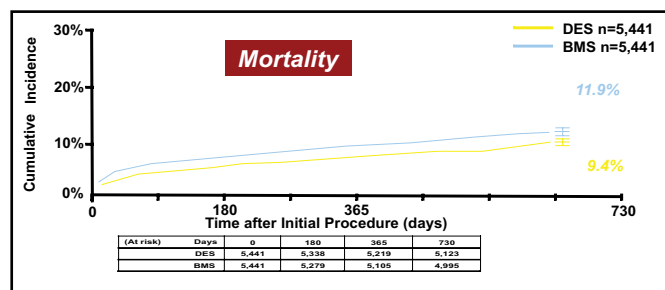underwent percutaneous coronary intervention (PCI) with stents from April 1, 2003 through September 30, 2004 at non-government hospitals in Massachusetts. The time period included the introduction of DES to the market, and patients were followed for 24 months following stent placement. The goal of the study was to determine long-term patient outcomes by stent type in a population representative of current United States medical practice.

A propensity score-matched analysis was performed using a logistic regression model created from 63 variables. The primary outcome measure was the matched risk differences between the two groups in mortality, myocardial infarction (MI), and revascularization at 2 years. A total of 17,726 patients that underwent placement of a bare metal stent (BMS) or DES were identified; patients that received both stent types were excluded. Sixty-five percent (11,516) of patients received DES compared with 35% (6,210) who received BMS. Of the DES, 72% were sirolimus-eluting, and 28% were paclitaxel-eluting stents. A total of 5,441 propensity matched pairs were analyzed for each of the 2-year outcomes. The DES group was significantly better in terms of mortality, 9.4% versus 11.9% (p<0.0001).

"Previous studies had presented differences in early and late hazards of DES compared to BMS. In fact, what we saw were consistent findings across all time periods," noted Dr. Mauri (Figure 1). Sensitivity analyses were employed in the following two areas to ensure that residual confounding was not present after the propensity match. The first sensitivity analysis included DES time on the market versus BMS over time, and the second analysis looked at a time-point where there would not be an expected difference in mortality between groups (2 days). The sensitivity analyses findings were consistent with the primary endpoint analyses, indicating that the data are robust. "This [study] demonstrated no increase in rates of death or myocardial infarction associated with DES compared with BMS use at 2 years," concluded Dr. Mauri.

Figure 1. 2-Year Mortality in Matched Patients After DES and BMS Treatment.

PCI Plus Optimal Medical Therapy Offers Benefit in Moderate-to-Severe Ischemia

A substudy analysis within the COURAGE trial indicated that percutaneous coronary intervention (PCI) plus optimal medical therapy (OMT) led to significantly improved outcomes in patients with moderate-to-severe ischemia. According to lead author Leslee Shaw, PhD, Emory University School of Medicine, Atlanta, GA, the substudy results clarify the primary results of the COURAGE trial, reported earlier this year. The main trial results demonstrated that elective PCI plus OMT did not reduce death or MI compared with OMT alone for patients with stable coronary artery disease.

"These findings do not invalidate the earlier results," said Dr. Shaw. "Rather, they clarify the results and show that there is a differential benefit of PCI in a particular subgroup. The benefit was greatest in patients with more severe ischemia at baseline."

The substudy involved 314 patients from the main COURAGE population who had rest and stress myocardial perfusion SPECT (MPS) before their assigned treatment and again at 6-18 months after randomization. The primary aim of the study was to compare changes in ischemic burden (defined as a reduction of at least 5% in myocardial ischemia) after an average of 1 year following random assignment to either PCI plus OMT or OMT alone.

The burden of ischemia at baseline on MPS was similar for both groups (8.2% for PCI plus OMT vs 8.6% for OMT alone). At an average of 1 year, the percentage of patients with a significant reduction (at least 5%) in ischemia (the primary endpoint) was greater for the PCI plus OMT group (33.3% vs 19.8%; p=0.004; Figure 1A). PCI was especially beneficial for patients who had moderate-to-severe ischemia at baseline (perfusion defect ≈10% of myocardium) (78% for the PCI plus OMT group vs 52%; p=0.007; Figure 1B). The mean reduction in ischemic myocardium was also greater in the PCI plus OMT group (-2.7% vs -0.5% for OMT alone; p<0.0001).

Figure 1A and 1B. Primary Endpoint: % with Ischemia Reduction ≥5% Myocardium (N=314) and % with Ischemia Reduction ≥ 5% Myocardium.
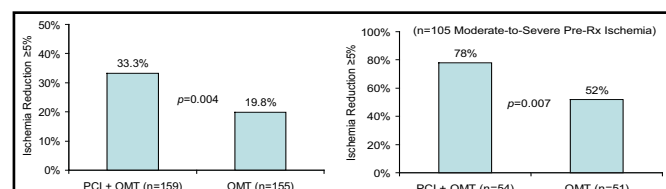
In addition, in an attempt to correlate the extent of myocardial ischemia to clinical outcomes, Dr. Shaw showed that the risk of death or MI was lower among patients who had a reduction in ischemia of at least 5% (13.4% vs 24.7%; p=0.037), particularly among patients with moderate-to-severe ischemia before treatment (16.2% vs 32.4%; p=0.001; Figure 2). The rates of death and MI ranged from 0-39% according to the amount of residual ischemia after PCI.

Figure 2. Risk of Death or MI Among Patients with Moderate-to-Severe Ischemia.
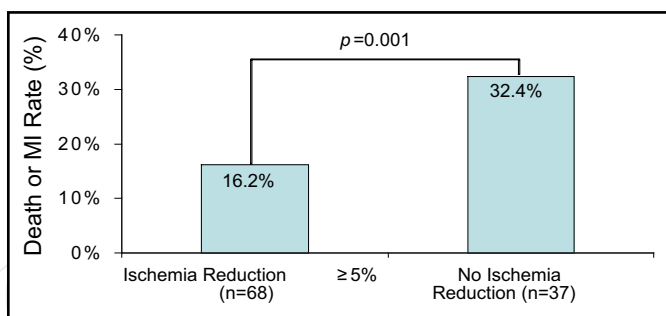
Dr. Shaw emphasized that although the findings suggest that MPS may be valuable for identifying patients at risk for death or MI, the prognostic findings in this substudy were exploratory with limited statistical power. Still, she said, "These findings suggest the potential value of MPS in identifying at-risk patients for targeting therapy and in guiding treatment strategies, particularly for patients with moderate-to-severe pre-treatment ischemia who may benefit with PCI as well as consideration of crossover to PCI for those patients with extensive residual ischemia following a course of medical management."

Duration of Eptifibatide Infusion after Uncomplicated PCI

This trial explored whether the infusion of eptifibatide after uncomplicated percutaneous intervention (PCI) with stenting could be safely shortened to <2 hours without increasing the risk of ischemic events and with the potential benefit of lowering the risk of major bleeding.

"This change in treatment [duration] reduces drug costs up to 37% of the standard regimen and significantly reduces the length of stay and associated costs," said Anthony Fung, MD, Vancouver General Hospital, Canada, who reported the findings of the Brief Infusion of Eptifibatide Following PCI (BRIEF-PCI) trial.

The BRIEF-PCI trial was designed to compare the standard 18-hour infusion of eptifibatide with a short infusion (<2 hours) after non-emergent PCI. Dr. Fung noted that contemporary PCI involves the use of dual oral antiplatelet therapy, including a loading dose of clopidogrel, and the routine use of coronary stents. The investigators' hypothesis, he said, was that this change in approach to PCI may obviate the need for prolonged infusion of eptifibatide.

The patients in the trial had stable angina, acute coronary syndromes, or recent (within <48 hours) ST-elevation myocardial infarction (STEMI). All patients received intravenous eptifibatide during PCI, and approximately two-thirds of the patients were treated with a loading dose of clopidogrel. After successful PCI, patients were randomly assigned to receive either standard eptifibatide (312 patients) or the short infusion (312 patients). The primary endpoint was ischemic myocardial injury within 24 hours after PCI, as determined by elevated levels of troponin-I and creatinine kinase MB at 6 and 18 hours compared with baseline. The trial was designed as a noninferiority study, with a reference event rate of the primary endpoint of 50% and an upper margin set at 10%. The study was powered at 80%, with a one-sided alpha of 0.05.

Dr. Fung reported that ischemic myocardial injury occurred in 30.1% of the patients who received the short infusion and in 28.3% of those who received the standard infusion (noninferiority margin, 1.8% [95% CI, 7.8%]; p<0.012 for noninferiority). There was also no difference between the two groups in the rate of the individual secondary endpoints of death, nonfatal MI, urgent target vessel revascularization, or a composite of these events. The incidence of minor bleeding did not differ between the two groups (17.6% vs 21.2%), but major bleeding occurred less frequently among patients who received the short infusion (1.0% vs 4.2%; p=0.02; Figure 1).

Figure 1. Bleeding and Quadruple Endpoints.