primary outcome was a composite of death and nonfatal myocardial infarction (MI) within 30 days following surgery. Secondary composite outcomes were 1) death, MI, or stroke, and 2) death, MI, revascularization, pulmonary embolism (PE), or deep vein thrombosis (DVT). Tertiary outcomes were death, MI, peripheral arterial thrombosis, PE, DVT, and acute kidney injury requiring dialysis.

The study enrolled patients who had been taking aspirin daily before surgery (aspirin-chronic; n=4382) as well aspirin-naïve patients (n=5628). For those in the first group, aspirin use was stopped ≥72 hours before surgery. All patients received placebo or 200 mg aspirin just before surgery. Postoperatively, the aspirin-naïve patients received 100 mg aspirin or placebo daily for 30 days, while aspirin-chronic patients received 100 mg aspirin or placebo for 7 days before resuming their presurgery aspirin regimen.

Both groups were similar; mean patient age 68.6 years, 53% male, 32% had known vascular disease, and 4.7% had a history of percutaneous coronary intervention. Surgeries for both groups in descending order of frequency were orthopedic (38%), general (32%), urologic or gynecologic (16%), vascular (6%), and other (11%). Prophylactic anticoagulant was administered to 65% of patients

There were no significant differences in the rate of the primary, secondary, or tertiary outcomes among patients randomized to aspirin compared with those receiving placebo with the exception of a trend towards higher rates of acute kidney injury in those randomized to aspirin (Table 1). Primary and secondary outcomes were similar for the aspirin-chronic and -naïve patients.

Table 1. Primary and Secondary Outcome Results

Outcome, n (%)	Aspirin (n=4998)	Placebo (n=5012)	HR (95% CI)	p Value
Primary (death or nonfatal MI)	351 (7.0)	355 (7.1)	0.99 (0.86–1.15)	0.92
Secondary no. 1 (death, MI, or stroke)	362 (7.2)	370 (7.4)	0.98 (0.85–1.13)	0.80
Secondary no. 2 (death, MI, revascularization, PE, or DVT)	402 (8.0)	407 (8.1)	0.99 (0.86–1.14)	0.90
Tertiary death	65 (1.3)	62 (1.2)	1.05 (0.74–1.49)	0.78
MI	309 (6.2)	315 (6.3)	0.98 (0.84–1.15)	0.85
Peripheral arterial thrombosis	13 (0.3)	15 (0.3)	0.87 (0.41–1.83)	0.71
PE	33 (0.7)	31 (0.6)	1.07 (0.65–1.74)	0.79
DVT	25 (0.5)	35 (0.7)	0.72 (0.43–1.20)	0.20
Acute kidney injury, dialysis	33 (0.7)	19 (0.4)	1.75 (1.00–3.09)	0.05

DVT=deep vein thrombosis; MI=myocardial infarction; PE=pulmonary embolism.

Aspirin users were significantly more likely to experience a major retroperitoneal, intraspinal, or intraocular bleed requiring infusions of red blood cells. They also experienced more (statistically nonsignificant) episodes of life-threatening bleeding (Table 2).

Table 2. Safety Outcome Results

Outcome, n (%)	Aspirin (n=4998)	Placebo (n=5012)	HR (95% CI)	p Value
Major bleed	230 (4.6)	188 (3.8)	1.23 (1.01–1.49)	0.04
Life-threatening bleed	87 (1.7)	73 (1.5)	1.19 (0.88–1.63)	0.26
Stroke	16 (0.3)	19 (0.4)	0.84 (0.43–1.64)	0.62

Life-threatening or major bleeding was an independent predictor of perioperative MI (HR, 1.82; 95% CI, 1.40 to 2.36; p<0.001). The investigators hypothesized that this might explain the efficacy of aspirin in the non-operative setting, where the risk of bleeding is less frequent, compared with the more neutral effect of aspirin in the perioperative setting, where the risk of bleeding is greater.

Perioperative Clonidine Does Not Reduce CV Events in Patients Having Noncardiac Surgery (POISE-2)

Written by **Brian Hoyle**

Clonidine, a centrally acting α-agonist, does not reduce the risk of perioperative myocardial infarction or death in noncardiac surgery; however, it did cause clinically significant bradycardia and hypotension. The findings of the Perioperative Ischemic Evaluation-2 Trial [POISE-2; Devereaux PJ et al. *N Engl J Med* 2014] were presented by Daniel I. Sessler, MD, Cleveland Clinic, Cleveland, Ohio, USA.

The trial randomized patients (aged >45 years) scheduled for noncardiac surgery to "low-dose" (0.2 mg) clonidine (n=5009) versus placebo (n=5001). Clonidine was started orally 2 to 4 hours before surgery and continued by patch for 72 hours. The primary outcome was a composite of death or MI at 30 days. The secondary outcome was death, MI, or stroke at 30 days.

Patients in both arms were similar. The mean age was 68.5 years. Approximately one third of subjects had a history of any vascular disease but few patients had a history of coronary revascularization (recent stenting was an exclusion). Vascular surgery comprised only 6% of the total surgeries. Approximately 30% of subjects were also taking β-blockers during the perioperative period. Over 96% of patients were randomized within 24 hours of the operation.

The primary and secondary outcomes were similar in patients receiving clonidine or placebo (Table 1).

Table 1. Results at Day 30

Outcome n (%)	Clonidine n=5009	Placebo n=5001	HR (95% CI)	p Value
Primary (death or MI)	367 (7.3)	339 (6.8)	1.08 (0.93–1.26)	0.29
Secondary (death, MI, or stroke)	380 (7.6)	352 (7.0)	1.08 (0.93–1.25)	0.30

MI=myocardial infarction.

Throughout the 30-day follow-up period, the composite of death or MI was greater, but not statistically significant, with clonidine versus placebo (HR, 1.08; 95% CI, 0.93 to 1.26; p=0.29). Of the assessed tertiary outcomes, nonfatal cardiac arrest was significantly more frequent in those given clonidine (n=16, 0.3%) versus placebo (n=5, 0.1%; HR, 3.20; 95% CI 1.17 to 8.73; p=0.02). Clinically important hypotension and bradycardia, but not stroke, were statistically more frequent in patients given clonidine (Table 2).

Table 2. Safety Outcomes

Outcome n (%)	Clonidine n=5009	Placebo n=5001	HR (95% CI)	p Value
Clinically important hypotension	2385 (48)	1854 (37)	1.32 (1.24–1.40)	<0.001
Clinically important bradycardia	600 (12)	403 (8)	1.49 (1.32–1.69)	<0.001
Stroke	18 (0.4)	17 (0.3)	1.06 (0.54–2.05)	0.87

Hypotension was an independent predictor of MI (adjusted HR, 1.37; 95% CI, 1.16 to 1.62; p<0.001). Hypotension was always more prevalent in patients given clonidine than placebo, especially during surgery and recovery, and decreasing over the next 3 days (Table 3). The duration of hypotension was markedly shorter during surgery and recovery, compared with the following 3 days (Table 3).

Table 3. Risk and Duration of Hypotension

Period	Prevalence of Hypotension			Duration of Hypotension		
	Clonidine (%)	Placebo (%)	p Value	Placebo, minutes	Clonidine, minutes	p Value
Surgery	39	32	<0.001	15	15	0.12
Post-anesthesia care unit	8	4	<0.001	30	30	0.30
Postop Day 1	8	5	<0.001	150	180	0.13
Postop Day 2	3	2	<0.001	110	160	0.03
Postop Day 3	1.1	0.6	0.004	109	214	0.07

The ineffectiveness of clonidine in reducing postoperative MI or death combined with the increase in frequency and duration of hypotension means that low-dose clonidine should not be given to patients having noncardiac surgery in an effort to lessen perioperative mortality or MI.

Consistent with the results of POISE-1 (β-blockers in noncardiac surgery), starting drugs that may have potent hemodynamic effects (eg, antihypertensive, sympatholytic) within 24 hours of major noncardiac surgery is not effective in a broad population of patients undergoing noncardiac surgery.

Methylprednisolone Not Beneficial in High-Risk Cardiac Surgery Patients (SIRS)

Written by Brian Hoyle

Findings of the Steroids in Cardiac Surgery Trial [SIRS Trial; NCT00427388] were presented by Richard Whitlock, MD, PhD, Hamilton Health Services/McMaster University, Hamilton, Ontario, Canada.

Inflammation triggered by cardiopulmonary bypass can be diminished using prophylactic steroids, which may produce clinical benefits. The SIRS trial assessed the hypothesis of whether methylprednisolone would reduce perioperative adverse events in high-risk patients undergoing cardiac surgery involving cardiopulmonary bypass.

A total of 7507 patients were randomized to intraoperative methylprednisolone (500 mg intravenously) (n=3755) or placebo (n=3752). The coprimary outcomes were total mortality within 30 days following surgery, and a composite of all-cause mortality, myocardial infarction (MI), stroke, renal failure, or respiratory failure over the same time. Secondary efficacy and safety outcomes were also evaluated.

The steroid and placebo groups were well-matched in terms of age (67.5±13.6 vs 67.3±13.8 years), male percentage (60.1% vs 60.8%), previous MI (26.2% vs 24.7%) or stroke (8.1% vs 8.4%), congestive heart failure (26.8% vs 27.2%), prevalence of diabetes (26.2% vs 26.4%), and EuroSCORE (both 7.1±2.0). The similarities between groups extended to any prior valve procedure (n=2646, 70.4% vs n=2723, 72.6%), prior coronary artery bypass graft (CABG; n=1838, 48.4% vs n=1796, 47.9%), isolated valve procedure (n=1206, 32.1% vs n=1228, 32.7%), and isolated CABG (n=826, 22.0% vs n=762, 20.3%)

Overall there was no difference in the rate of the coprimary outcomes between patients receiving steroids compared with those receiving placebo at 30 days (Table 1). Analysis of the individual components of the composite outcome revealed a significantly higher rate of MI in patients randomized to methylprednisolone (Table 1). In subanalyses, the results were consistent when stratified by gender, diabetes, age, EuroSCORE, type of surgery, and duration of cardiopulmonary bypass.