Table 1. Coprimary Outcomes

30-Day Outcome n (%)	Steroid n=3755	Placebo n=3752	Relative Risk (95% CI)	p Value
Death	155 (4.1)	176 (4.7)	0.88 (0.71–1.09)	0.23
Composite of death, MI, stroke, new renal failure, respiratory failure	908 (24.2)	869 (23.2)	1.04 (0.96–1.13)	0.30
Components of Composite				
MI	500 (13.3)	408 (10.9)	1.22 (1.08–1.38)	0.001
Stroke	72 (1.9)	80 (2.1)	0.90 (0.66–1.23)	0.51
New renal failure	105 (2.8)	114 (3.0)	0.92 (0.71–1.20)	0.53
Respiratory failure	343 (9.1)	375 (10.0)	0.91 (0.79–1.05)	0.21

MI=myocardial infarction.

Of the secondary outcomes, the prevalence of death or MI, and the postoperative level of insulin were significantly greater in the steroid group (Table 2).

Table 2. Secondary Outcomes of Efficacy and Safety

30-Day Outcome n (%)	Steroid n=3755	Placebo n=3752	Relative Risk (95% CI)	p Value
Efficacy				
Death or MI (%)	620 (16.5)	536 (14.3)	1.16 (1.04–1.29)	0.008
New atrial fibrillation (%)	821 (21.9)	846 (22.5)	0.97 (0.89–1.06)	0.53
Any transfusion (%)	1932 (48.8)	1865 (49.7)	0.98 (0.94–1.03)	0.43
Length of intensive care unit stay (hours)	46.0 (23.0–90.0)	47.0 (24.0–91.0)		0.05
Length of hospital stay (days)	9.0 (7.0–13.0)	9.0 (7.0–13.0)		0.06
Safety				
Infection (%)	464 (12.4)	494 (13.2)	0.94 (0.83–1.06)	0.29
Delirium (%)	295 (8.4)	290 (8.3)	1.01 (0.87–1.19)	0.84
Surgical site infection (%)	150 (4.0)	150 (4.0)	1.00 (0.80–1.25)	0.99
Gastrointestinal perforation or hemorrhage (%)	55 (1.5)	46 (1.2)	1.19 (0.81–1.76)	0.37
Peak blood glucose (mmol/L)	12.7±7.2	12.1±18.7		0.04
Postoperative insul1in (u)	50.3±66.3	32.6±52.9		<0.00001

MI=myocardial infarction.

The investigators concluded that the trial demonstrated that routine use of methylprednisolone in high-risk patients undergoing cardiac surgery with the use of cardiopulmonary bypass was ineffective in reducing death or major morbidity at 30 days and appeared to increase the risk of early postoperative MI.

Metformin Doses Not Reduce Heart Failure After STEMI in Patients Without Diabetes (GIPS-III)

Written by Brian Hoyle

Results of a double-blind, randomized, placebo-controlled, parallel-group trial do not support the routine use of metformin in nondiabetic patients after ST-segment elevation myocardial infarction (STEMI) for the purpose of preserving myocardial function. Findings of the Metformin to Reduce Heart Failure After Myocardial Infarction trial [GIPS-III; Lexis CPH et al. *JAMA* 2014] were presented by Chris P. H. Lexis, MD, University Medical Center, Groningen, Groningen, The Netherlands.

MI diminishes left ventricular function (LVF) in up to 50% of subjects and leads to clinical heart failure in up to 40% [Steg PG et al. *Eur Heart J* 2012]. Animal experiments and observational suggest metformin may have protective effects on the myocardium in the setting of ischemia-reperfusion; the mechanism of action being independent of the drug's glucose-lowering effect. The GIPS-III trial tested whether 4 months of metformin treatment started after successful percutaneous coronary intervention (PCI) for MI could preserve left ventricular ejection fraction (LVEF) in patients without diabetes at 4 months.

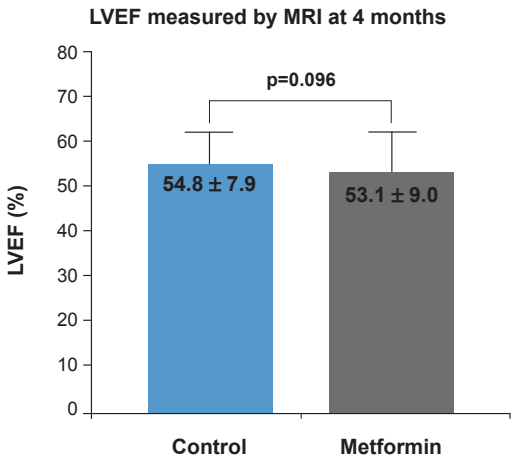
Acute STEMI patients, post-PCI with stenting, and with TIMI post-PCI flow Grade ≥2 were eligible for the trial. Key exclusion criteria were diabetes, prior MI, prior CABG, need for cardiothoracic surgery, contraindication for magnetic resonance imaging (MRI), and severe renal impairment. Three-hundred and eighty patients were randomized 1:1 to receive metformin 500 mg BID (n=191) or placebo BID (n=189) beginning immediately after PCI and continuing for 4 months. The primary endpoint was the LVEF measured in a blinded fashion at 4 months using a 3.0 Tesla MRI. The principal secondary endpoint was N-terminal brain natriuretic peptide (NT-proBNP) at 4 months. cardiovascular outcomes, adverse events, and markers of glycometabolic state were also collected.

Time from onset of symptoms to first coronary intervention was 161 minutes (IQR, 109-250). Time to administration of first dose of study drug after first coronary intervention was approximately 100 minutes in each arm. The two arms were similar at baseline for demographic and physiologic characteristics including specific angiographic parameters. Angiographic markers of successful reperfusion were less successful for patients receiving metformin versus placebo (TIMI post-PCI flow Grade <3, 12.6% vs 5.3%; myocardial blush Grade ≤1: 13.8% vs 5.9%).

In both arms, over 25% of subjects did not undergo MRI; 55 and 50 patients in the metformin and placebo

arms, respectively. For those that had a successful MRI, the primary endpoint of LVEF at 4 months was similar for both arms (53.1±9.0 vs 54.8±7.9; p=0.096; Figure 1), as was the secondary endpoint of NT-proBNP and other relevant laboratory markers (Table 1).

Figure 1. MRI Determination of LVEF



LVEF=left ventricular ejection fraction; MRI=magnetic resonance imaging.
Reproduced with permission from CPH Lexis, MD.

Table 1. Principal Secondary Endpoint and Laboratory Markers at 4 Months

	Metformin Group	Placebo Group	p Value
Principal secondary endpoint			
NT-proBNP at 4 months; IQR, ng/L	167 (65–393)	167 (74–383)	0.66
Laboratory markers at 4 months			
Creatinine; IQR, µmol/L	79 (70–87)	79 (72–89)	0.61
Glucose; IQR, mmol/L	5.7 (5.2–6.3)	5.6 (5.2–6.2)	0.96
HbA1C; IQR, %	5.9 (5.6–6.1)	5.9 (5.7–6.1)	0.15

IQR=interquartile range; N-proBNP=N-terminal brain natriuretic peptide.

Adverse events were similar in both arms, with no deaths or episodes of lactic acidosis. There was no evidence of superiority of metformin in subgroup analyses by sex, age, body mass index, MI location, TIMI flow pre-PCI, admission levels of glucose, or NT-proBNP.

Metformin 500 mg twice daily beginning after PCI and continuing for 4 months does not preserve LVEF after STEMI in patients without diabetes. Even though metformin appears to be safe, the current results do not support its routine use in this patient setting.

Bariatric Surgery for Treatment of Type 2 Diabetes in Obese Patients: 3-Year Outcomes (STAMPEDE)

Written by Brian Hoyle

Of the more than 25 million Americans with type 2 diabetes mellitus (T2DM), fewer than half can attain adequate glycemic control. Bariatric surgery has resulted in improved glycemic and cardiovascular risk factor control in observational and short-term randomized studies, including the 1- year results of the Surgical Treatment and Medications Potentially Eradicate Diabetes Efficiently trial [STAMPEDE; Schauer P et al. *N Engl J Med* 2012]. The 3-year STAMPEDE data, presented by Sangeeta R. Kashyap, MD, Cleveland Clinic, Cleveland, Ohio, USA, compared the effect of bariatric surgery with intensive medical therapy versus intensive medical therapy alone on glycemic control [Schauer PR et al. *N Engl J Med* 2014].

In the single-center trial, 150 patients aged 20 to 60 years with uncontrolled diabetes (HbA1C >7.0%) and body mass index (BMI) 27 to 43 kg/m^2 were randomized to medical therapy alone (MT; n=50), MT plus laparoscopic Roux-en-Y gastric bypass (n=50), or MT plus laparoscopic sleeve gastrectomy (n=50). The MT regimen involved regular follow-up with extensive medication titration to achieve a target HbA1C of 6.0%. Subjects were encouraged to participate in a weight management program, such as Weight Watchers. The primary endpoint was the 3-year success rate in achieving HbA1C ≤6%. Secondary endpoints were changes in fasting plasma glucose (FPG), lipids, blood pressure, BMI, carotid intima media thickness (CIMT), medication usage, adverse events, and quality of life.

Thirteen patients (9%) were either lost to follow up (n=4) or withdrew consent (n=9), such that the 3-year analysis included 40, 48, and 49 patients in the MT alone, gastric bypass and sleeve gastrectomy arms, respectively. The three arms were comparable at baseline. The primary outcome, attainment of an HbA1C ≤6%, occurred in 5%, 38% and 24%, respectively, in the MT, gastric bypass, and sleeve gastrectomy arms with no significant differences between surgical arms (Table 1). Bariatric surgery also resulted in significant improvements in a number of secondary outcomes, including FPG, high-density lipoprotein, triglycerides, and medication usage. Both bariatric surgery approaches similarly reduced the percentage of patients on insulin, compared to MT alone. At 3 years, the percentage of patients requiring insulin in the MT, gastric bypass, and sleeve gastrectomy arm was 55%, 6%, and 8%, respectively. Requirement for cardiovascular medications was also substantially reduced by bariatric surgery. Only gastric bypass was associated with significantly diminished relapsed glycemic control compared with MT (Table 1).