Case History: Antiplatelet Therapy in the Management of STEMI Treated With PCI

Written by Maria Vinall

Management of antiplatelet therapy in the treatment of patients with ST segment elevation myocardial infarction (STEMI) undergoing percutaneous coronary intervention (PCI) has many decision points. Using evidence-based findings, Marcus St. John, MD, Miami Cardiac and Vascular Institute, Miami, Florida, USA, described the decisions made to treat a 44-year-old man who presented with severe substernal chest pain (Canadian Cardiovascular Society class IV angina). He had a history of hypertension, diabetes, and dyslipidemia, and he was a smoker. There was no history of stroke or bleeding. An electrocardiogram revealed inferior ST elevations and depressions in leads 1 and L. His vital signs were normal, and there were no signs of congestive heart failure.

The patient received aspirin and heparin in the emergency department. While there, he suffered an episode of hematemesis, which may have influenced his clinical course. The first decision point in his treatment was deciding which antiplatelet therapy to use. The decision was based on the 2013 American College of Cardiology/American Heart Association STEMI guidelines [O'Gara PT et al. *Circulation* 2013]. Aspirin (162 to 325 mg) and a loading dose of a $P2Y_{12}$ inhibitor were given to the patient. The choices for $P2Y_{12}$ were clopidogrel (600 mg), prasugrel (60 mg), or ticagrelor (180 mg). Ticagrelor was chosen based on the PLATO study, which reported that patients with acute coronary syndrome treated with it had significantly fewer deaths, myocardial infarctions (MIs), or strokes (9.8% vs 11.7%; $p < .001$ for the composite end point) at 1 year, with an acceptable bleeding profile, when compared with clopidogrel [Wallentin L et al. *N Engl J Med* 2009].

The next decision point was to initiate bivalirudin in the catheterization laboratory. This decision was based on the ACUITY study, which showed that bivalirudin monotherapy was associated with similar rates of ischemia (8.8% vs 8.2%; $p = .45$), significantly lower rates of bleeding (3.5% vs 6.8%; $p < .001$), and improved net clinical outcome (11.6% vs 13.3%, $p < .057$) when compared with heparin plus glycoprotein (GP) IIb/IIIa inhibitors [Stone GW et al. *N Engl J Med* 2006].

Note, however, that a more recent and somewhat controversial HEAT PCI trial reported that major adverse ischemic cardiac events were significantly more common with bivalirudin (8.7%) than heparin (5.7%; $p = .01$) [Shahzad A et al. *Lancet* 2014. This difference was driven by a 4-fold increase in the rate of stent thrombosis observed with bivalirudin (3.4%) therapy versus heparin (.9%; $p = .001$). There was no difference in the rate of major bleeding, which may be explained by the high proportion of patients treated by radial access. In addition, it has been suggested that in the hands of experienced operators, PCI patients have better outcomes with radial versus femoral access [Mehta SR et al. *J Am Coll Cardiol* 2012]. Therefore, the use of bivalirudin in this setting has been questioned, as highlighted by results of a recent meta-analysis (Cavander LANCET).

The patient received a bare metal stent along with manual aspiration thrombectomy. Specifically, a bare metal stent was chosen relative to a drug-eluting stent to reduce the risk of stent thrombosis if his adenosine diphosphate receptor blocker needed to be discontinued because of bleeding before 1 year. New data, however, suggest that later-generation drug-eluting stents have lower rates of stent thrombosis compared to early-generation drug-eluting stents. In particular, cobalt-chromium everolimus-eluting stents appear to be associated with significantly lower rates of stent thrombosis within 2 years of implantation compared with bare metal stents [Palmerini T et al. *Lancet* 2012].

Another decision point was reached when the patient complained of recurrent chest pain and had signs of inferior ST elevations 30 minutes after the procedure. Another angiogram was performed. The patient was given a double bolus of eptifibatide, and bivalirudin drip was resumed. Fetch thrombectomy revealed a red thrombus in aspirate. After further balloon dilation, intravascular ultrasound

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revealed adequate stent apposition. Postprocedure coronary blood flow was normal (TIMI 3), and there was good myocardial blush. Dr. St. John speculated that secondary problems in this patient may have increased the risk of stent thrombosis, such as lack of absorption of antiplatelet therapy in the setting of vomiting and the very quick time from door to balloon. This was based on a study that showed that among patients with STEMI undergoing primary PCI, antiplatelet action by ticagrelor (46% of platelets still active) was significantly delayed at 2 hours [Alexopoulos D et al. *Circ Cardiovasc Interv* 2012]. In addition and as noted, this patient received bivalirudin, which has been associated with increased rates of acute stent thrombosis relative to heparin.

The patient was admitted to the intensive care unit, placed on beta-blockers, angiotensin-converting enzyme I, and statins. He was discharged 4 days later and subsequently lost to follow-up.

Dr. St. John's key message was that there are many decision points along the way from door to balloon and decisions should be made according to evidence-based medicine. Platelet inhibition with newer agents is rapid but not instantaneous. Depending on time to PCI and risk factors for poor absorption (cardiogenic shock, vomiting), physicians should consider adjunctive treatment with a GP IIb/IIIa receptor antagonist IIb/IIIa as a "bridge" to adequate platelet inhibition with oral agents.

An additional lesson in this case is the importance of systems to maximize patient follow-up. This patient's risk of recurrent event is highest in the first year after his MI, particularly in the first 30 days. Compliance with evidence-based medications, including aspirin, ticagrelor (twice daily), statin therapy, and beta-blocker therapy, is critical; however, he was lost to follow-up after discharge. Should he remain stable for 1 year after his MI the next decision point with regard to antiplatelet therapy will be whether to continue his ticagrelor beyond 1 year. Currently, there are no data to answer this question. Nonetheless, the DAPT trial is anticipated to report in 2014 and the PEGASUS-TIMI 54 trial in 2015, and these will provide important evidence to support clinical decision making.

Improving Outcomes in HF and Aortic Valve Stenosis With Advanced Technologies

Written by Toni Rizzo

Brian T. Bethea, MD, Tenet Florida Region, Florida, USA, discussed advanced treatments for heart failure (HF) and severe aortic stenosis (SAS). Patients with advanced HF require special intervention, including left ventricular assist device (LVAD) implantation. Studies of the HeartMate II LVAD reported 79% to 90% rates of survival to transplant, recovery, or ongoing device support at 180 days [John R et al. *Ann Thorac Surg* 2011; Starling RC et al. *J Am Coll Cardiol* 2011; Pagani FD et al. *J Am Coll Cardiol* 2009; Miller LW et al. *N Engl J Med* 2007] and 58% to 63% 2-year survival [Park SJ et al. *Circ Heart Fail* 2012; Slaughter MS et al. *N Engl J Med* 2009].

The Heartware Bridge to Transplant trial reported 82% survival at 2 years, with 34% still on the device, 40% transplanted, and 8% recovered [Strueber M et al. *J Am Coll Cardiol* 2011].

Recent LVAD improvements include decreased size and increased durability. Next-generation LVADs include the HeartMate III, HeartMate X, and HeartMate FILVAS.

SAS is life-threatening, and it progresses rapidly. In the PARTNER trial, 50% of inoperable patients died within 1 year [Leon MB et al. *N Engl J Med* 2010]. The 2014 Valvular Heart Disease guidelines recommend valve replacement for most patients with SAS promptly after symptom onset [Nishimura RA et al. *J Am Coll Cardiol* 2014]. Surgical aortic valve replacement (SAVR) is recommended for low- to moderate- and high-risk patients; transcatheter aortic valve replacement (TAVR) is recommended for high- and greater-risk patients.

The PARTNER trial evaluated TAVR versus SAVR in high-risk operable SAS patients (cohort A) [Smith CR et al. *N Engl J Med* 2011] and TAVR versus standard therapy in inoperable SAS patients (cohort B) [Leon MB et al. *N Engl J Med* 2010]. At 1 year, all-cause mortality in cohort A was 24.3% versus 26.8% in the TAVR and SAVR arms, respectively ($p = .001$ for noninferiority). Symptom improvement and hemodynamic performance were similar in both groups. There was no significant difference in stroke rates despite increased periprocedural events after TAVR at 30 days or 1 year; rates of all neurologic events were higher in the TAVR group at 30 days and 1 year ($p = .04$, both). In cohort B, TAVR versus standard therapy patients had a 25% absolute mortality reduction. Major vascular complications and major bleeding were more significant in the TAVR group at 30 days and 1 year ($p < .001$, all).

The CoreValve pivotal trial had superior 1-year all-cause mortality with TAVR (14.2%) versus SAVR (19.1%; $p = .04$) [Popma et al. *N Engl J Med* 2014]. Several next-generation valve systems are under development.

Dr. Bethea stressed the importance of a multidisciplinary approach to the treatment of HF and SAS patients, using a "shared care model" [Dickstein K et al. *Eur Heart J* 2008].