The Use of Drug-Eluting Stents in Patients with ST-Elevation Myocardial Infarction Increases Mortality Compared to Bare Metal Stenting at 2-Years

According to results presented by P. Gabriel Steg, MD, Hôpital Bichat-Claude Bernarde, Paris, France, the use of drug-eluting stents (DES) vs bare metal stents (BMS), in patients with ST-elevation myocardial infarction (STEMI) increases all-cause mortality at 2 years.

Prof. Steg presented the results of an analysis from GRACE (Global Registry of Acute Coronary syndromEs), an ongoing, observational registry of patients with ACS hospitalized in 94 hospitals in 14 countries across 4 continents. The analysis is based on data from 6,447 patients who received either DES (n=2,126) or BMS (n=4,321).

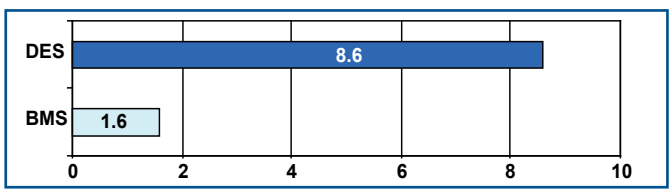
All Patients

Overall, patients with acute coronary syndrome (ACS) who had a DES implanted had a significantly lower in-hospital death rate (1.1%) than BMS patients (2.7%; p<0.0001), although mortality of the two groups was identical at 6 months (2.2% BMS; 2.3% DES). The use of dual antiplatelet therapy, (70% for DES vs 50% for BMS), was significantly higher in DES patients at 6 months (p<0.001). This difference continued up to the 2-year follow-up, at which point 38% of DES patients were still receiving dual antiplatelet therapy vs 12.9% of patients with BMS (p<0.001).

Between 6 months and 2 years there was a significant difference in the rate of reinfarction in favor of BMS (2.9%) vs DES (5.4%) (p=0.046). However, no difference in mortality between 6 months and 2 years (DES 4.8%, BMS 4.6%) was found in the overall cohort of patients with ACS.

When patients were analyzed based on a diagnosis of STEMI or non-STEMI/unstable angina (NSTE-ACS), there was a significant difference in mortality rate between STEMI patients who received DES (8.6%) vs those who received BMS (1.6; p<0.001; Figure 1).

Figure 1. Mortality – STEMI Patients - 6 Months to 2 Years.



STEMI Patients

Of the 2,298 patients in the STEMI population, 569 received DES and 1,729 received BMS. At 6 months the unadjusted rate of hospital mortality was significantly lower in DES (2.0%) vs BMS (3.8%) patients (p=0.018). A landmark analysis was performed to compare post-discharge survival between the two stent groups. Results of this analysis showed no difference in risk for the two groups between hospital discharge and month 6 (HR 0.99) but a marked increase in the risk of death for STEMI patients treated with DES began at month 6 and continued to 2 years (HR 4.67). A significant increase in the risk of death at 2 years persisted after adjustment for GRACE risk score, number of dilated vessels, diabetes, and type of PCI (HR 6.69; p=0.002).

Although acknowledging the limitations of observational studies, according to Prof. Steg, these data suggest that DES should be used cautiously in patients with STEMI until further evidence of long-term safety is accumulated. "There is now a need for a large prospective randomized trial with long-term follow-up," said Prof. Steg.

Lowering Blood Pressure in Patients with Type 2 Diabetes Significantly Reduces the Risk of Death from Diabetic Complications Even in Patients with Normal Blood Pressure

Data from the ADVANCE study (Action in Diabetes and Vascular Disease) presented by Stephen MacMahon, MD, The George Institute for International Health, Australia, demonstrated that lowering blood pressure in patients with diabetes significantly reduces mortality. The benefits were evident independent of baseline blood pressure and whether patients were receiving concomitant treatment with other blood pressure-lowering, lipid-lowering, or antiplatelet therapies.

The UK Prospective Diabetes Study showed that lowering systolic blood pressure (SBP) from 155-145 mmHg in diabetic patients with hypertension resulted in a significant reduction in mortality (Turner R et al. *BMJ* 1998). The objectives of the current study were to determine whether additional benefits could be achieved by further lowering SBP to <145 mmHg, whether the benefits would be similar for non-hypertensive patients, and whether those benefits would be in addition to those produced by other cardiovascular preventive therapies.

The study population included 11,140 patients (mean age 66 years; mean SBP 145 mmHg) who were randomly assigned to receive combination perindopril/indapamide 2.0mg/0.625mg for 3 months followed by 4.0mg/1.25mg thereafter (n=5,569) or placebo (n=5,571). Patients received ancillary treatment at the discretion of the treating physician. The primary study outcomes were macrovascular (nonfatal stroke or MI or death from any cardiovascular cause) and microvascular events (new or worsening nephropathy or diabetic eye disease).

Baseline patient characteristics were similar between groups. Average patient follow-up was 4.3 years at which point 73% of those receiving active therapy and 74% of those receiving placebo remained on therapy. Mean systolic and diastolic blood pressure (DBP) declined by 5.6 and 2.2 mmHg, respectively, in patients receiving combination perindopril/indapamide vs placebo (p<0.001 for both systolic and DBP). Blood pressure dropped from 145/81 mmHg at baseline to 135/75 mmHg in the treatment arm and 140/77 mmHg in the control group.

In patients receiving combination perindopril/indapamide there was a significant relative risk reduction (RRR) of 14% in all-cause mortality (p=0.025) which was driven primarily by an 18% RRR in cardiovascular deaths (p=0.027).

The overall RRR of a macrovascular or microvascular event was 9% (p=0.041).

Additional secondary endpoint analyses showed a 14% reduction (8.4% vs 9.6%, p=0.020) in the risk for coronary heart disease and a 21% reduction (22.3% vs 26.9%, p<0.0001) in all renal events. There was no difference in cerebrovascular or diabetic eye events. Similar benefits were achieved for those with or without hypertension and in the presence or absence of treatment with other blood pressure lowering drugs, statins, or anti-platelet drugs (Table 1).

Table 1. Relative Risk Reduction by Subgroup.

Subgroup	Perindopril/ Indapamide n=5569	Placebo n=5571	Relative Risk Reduction (95% CI)
History of hypertension			
No	121 (12.7%)	136 (13.8%)	9% (-1.7, 29)
Yes	740 (16.0%)	802 (17.5%)	9% (0, 18)
Any blood pressure lowering therapy			
No	177 (12.6%)	183 (13.3%)	6% (-15, 24)
Yes	684 (16.4%)	755 (18.0%)	10% (0, 19)
Statin therapy			
No	638 (15.8%)	687 (17.3%)	10% (0, 19)
Yes	223 (14.5%)	251 (15.6%)	8% (-10, 23)
Anti-platelet therapy			
No	408 (13.7%)	454 (15.3%	11% (-2, 22)
Yes	453 (17.4%	484 (18.6%)	7% (-5, 18)

Source: ADVANCE Collaboration Group. *Lancet* 2007. Published Online September 2, 2007

Prof. MacMahon called for routine blood pressure reduction for all patients with type 2 diabetes. "In absolute terms", said Prof. MacMahon, "one death would be avoided for every 78 patients treated with the fixed combination of perindopril and indapamide over 5 years. Lowering blood pressure is what counts, not the way by which it is lowered"

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The importance of monitoring weight in patients with HF was reinforced by the findings of a study in which weight loss and leanness simultaneously predicted poor prognosis in a broad spectrum of HF patients. The study was carried out by Joanna Dobson, MD, London School of Hygiene, UK, who reports that weight loss at 6 months predicted poor prognosis in the long-term. In the study, for every 1% weight loss, there was an 11.2% increase in mortality hazard. Prof. Dobson advocates for more intense monitoring of weight loss as well as optimizing treatment when weight loss is detected.

Patient Education

According to the Study group on Heart failure Awareness and Perception in Europe (SHAPE) study, only 3% of 7,958 respondents to a European survey could correctly identify HF from a description of typical signs and symptoms [Remme WJ et al. *Eur Heart J* 2005]. This was much lower than the rates for recognition of any other cardiovascular disease. To address this knowledge gap, the Heart Failure Association of the ESC developed the website www.heartfailurematters.org. "The website is designed to empower patients to know what they can do to help themselves," says Prof. Dickstein. It offers a description of HF and its treatment in simple language and features an optional narrative guide to help older visitors to the site. Prof. Dickstein encouraged physicians to tell their patients about the website as a way to improve patient compliance with treatment and lifestyle changes that can help enhance their quality of life and improve survival.

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elevated TC/HDL-C ratio defines a group of patients at higher risk for ACS.

The results of these studies indicate that enhanced efforts to increase the HDL-C level and to decrease the TC/HDL-C ratio may be of benefit, especially in individuals with ACS or at high risk for the disease; the cardioprotection offered by HDL-C stemming from its direct relationship with anti-inflammatory markers.