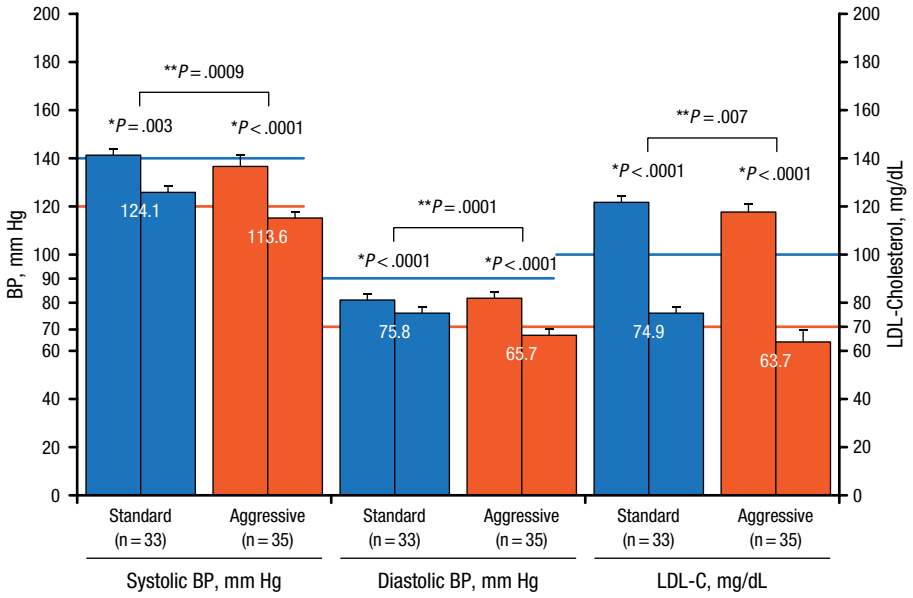
Figure 1. Effect of Aggressive Therapy for BP and LDL-C Lowering



BP, blood pressure; LDL-C, low-density lipoprotein cholesterol.

*Paired t-test.

**Unpaired t-test.

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and LDL-C to <70 mg/dL [Kawashiri MA et al. *Heart Vessels*. 2014]. Patients were excluded if the percutaneous coronary intervention was unsuccessful, they had type 1 diabetes or poorly controlled diabetes, they were receiving insulin therapy, had secondary hypertension, were using dihydropyridine calcium channel antagonist for >6 months, used an intensive lipid-lowering statin agent, had familial hypercholesterolemia, or were aged ≥80 years. Baseline characteristics were similar between the 2 arms.

Among the 68 patients who completed the study, the primary end point of this study, the percent change in coronary plaque volume, decreased in the standard treatment arm (n = 33; $P = .006$) and the aggressive treatment arm (n = 35; $P = .008$), but there were no differences between the 2 therapies. In addition, BP and LDL-C were significantly reduced in both arms, with a greater reduction in the aggressive treatment arm compared with the standard treatment arm (BP, $P = .0009$; LDL-C, $P = .007$; Figure 1). There was no significant difference in percent change in lumen and vessel volume between the 2 arms.

Dr Kawashiri concluded that the data from the MILLION trial suggest that both standard and aggressive BP and lipid-lowering regimens were effective; however, a greater decrease in BP and LDL-C was evident in the aggressive treatment group compared with standard therapy.

OUTSIDE START: Successful MACE-Free Cilostazol Bridging to Surgery in Patients With DES

Written by Toni Rizzo

Dual antiplatelet therapy (DAPT) with a $P2Y_{12}$ inhibitor plus aspirin decreases drug-eluting stent (DES) thrombosis [Mauri L et al. *N Engl J Med.* 2014]. Each year, approximately 5% to 10% of patients with a DES must interrupt DAPT to reduce perioperative bleeding. Premature discontinuation of DAPT, especially during the first postoperative year, results in stent thrombosis rates of 10% to 35%, inversely related to duration after stent placement [Moussa ID, Colombo A. *Catheter Cardiovasc Interv.* 2009; van Kuijk JP et al. *Am J Cardiol.* 2009]. The highest stent thrombosis rates have been observed in patients with a paclitaxel-eluting stent (PES) during DAPT discontinuation, leading to increased major adverse cardiac events (MACEs) for prolonged durations, up to 30 months post-stenting [Garratt KN et al. *Circulation.* 2015].

Currently, there is no consensus on the best bridging strategy for patients with a DES discontinuing DAPT preoperatively [Kern MJ et al. *Catheter Cardiovasc Interv.* 2014]. DES bridging has been attempted with aspirin, heparin, glycoprotein IIb/IIIa inhibitors, low molecular weight

heparins, and intravenous cangrelor, but success has been limited. Cilostazol, a phosphodiesterase inhibitor–type 3 that reversibly inhibits platelet activation and aggregation has shown promise as a third antiplatelet agent for high-risk patients and, given its shorter half-life, may be a consideration for perioperative bridging.

The OUTSIDE START Cilostazol Bridge Study, presented by Charles L. Laham, MD, Holy Family Memorial Hospital, Manitowoc, Wisconsin, USA, was a retrospective analysis conducted in patients who required surgery during the first 6 to 12 months after PES placement and discontinued DAPT. The analysis included consecutive patients who were bridged with cilostazol from 2 weeks to 60 months after a PES placement over an 8-year period.

The patients stopped DAPT 8 days before surgery and started cilostazol 100 mg BID on the seventh day preoperatively. Two dosing regimens of cilostazol 1300 mg were used to reduce the risk and degree of perioperative bleeding. Patients undergoing surgery with a low to moderate risk of bleeding had a goal of cilostazol 1300 mg, which they discontinued 24 to 30 hours before surgery. DAPT was resumed 12 to 24 hours after surgery. The goal for patients undergoing high-bleeding-risk surgery was cilostazol 1000 mg, which they stopped 54 to 60 hours prior to surgery. They restarted DAPT 24 to 36 hours after surgery. The primary end points were perioperative bleeding and MACE (cardiac death, myocardial infarction, or urgent revascularization) within the bridged period and up to 1 month after surgery.

A total of 108 patients with ≥1 PES who underwent 183 consecutive surgeries stopped DAPT and were bridged by cilostazol (Table 1). Of these, 104 (57%) surgeries were bridged with cilostazol 1300 mg, 60 (32%) with cilostazol 1000 mg, and 10 (5.5%) with 650 to 900 mg. A total of 171 surgeries were adequately bridged with >600 mg of cilostazol. The remaining 12 patients received an inadequate preoperative dose of 0 to 600 mg cilostazol and failed to resume DAPT postoperatively. No MACE occurred among patients who were successfully bridged with cilostazol. Among patients who were not adequately bridged perioperatively, 1 MACE occurred in the first year, and of note, 3 occurred beyond 12 months, of which 1 occurred up to 40 months post-PES stent placement. The study results are shown in Table 1.

Perioperative cilostazol for DES bridging is feasible in patients at the highest risk of stent thrombosis with PES and completely off DAPT. No MACE or bleeding other than minor nuisance bleeding was reported in patients who were successfully bridged with cilostazol. Dr Laham concluded that this was a clinically driven hypothesis-generating feasibility study. The results should be verified in controlled trials using current-generation DES and bare metal stents with antiplatelet agents in current use.

Table 1. OUTSIDE START Cilostazol Bridge Study: 8-Year Results, No. (%)

Timing of Surgical Bridging[a]	Adequate Bridging/DAPT Resumption	Suboptimal or No Cilostazol Bridge and/or Failed DAPT Resumption (Controls)	
	No MACE	No MACE	MACE[b]
<6 (26)	23 (88)	3 (12)	—
6-12 (29)	25 (86)	3 (10)	1 (3.4)[c]
>12-24 (49)	48 (98)	—	1 (2.0)[d]
>24-36 (48)	45 (94)	2 (4.2)	1 (2.1)[e]
>36-60 (31)	30 (97)	—	1 (2.9)[f]
Total (183)	171 (93)	8 (4.4)	4 (2.2)

Data presented in No. (%) unless otherwise indicated.

DAPT, dual antiplatelet therapy; MACE, major adverse cardiac event; PCI, percutaneous coronary intervention; PES, paclitaxel-eluting stent.

[a]Months post-PES (No. of bridged).

[b]Actual MACE by type and timing post-PES placement (events occurred only in those without adequate bridging).

[c]Urgent repeat PCI at 7.5 months.

[d]Death at 12.5 months.

[e]Urgent repeat PCI at 28 months.

[f]Myocardial infarction at 40 months.

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TRIAGE: Similar Ischemic and Bleeding Outcomes With Prasugrel and Clopidogrel

Written by Alla Zarifyan

Jaya Chandrasekhar, MBBS, Icahn School of Medicine at Mount Sinai, New York, New York, USA, presented results of the TRIAGE study [NCT01582217], demonstrating that patients with high on-treatment platelet reactivity (HTPR) receiving prasugrel and patients with low on-treatment platelet reactivity (LTPR) treated with clopidogrel had similar ischemic and bleeding outcomes.

HTPR in patients treated with clopidogrel is associated with a greater incidence of adverse cardiac events such as stent thrombosis, myocardial infarction (MI), and even death. However, testing platelet function prior to thienopyridine selection in patients undergoing percutaneous coronary intervention (PCI) has not been shown to correlate with improved outcomes in recent randomized trials, and the role of screening for platelet function in the context of ischemic and bleeding risks has not been investigated.

TRIAGE was a multicenter, prospective, observational study. The objective was to compare outcomes in patients treated with prasugrel vs clopidogrel at PCI