

# CLINICAL CASE UPDATE

## Compounding the Bleeding Reduction Effects of Transradial PCI and Bivalirudin in a High-Risk Patient Undergoing Complex PCI

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### Case Report

An 85-year-old Caucasian female with history of hypertension, hyperlipidemia (intolerant to statins), and chronic kidney disease, and a baseline serum creatinine of 1.5 mg/dL, was referred for management of severe aortic stenosis. A few months before presentation, the patient had suffered a non-ST-elevation myocardial infarction (MI) with significant gastrointestinal (GI) bleed and need for transfusions. Cardiac catheterization was not performed at that time.

Her chief complaints were severe dyspnea and congestive heart failure NYHA Class IV. Echocardiography demonstrated preserved ejection fraction of 55% and apical and septal hypokinesis. The aortic valve was severely calcified with peak/mean gradients of 126/76 mmHg and an aortic valve area of 0.3 cm<sup>2</sup>.

A cardiothoracic surgery consultant considered that she was not eligible for surgical aortic valve replacement because of her multiple comorbidities, small body size (height: 150 cm; weight: 53 Kg), and a Society of Thoracic Surgeons (STS) score of 9.3%. She was then referred for cardiac catheterization and possible balloon aortic valvuloplasty (BAV) as a bridge for transcatheter aortic valve replacement (TAVR).

The procedure, performed via transfemoral access, demonstrated three-vessel disease, as depicted in Figure 1, and severe aortic stenosis with a peak aortic gradient of 110 mmHg and an aortic valve area of 0.37 cm<sup>2</sup>. The 6 Fr sheath used for the diagnostic part of the study was exchanged for a 12F sheath. A 5 cm x 22 mm ZMed balloon was used for valvuloplasty (Figure 1D). The peak aortic gradient decreased to 32 mmHg and the valve area increased to 0.67 cm<sup>2</sup>.

A few minutes later, ST elevation was noted in the monitor. Repeat coronary angiography demonstrated a complete occlusion (TIMI 0) of the mid-right

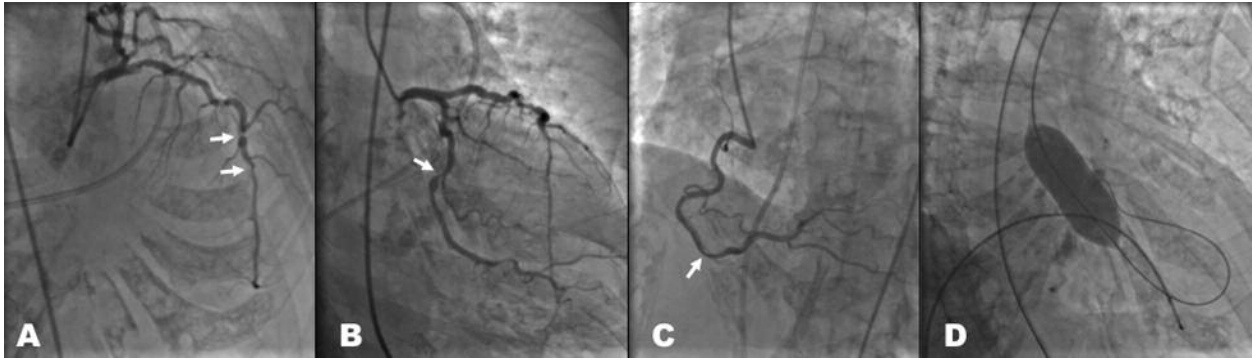
coronary artery (RCA) that was immediately treated with a bare-metal stent (Figure 2). Unfractionated heparin was given during the procedure, and manual pressure was used for hemostasis. The activated clotting time during the procedure was maintained between 250 and 300 seconds. There was a mild rise in postprocedural cardiac enzymes with a peak CK-MB of 9.6 ng/mL and Troponin I of 2.59 ng/mL (ULN < 0.04 ng/mL).

Over the next 24 hours, hemoglobin levels dropped significantly from a baseline of 11.9 g/dL to 8.5 g/dL despite the transfusion of 2 units of blood. A computerized tomography of the pelvis showed a groin hematoma but ruled out a significant retroperitoneal bleed. She was discharged 48 hours later on clopidogrel 75 mg and aspirin 81 mg daily, but had to be readmitted for GI bleeding with need for transfusions. She was then discharged to a rehabilitation facility, where she recovered with significant improvement in her heart failure symptoms (NYHA Class II).

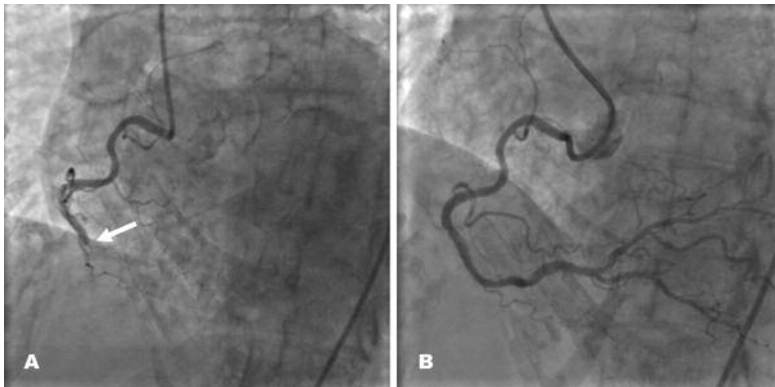
Complete revascularization with treatment of the left anterior descending (LAD) and left circumflex (LCx) lesions was needed before she could be considered a candidate for TAVR. After the patient finally recovered from the initial BAV and right coronary artery (RCA) percutaneous coronary intervention (PCI) procedures and complications, a 2-vessel PCI was scheduled approximately 50 days later. The patient and her family demanded transradial arterial access.

After some initial difficulties advancing a 6 Fr EBU 3.5 guiding catheter through the vasculature of the right upper extremity, the left main coronary artery was selectively cannulated (Figure 3A). Bivalirudin (bolus of 0.75 mg/kg followed by an infusion of 1.75 mg/kg/h) was used for anticoagulation. A clopidogrel loading dose of 300 mg was administered two hours prior to the procedure. The mid-LAD lesion was successfully treated with rotational atherectomy using a 1.5 mm burr, and two 3.0 x 24 mm bare-metal stents. Intravascular ultrasound demonstrated good stent apposition and expansion

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**Figure 1.** Coronary angiography demonstrated severe 3-vessel CAD with complex disease in the mid LAD (A), a 95% lesion in the mid LCx (B), and a 75% lesion in the mid/distal RCA (C). After diagnostic angiography, balloon aortic valvuloplasty was performed using a 5 cm x 22 mm ZMed balloon.



**Figure 2.** Immediately after balloon aortic valvuloplasty, ST elevation was noticed in the ECG monitor. Repeat angiography demonstrated an occluded right coronary artery with TIMI 3 flow (A). The vessel was promptly intervened with placement of a bare metal stent and restoration of TIMI 3 flow (B).

(Figure 3B). The LCx lesion was treated with a 2.75 x 12 mm bare-metal stent (Figure 3C). RCA angiography demonstrated a patent stent without restenosis. The hydrophilic-coated sheath was manually removed immediately after the procedure and a compression band was left in place for about two hours. The patient was discharged the next day on dual antiplatelet therapy. Her course was uneventful without bleeding or recurrent ischemia.

One month later, the patient exhibited mild dyspnea on exertion. Echocardiography demonstrated preserved ejection fraction with significant restenosis of the aortic valve with an area of 0.5 cm<sup>2</sup> and a peak gradient of 83 mmHg. Transapical TAVR was performed a month later using a 23 mm Edwards-Sapien balloon-expandable bovine valve (Figure 4).

The postoperative course was complicated with acute-on-chronic renal failure, altered mental status, diarrhea, and pneumonia. She was successfully treated for all these conditions while she remained hospitalized for a total of 20 days. At three-month follow-

up, the patient had some fatigue and back pain, but did not complain of shortness of breath or other cardiac-related symptoms. All laboratory values had returned to baseline.

### Discussion

This case illustrates the complexities associated with treating elderly patients with complex coronary disease and severe aortic stenosis, who until not long ago had no treatment options for their valvular conditions. In the TAVR era, an increasing number of very elderly patients undergo catheterization procedures including BAV and PCI for clinical stabilization before percutaneous valve replacement.<sup>1</sup>

These patients are inherently at high bleeding risk due to their older age, higher proportion of female gender, compromised renal function, baseline anemia, and use of large femoral sheath size.<sup>2,3</sup> Over the past decade, bleeding and transfusions have been recognized as predictors of increased mortality and recurrent myocardial ischemia.<sup>4,5</sup> As a matter of fact, incidents of bleeding and acute MI have a similar and independent association with 30-day and 1-year mortality in moderate- to high-risk ACS patients managed with an invasive strategy.<sup>6</sup>

With the recognition of the impact of bleeding on patient outcomes, most primary endpoints in recent clinical trials include a composite of ischemic and bleeding outcomes.<sup>7</sup> The mechanisms linking bleeding and transfusions with increased mortality are multiple and include the bleed location (cerebral, GI, retroperitoneal), its hemodynamic effects, cessation of antithrombotic agents, and the prothrombotic effects — decreased oxygen delivery and proinflammatory effects of stored blood products.<sup>8</sup>

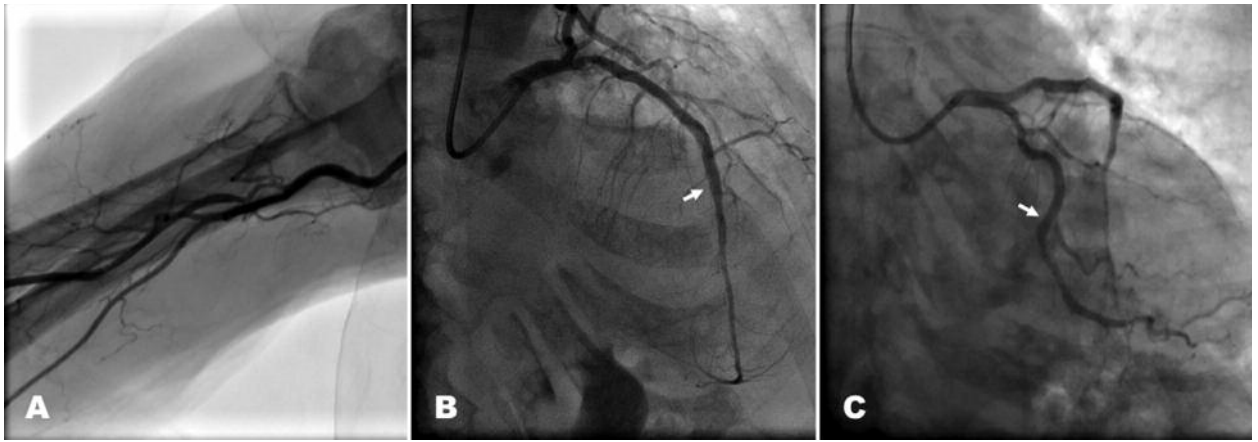


Figure 3. The second procedure was performed using transradial access. A localized angiography of the radial artery was necessary because of difficulties advancing a 6F EBU 3.5 guiding catheter (A). The LAD was treated with rotational atherectomy (1.5 mm burr) and 2 bare metal stents with good angiographic result (B). The LCx was treated with a bare metal stent (C).

Our patient had almost every predictor for bleeding and, in fact, she experienced a major GI bleed after the first procedure. In elective PCI cases, the majority of bleeds are usually associated with the vascular access site (approximately 70%), with a minority from non-access sites (30%).<sup>9</sup> Transradial access has been shown to effectively decrease bleeding risk in PCI. Transradial access was associated with a significant 73% relative reduction of major bleeding in a large meta-analysis and a 63% relative reduction in the incidence of major vascular access site complications in the recently published RIVAL trial.<sup>10,11</sup>

However, non-access-site bleeds represent approximately two-thirds of all bleeds in patients treated for acute coronary syndromes, as they are exposed to more potent antithrombotic agents for longer periods of time compared to patients undergoing elective PCI.<sup>9,12</sup> In the ACUTY trial, GI bleeding occurred in approximately 4% of patients older than 80 and was usually severe and associated with increased mortality.<sup>13</sup>

Transradial access is unquestionably safe but does not reduce non-access-site bleeds. Therefore, the clinician must individualize the bleeding risk and tailor antithrombotic strategies accordingly. Bivalirudin, with its favorable pharmacokinetic profile, including a short plasma half-life of 25 minutes after intravenous injection and a 20% renal excretion, as well as a lack of stimulatory effect on platelets, has been associated with decreased bleeding risk across clinical trials.<sup>14-19</sup>

In our particular case, after the initial BAV and PCI

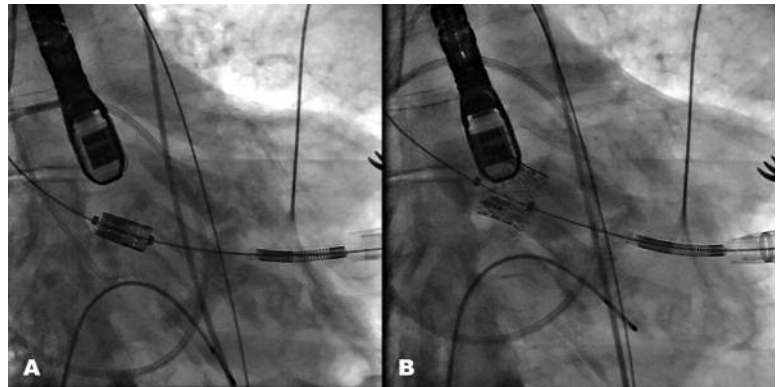


Figure 4. Three months after PCI, the patient showed evidence of aortic valve restenosis and underwent successful TAVR with a 23 mm Edwards-Sapien balloon-expandable bovine bioprosthetic valve that was implanted via transapical access. The valve was initially positioned under echocardiographic and angiographic control (A) and then deployed (B).

procedure complicated with GI bleeding, we chose to perform the second procedure via transradial access using bivalirudin. Radial access did not prevent us from performing a highly complex 2-vessel PCI in a heavily calcified vessel with use of rotational atherectomy and intravascular ultrasound in an elderly patient of short stature. Older age and short height have been identified as predictors of transradial PCI failure, because these 2 factors are usually associated with subclavian calcification and tortuosity.<sup>20</sup> Our choice of guiding catheter (EBU 3.5) was ideal to provide the support needed for this type of intervention.

Multiple studies have shown that complex PCI for bifurcations, chronic total occlusions, and other high-risk clinical settings is feasible using the transradial route without any disadvantages in comparison with transfemoral access.<sup>21-23</sup> The compounded

safety of transradial vascular access and bivalirudin resulted in excellent outcomes in this high-risk patient undergoing a complex procedure.

As new transcatheter valve therapies become available, an increasing number of non-operable elderly patients at high risk for bleeding — such as our patient — will be considered for percutaneous procedures in anticipation of definitive valve therapy. Transradial access for coronary interventions and bivalirudin for either coronary interventions or BAV are safe options that decrease bleeding rates and improve outcomes.

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