Reappraisal of the Current Guidelines With Respect to Preloading Before PCI May Be Warranted

Written by Phil Vinall

Both the European Society of Cardiology and the European Association for Cardio-Thoracic Surgery myocardial revascularization guidelines [Wijns W et al. *Eur Heart J* 2010] and American College of Cardiology Foundation, American Heart Association, and Society for Cardiovascular Angiography and Interventions percutaneous coronary intervention (PCI) guidelines [Levine GN et al. *J Am Coll Cardiol* 2011] recommend (with a Class I recommendation) the use of a loading dose of a $P2Y_{12}$ receptor inhibitor before PCI with stenting. David J. Cohen, MD, MSc, University of Missouri at Kansas City, Kansas City, Missouri, USA, suggested that despite the Class I recommendation, data supporting $P2Y_{12}$ inhibitor preloading before PCI are uncertain, as they are based predominantly on older trials that used conservative management strategies with prolonged treatment delays and with a substantial proportion of benefit occurring before the PCI.

The data for the current preloading guidelines come from 3 early trials: Percutaneous Coronary Intervention–Clopidogrel in Unstable Angina to Prevent Recurrent Events [PCI-CURE; Mehta SR et al. *Lancet* 2001], Clopidogrel for the Reduction of Events During Observation [CREDO; Steinhubl SR et al. *JAMA* 2002], and Clopidogrel as Adjunctive Reperfusion Therapy–Percutaneous Coronary Intervention [CLARITY-PCI; Sabatine MS et al. *JAMA* 2005], only 2 of which (PCI-CURE and CLARITY-PCI) showed significant reductions in end points with preloading. Of note, 2 of these trials (PCI-CURE and CLARITY-PCI) were subgroup analyses of larger trials based on post-randomization management and therefore were not truly randomized comparisons. CREDO, the only true randomized controlled trial of the 3, failed to show a benefit with preloading. The major concern with all 3 trials is the length of time between preload and PCI (median, 6 days in PCI-CURE; 3–24 hours in CREDO; and 2–8 days in CLARITY-PCI).

Upstream use of $P2Y_{12}$ loading prior to PCI with ticagrelor was superior to clopidogrel in the Platelet Inhibition and Patient Outcomes trial. However, there has been no study evaluating the potential benefit of pretreatment versus treatment at the time of PCI with ticagrelor.

A Comparison of Prasugrel at PCI or Time of Diagnosis of Non-ST-Elevation Myocardial Infarction [ACCOAST; Montalescot G et al. *N Engl J Med* 2013] was a Phase 3 trial designed to compare 2 prasugrel loading-dose regimens in patients with non–ST-segment elevation myocardial infarctions (NSTEMIs) with elevated troponin (≥1.5 times the upper limit of normal) who were intended to undergo an early (within 24 hours) invasive management strategy [Montalescot G et al. *Am Heart J* 2011]. Participants were randomized to either placebo (n=1996) or prasugrel 30 mg (n=2037) [Montalescot G et al. *N Engl J Med* 2013]. Following coronary angiography, subjects in the placebo group intended for PCI received the full loading dose of prasugrel 60 mg, while those in the prasugrel 30 mg group who were intended for PCI received an additional 30 mg of prasugrel. After PCI, all subjects received 5 or 10 mg of prasugrel daily (based on age and weight) for 30 days. The primary end point was a composite of cardiovascular (CV) death, MI, stroke, urgent revascularization, or glycoprotein (GP) IIb/IIIa bailout, at 7 days. Key safety end points include Thrombolysis In Myocardial Infarction (TIMI) major and minor bleeding risks [Montalescot G et al. *Am Heart J* 2011]. ACCOAST was stopped early because of an increase in major and life-threatening bleeding and no reduction in CV events.

Subjects were aged 64 years (mean) and mostly men; about one-quarter were high risk according to the Global Registry of Acute Coronary Events risk score. The median time from first loading dose to coronary angiography was 4.4 hours in the pretreated group and 4.2 hours in the placebo group.

At Day 30, preloading was not associated with an incremental benefit on the composite primary end point of CV death, MI, stroke, urgent revascularization, or GP IIb/IIIa bailout (HR,

Official Peer-Reviewed Highlights From
SCAI 2014
Las Vegas, NV | May 28-31, 2014

0.997; 95% CI, 0.83 to 1.20; p = .98). The absence of additional benefit was consistent for each of the individual end points and among the subgroup of participants who underwent PCI (the majority but not all trial subjects).

Although relatively infrequent, there was a doubling of TIMI major bleeding among subjects who received the 30-mg prasugrel preload (HR, 2.0; 95% CI, 1.3 to 3.1; p = .002).

Dr. Cohen concluded that in patients with NSTEMIs undergoing invasive management within 48 hours of admission, pretreatment with prasugrel (compared with treatment started only at the time of PCI) does not decrease major ischemic events but increases major bleeding complications. It is unknown whether these findings apply to patients with longer waiting times or to those treated with other agents (eg, clopidogrel, ticagrelor). Thus, the results showed no benefit of pretreatment, and reexamination of the current guidelines may be warranted.

Operator Radiation Exposure Reduced by One-Third With Bleeper Sv Radiation Monitoring Device

Written by Toni Rizzo

Radiation exposure during cardiac catheterization can result in injury to both the operator and the patient. Operator exposure has been associated with cataract formation [Ciraj-Bjelac O et al. *Catheter Cardiovasc Interv* 2010] and implicated in brain tumors [Roguin A et al. *EuroIntervention* 2012]. Skin injury and cancer in patients have been linked to radiation exposure during catheterization as well.

Georgios Christopoulos, MD, Veterans Administration North Texas Health Care System and University of Texas Southwestern Medical Center, Dallas, Texas, USA, presented results of the Effect of a Real Time Radiation Monitoring Device on Radiation Exposure During Cardiac Catheterization trial [RadiCure; NCT01510353]. The study objective was to examine the effect of the Bleeper Sv radiation monitoring device on operator and patient radiation exposure during cardiac catheterization. The Bleeper Sv device provides real-time operator dose reporting through auditory feedback. Device feedback enables the operator to take protective measures, such as using radiation only when necessary, repositioning the camera, stepping farther away from the source, or adjusting the lead shielding.

The study included patients undergoing clinically indicated coronary angiography or percutaneous coronary intervention (PCI). A total of 505 patients were randomized to the Bleeper Sv (n = 253) or to the control group (n = 252). The primary end point was operator radiation exposure. Secondary end points were patient radiation exposure, fluoroscopy time, and contrast volume.

Similar proportions of patients in both groups received diagnostic, PCI, and diagnostic + PCI procedures. There were no significant differences in procedural characteristics between the 2 groups (p = .852).

The first operator radiation exposure in the Bleeper Sv group was reduced compared with control for diagnostic procedures (0.7 vs 1.0 millirem [mrem]; p < .001), PCI (1.1 vs 1.4 mrem; p = .323), and both (0.9 vs 1.4 mrem; p < .001), for a 36% relative reduction in overall radiation exposure. The second operator radiation exposure in the Bleeper Sv group was reduced versus control for diagnostic procedures (0.4 vs 0.7 mrem; p < .001), PCI (0.4 vs 0.6 mrem; p = .197), and both (0.5 vs 0.07 mrem; p < .001), for a 29% relative reduction in overall radiation exposure.

There were no significant differences between the Bleeper Sv and control groups in patient air kinetic energy released per unit mass (kerma) for diagnostic procedures (p = .189), PCI (p = .631), or both (p = .153). Nor were significant differences observed between the Bleeper Sv and control groups in patient dose area product radiation dose for diagnostic procedures (p = .269), PCI (p = .511), or both (p = .125). No significant differences were observed in procedural outcomes between the 2 groups.

The Bleeper Sv effect on the first operator exposure remained consistent in various subgroups. The device effect during consecutive periods across the study was consistent, showing that a learning curve was not required.

Limitations of the study included that it was conducted in a single center and that there was no blinding. Additionally, the trial was not adequately powered for differences in patient radiation exposure and did not include a formal protocol for reducing radiation exposure apart from Bleeper Sv use. Dr. Christopoulos concluded that use of the Bleeper Sv device during cardiac catheterization resulted in a 29% to 36% decrease in operator radiation exposure.

Similar Rates of Lesion Misclassification With Nonhyperemic Indices of Stenosis Severity (iFR and Pd/Pa)

Written by Toni Rizzo

Stuart Watkins, MD, Golden Jubilee National Hospital, Glasgow, Scotland, United Kingdom, presented the results of the Verification of Instantaneous Wave-Free Ratio and Fractional Flow Reserve for the Assessment of