News and Views from the Literature

Myocardial Infarction

Initial Results from the EPHESUS Trial

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Eplerenone Reduces Mortality 30 Days After Randomization Following Acute Myocardial Infarction in Patients with Left Ventricular Systolic Dysfunction and Heart Failure

Pitt B, White H, Nicolau J, et al.

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A significant number of patients who suffer myocardial infarction (MI) develop systolic left ventricular dysfunction, accompanied by signs and symptoms of heart failure. Patients who develop signs of heart failure following acute MI are at a 3- to 4-fold increased risk of in-hospital mortality.[1] Early intervention in this population with revascularization and angiotensin-converting enzyme inhibitor, β-blocker, and anti-platelet agent therapies has been shown to be particularly effective, if administered as early as possible following the ischemic event.[2] The use of selective aldosterone blockade during the in-hospital phase of acute MI management has been shown to have beneficial effects on left ventricular remodeling and collagen formation, as well as improving myocardial neuronal norepinephrine uptake, decreasing plasma norepinephrine levels, and improving heart rate variability and baroreceptor function. The Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study (EPHESUS) has demonstrated the ability of eplerenone therapy to reduce all-cause mortality and a composite endpoint of cardiovascular mortality and cardiovascular hospitalizations by 15% and 13%, respectively, with a mean follow-up of 16 months, when added to conventional post-MI therapy.[3]

During the first 30 days post-MI, patients with left ventricular dysfunction and heart failure are exposed to significant mortality risk, including sudden cardiac death. There is a gap for the use of internal cardiac defibrillators for primary prevention of sudden cardiac death. Therefore, it is critical that life-saving treatments be initiated as early as possible. In this study, eplerenone at a dose of 25 mg daily was initiated at an average of 7 days following acute MI in patients with left ventricular dysfunction (left ventricular ejection fraction $\leq$ 40%) and clinical signs of heart failure. A 31% relative risk reduction for all-cause mortality ($P = 0.004$), a 32% reduction in cardiac mortality ($P = 0.003$), and a reduction of 37% for the risk of sudden cardiac death ($P = 0.051$) were measured when the eplerenone dose was added to conventional therapy.[4] Of the total patient cohort, 86% were taking angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, 75% β-blockers, 60% diuretics, 88% aspirin, and 47% statin therapy at the time of randomization. Of note, patients excluded from this study included those

with a serum potassium concentration greater than 5.0 mmol/L or serum creatinine levels greater than 2.5 mg/dL. There was no difference in the occurrence of hyperkalemia between the study and control populations.

Based on the results of this study, one would consider the early use of eplerenone to be an integral part of a life-saving regimen for patients with acute MI and reduced left ventricular function with clinical signs of heart failure. Caution should be used when treating patients with moderate to severe chronic kidney disease and baseline hyperkalemia. ■

References

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Coronary Artery Disease

Randomized Trials, Registries, and Revascularization

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Long-Term Outcomes of Coronary Artery Bypass Grafting Versus Stent Implantation

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This large study from the New York State Registry analyzed 3-year outcomes in patients with multivessel disease who underwent coronary artery bypass grafting (CABG, n = 37,212) or percutaneous coronary intervention (PCI) with stenting (n = 22,102), between January 1997 and December 2000.[1] Patients with left main coronary artery disease, prior revascularization, or myocardial infarction within 24 hours of revascularization were excluded. The CABG group were older, slightly less likely to be female, more likely to be white, and less likely to be Hispanic. There was also a higher prevalence of patients with left ventricular dysfunction and comorbidities including chronic obstructive pulmonary disease, diabetes, renal failure, peripheral vascular disease, carotid or cerebrovascular disease, aortoiliac disease, or prior stroke in this group.

Unsurprisingly, over a follow-up of approximately 3 years, rates of subsequent revascularization were much higher after stenting when compared to rates following coronary bypass surgery (7.8% versus 0.3% for subsequent CABG and 27.3% versus 4.6% for subsequent PCI). Unadjusted survival data demonstrated a higher mortality rate after CABG in patients with 2-vessel disease and no involvement of the proximal left anterior descending coronary artery (LAD). There was no significant difference in those with 2-vessel disease and proximal LAD involvement, a nonsignificant trend in favor of surgery in patients with 3-vessel disease without proximal LAD involvement, and a highly significant benefit for surgery in patients with 3-vessel disease and proximal LAD involvement. In most subgroups with 3-vessel disease, with or without proximal LAD involvement, the presence of an ejection fraction of less than 40% favored CABG.

Adjusted analyses, which take into account the sicker state of the surgical patients, demonstrated a survival advantage for CABG in virtually all anatomical subgroups. The adjusted hazard ratio for the long-term risk of death after CABG, relative to stent implantation, was 0.64 (95% confidence interval [CI], 0.56-0.74) for patients with 3-vessel disease and proximal LAD involvement and 0.76 (95% CI, 0.60-0.96) for patients with 2-vessel disease with involvement of the nonproximal LAD. In general, the benefits of surgery were enhanced in the subgroups with diabetes, particularly in patients with an ejection fraction of less than 40%.

The major conclusion from this study was that, for patients with 2 or more diseased coronary arteries, coronary bypass surgery is associated with higher adjusted rates of long-term survival than stenting. When one looks at the unadjusted data, it appears that bypass surgery is clearly associated with greater survival in comparison to stenting in all patients with 3-vessel disease, and in patients with 2-vessel disease associated with proximal LAD involvement and/or ejection fractions of less than 40%.