Metformin Does Not Improve Diastolic Function in Nondiabetic Patients With STEMI

Written by Brian Hoyle

Metformin has no effect on diastolic function following acute myocardial infarction (MI) in nondiabetic patients. The disappointing finding from the Glycometabolic Interventions in Patients Presenting With ST-Segment Elevation Myocardial Infarction trial [GIPS-III; Lexis CP et al. *JAMA* 2014] was reported by Chris P. H. Lexis, MD, University Medical Center Groningen, Groningen, the Netherlands.

Left ventricular dysfunction following MI occurs in 30% to 50% of patients, of which 15% to 30% will develop heart failure. Left ventricular dysfunction is the strongest predictor of poor outcomes following an ST-segment elevation MI (STEMI). Post-STEMI patients experiencing heart failure at admission or during initial hospitalization are at markedly higher risk when compared to patients with no heart failure [Steg PG et al. *Circulation* 2004]. The researchers became interested in the possible benefit of metformin—the number one–prescribed antihyperglycemic drug—given animal studies that found that metformin improved left ventricular ejection fraction. In addition, some studies found an association between reduced all-cause mortality in patients with diabetes treated with metformin [UK Prospective Diabetes Study Group. *Lancet* 1998].

GIPS-III was a double-blind, placebo-controlled, parallel-group trial that comprised 379 patients. The 371 patients that received at least an assessment of diastolic function were randomly assigned (1:1) to receive metformin (500 mg, twice a day [BID]; n=187) or placebo (BID; n=184). The treatments commenced immediately after percutaneous coronary intervention (PCI) and continued for 4 months. The objective of the study was to evaluate the effect of metformin on left ventricular diastolic function during hospitalization and at 4 months in nondiabetic patients with STEMI.

Patients were eligible if they were at least 18 years old with STEMI, had received a primary PCI with ≥3.0-mm-diameter stents, and had a thrombolysis in MI flow grade ≥2 after PCI. Patients were excluded if they were diabetic, had a prior MI, required cardiothoracic surgery, were contraindicated for magnetic resonance imaging, or had severe renal impairment. Transthoracic echocardiography was done in the left decubital position during hospitalization to assess the short-term effect and again at 4 months. Assessors were blinded to treatment and clinical information. Diastolic individual assessment parameters (grade 0 to 3) included age, heart rate, size and mass, left atrial volume index, E/A ratio, deceleration time, e', E/e' ratio, and estimated pulmonary pressure.

The baseline characteristics of the 2 groups were similar, except for the higher prevalence of dyslipidemia and previous PCI in the placebo group and the longer ischemia time and greater creatinine kinase elevation in the metformin group.

The metformin and placebo groups were not appreciably different in the extent of normal and abnormal diastolic function during hospitalization and at 4 months. Similar grades of diastolic dysfunction and change of diastolic function were evident between groups at both times. Finally, all the assessed parameters were similar during hospitalization and at 4 months.

Dr. Lexis and colleagues concluded that metformin (500 mg, BID) started right after PCI in nondiabetic patients does not improve left ventricular diastolic function after STEMI as compared with placebo, both during hospitalization and at 4 months after discharge.

Spironolactone Misses Primary Endpoint in TOPCAT

Written by Emma Hitt Nichols, PhD

Spironolactone treatment of heart failure (HF) with preserved ejection fraction (HFpEF) did not significantly reduce cardiovascular death, hospitalization due to HF, or resuscitated cardiac arrest compared with placebo. Bertram Pitt, MD, University of Michigan School of Medicine, Ann Arbor, Michigan, USA, presented updated data from the Aldosterone Antagonist Therapy for Adults With Heart Failure and Preserved Systolic Function trial [TOPCAT; Shah SJ et al. *Circ Heart Fail* 2012].

Previous trials have demonstrated that mineralocorticoid receptor antagonists improve survival in patients with mild to severe reduced ejection fraction and postmyocardial infarction left ventricular dysfunction compared with placebo [Zannad F et al. *N Engl J Med* 2011; Pitt B et al. *N Engl J Med* 2003; Pitt B et al. *N Engl J Med* 1999]. The purpose of the TOPCAT trial was to evaluate the effect of spironolactone in patients with HFpEF.

In the multicenter TOPCAT trial, 3445 patients with HFpEF were randomly assigned to receive a target dose of 30 mg of spironolactone (n=1722) or placebo (n=1723) over a mean follow-up of 3.3 years [Desai AS et al. *Am Heart J* 2011]. Randomly assigned patients had a mean age of 69 years and a New York Health Association class II or III HF, with a mean left ventricular ejection fraction of 56% [Shah SJ et al. *Circ Heart Fail* 2012].