Hospital, Boston, MA. In addition, PCI is associated with unique limitations in the diabetic population, such as a higher risk of restenosis, MI, and cardiac mortality.

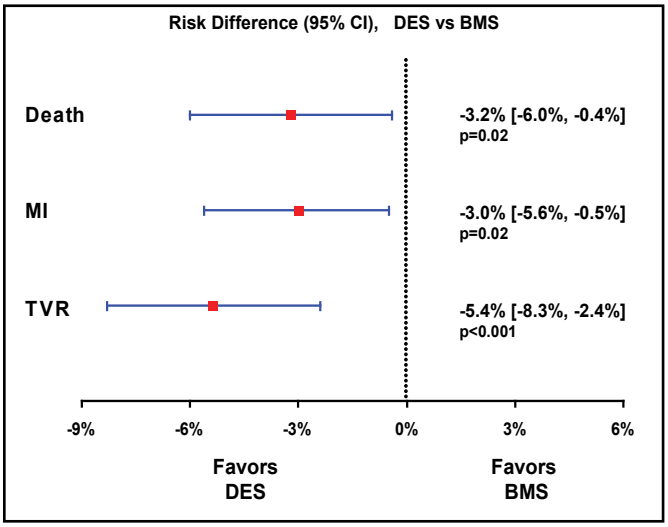
Dr. Mauri presented results of the Mass-DAC trial, which were simultaneously published online in *Circulation* [Garg P et al. *Circulation* 2008].

The Mass-DAC analysis included data from all adults who underwent PCI in Massachusetts from April 1, 2003 through Sept. 30, 2004 and completed a 3-year follow-up (n=21,045). Of the 5051 patients with diabetes, 3341 received a DES and 1710 received a BMS. Patients who received both types of stent were excluded from the analysis.

Because Mass-DAC was an observational study in which patients were not randomly assigned to different treatment groups, several baseline characteristics differed in the 2 groups. Therefore, propensity score matching using 67 clinical variables was used to compare outcomes in the DES and BMS groups. The primary endpoints were mortality, MI, and target vessel revascularization after 3 years.

The unadjusted mortality rate was 14.4% for patients who received DES and 22.2% for those who received BMS. According to propensity score analysis, DES were associated with a 3.2% absolute reduction in the risk of death compared with BMS (17.5% vs 20.7%; p=0.02), a 3% absolute reduction in the risk of MI (13.8% vs 16.9%; p=0.02), and a 5.4% absolute reduction in the risk of target vessel revascularization (18.4% vs 23.7%; p<0.001; Figure 1).

Figure 1. Drug-Eluting and Bare-Metal Stenting for Diabetes Mellitus - Matched Risk Differences at 3 Years.



Dr. Mauri noted that the mortality curves for the DES and BMS groups stayed roughly parallel from 6 months through 3 years. The durability of the restenosis benefit with the small but persistent survival benefit that was associated with DES suggests that they should be the preferred therapy in patients with diabetes, she concluded.

Early Invasive Management Beneficial for High-Risk NSTEMI Patients

An early invasive strategy is as safe as delayed invasive management in patients with unstable angina or non-ST-segment elevation myocardial infarction (NSTEMI), according to findings from the TIMACS (Timing of Intervention in Patients with Acute Coronary Syndromes; NCT00552513) trial. However, early invasive care does not significantly reduce the risk of death, new myocardial infarction (MI), or stroke compared with a delayed invasive strategy in most patients, except for those who are at the highest risk for adverse events.

The TIMACS trial included 3031 patients who were randomly assigned to an early invasive strategy that included coronary angiography within 24 hours followed by percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) as needed (n=1593), or to a delayed strategy in which patients received angiography, PCI, or CABG 36 hours or more after the onset of symptoms (n=1438). The median times to angiography in the early and delayed groups were 14 and 50 hours, respectively.

Patients in the early and delayed management groups had similar rates of the primary composite endpoint of death, MI, or stroke within 6 months (9.7% vs 11.4%, HR, 0.85; 95% CI, 0.68 to 1.06; p=0.15; Figure 1). In a secondary endpoint analysis, early invasive management reduced the risk of refractory ischemia compared with delayed management (1.0% vs 3.3%; HR, 0.30; 95% CI, 0.17 to 0.53; p<0.00001), without increasing the risk of major bleeding during the index hospitalization (3.1% vs 3.5%; p=0.53).

Early management also reduced the risk of death or cardiovascular events among patients who were at high risk for adverse events, as determined by GRACE (Global Registry of Acute Coronary Events) scores ≥140. For patients with low or intermediate risk according to GRACE scoring, the 6-month risk of death, MI, or stroke was similar in the early and delayed management groups (7.7% vs 6.7%; p=0.43). However, among patients in the

high-risk group, early management reduced this risk by 35% compared with delayed management (14.1% vs 21.6%; HR, 0.65; 95% CI, 0.48 to 0.88; p=0.005; Figure 2).

Figure 1. Primary Outcome of Death, MI, or Stroke at 180 Days.

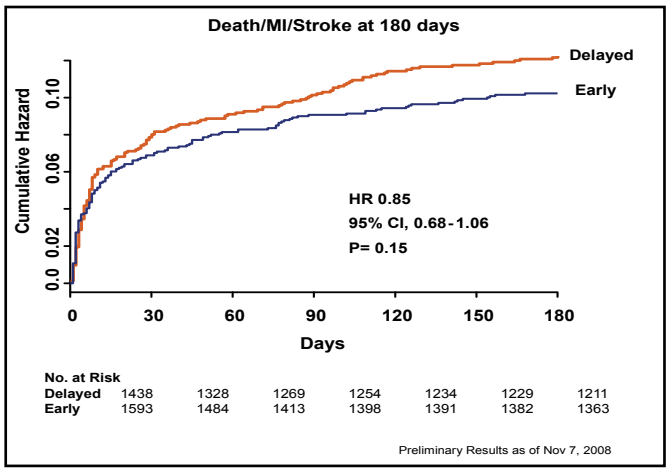
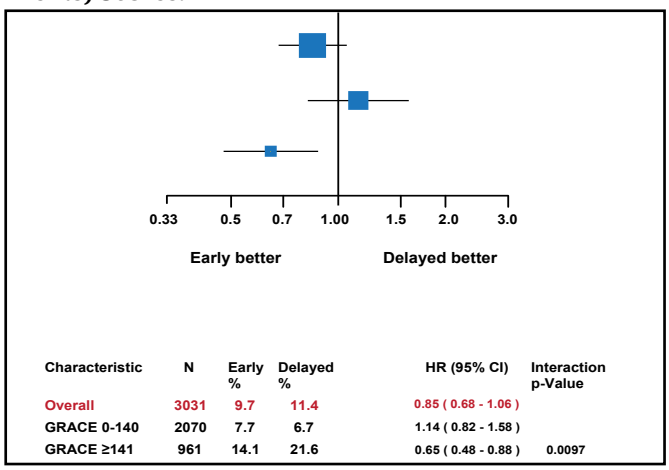


Figure 2. GRACE (Global Registry of Acute Coronary Events) Scores.



"Most patients with acute coronary syndromes can be managed safely with either an early or a delayed invasive strategy," said Shamir R. Mehta, MD, MSc, McMaster University, Hamilton, Ontario, Canada, who reported the TIMACS findings. However, early intervention appears to be superior for high-risk patients, who should be considered for early heart catheterization, he said.

"In all other patients with acute coronary syndrome, the decision regarding timing of intervention can depend on other factors, such as catheterization laboratory availability, health care system, convenience and economic considerations," Dr. Mehta concluded.

Tailored Clopidogrel Dosing Reduces Adverse Events in Patients With Clopidogrel Resistance Undergoing PCI

For patients who undergo nonemergent percutaneous coronary intervention (PCI), tailoring the loading dose of clopidogrel according to platelet reactivity reduced the rate of early stent thrombosis, according to findings from a new trial. Individualized dosing also reduced the incidence of major adverse cardiovascular events (MACE) without increasing bleeding events.

Franck Paganelli, MD, Hôpital Université Nord, Marseilles, France, reported findings from the Tailored Clopidogrel Loading Dose According to Platelet Reactivity Monitoring to Prevent Stent Thrombosis study at the American Heart Association Scientific Sessions meeting in New Orleans.

Clopidogrel resistance has been linked to increased adverse events in patients who are undergoing PCI. Dr. Paganelli and colleagues have been exploring the role of the vasodilator-stimulated phosphoprotein (VASP) index, a measure of platelet reactivity that is specific to the $P2Y_{12}$ receptor, to guide clopidogrel dosing. The present study examines whether additional loading doses of clopidogrel, based on the VASP index, can overcome problems that are related to clopidogrel resistance, including stent thrombosis and MACE, which have been shown to occur more frequently in patients with elevated platelet reactivity (elevated VASP index).

The trial included 429 "low responders" to clopidogrel, whose VASP index remained ≥50% (elevated platelet reactivity) after an initial loading dose of clopidogrel 600 mg. These patients were randomly assigned to additional VASP-guided clopidogrel dosing, with the goal of achieving a VASP index <50% (low platelet reactivity) prior to PCI (n=214), or PCI without additional clopidogrel dosing (n=215). In the VASP-guided arm, up to 3 additional loading doses of 600 mg of clopidogrel (maximum clopidogrel dose 2400 mg) were administered before PCI.

After the second clopidogrel dose in the VASP-guided group, 132 patients (61%) had a low VASP index of <50% and proceeded to PCI. Of the remaining patients, 83 (38%) required third doses and 40 (18%) required fourth doses of clopidogrel prior to intervention. The latter group included 17 patients (8%) whose VASP index remained elevated (>50%) despite a total of 2400 mg of clopidogrel. The primary endpoint was the rate of early definite stent thrombosis.