</sup>

In the economic substudy of ACUITY, which included more than 7800 patients, bivalirudin use was associated with a net cost savings of approximately \$600 per patient compared with heparin + routine upstream GP IIb/IIIa and approximately \$200 per patient compared with heparin + catheterization lab GP IIb/IIIa.<sup>28</sup> For both substudies, the overall cost savings was driven by reductions in bleeding complications and lengths of stay.

The economic impact of bivalirudin versus heparin alone, however, remains less clear. When validated risk models are applied, bivalirudin demonstrates clear cost savings over heparin alone for patients with high predicted bleeding risks (> 20%).<sup>29</sup> In the context of large case volumes and with the potential for additional cost savings in PCI, there are tremendous economic considerations for a combined transradial/bivalirudin approach.

In addition to cost considerations, the radial approach allows for reduced post-procedural recovery time, earlier ambulation, and earlier discharge, resulting in higher quality-of-life measures.<sup>30,31</sup> Ambulatory times

after the radial approach are possible immediately after the procedure. Post-procedural complications due to prolonged bed rest in the femoral approach are also more accentuated in the elderly and in patients with preexisting back pain or urinary problems. From a patient comfort perspective, this makes the radial approach more advantageous and, in patients who have experienced both femoral and radial approaches, more preferred for repeat procedures.

## Summary

It is clear that an individualized approach to PCI that mitigates both access-site and non-access-site bleeding is a necessity, especially in high-risk elderly patients as described in this clinical case update. Using available techniques that also reduce hospital costs and improve post-procedure quality of life are equally important. The combination of a transradial approach and bivalirudin provided an excellent procedural outcome with lower potential for bleeding, vascular complications, post-procedure discomfort, and inflated cost.

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