2012. The primary analysis group included all patients with an undetectable hs-cTnT (<5 ng/L) and no significant ST-elevation or depression on ECG. The primary endpoint was fatal or nonfatal MI within 30 days. Secondary endpoints included MI at 180 and 365 days and all-cause mortality at 30, 180, and 365 days. The hs-cTnT assay (Roche Diagnostics) has a detection limit of 2 ng/L, a 99th-percentile cutoff point of 14 ng/L, and a coefficient of variation of <10% at 13 ng/L.

A total of 330,821 patients visited the ED within the study period. Of these, 14,636 (4.4%) were aged ≥25 years with chest pain and had at least one hs-cTnT measured. The hs-cTnT was <5 ng/L (undetectable) in 61%, 5 to 14 ng/L in 21% (detectable but <99th percentile), and >14 ng/L (>99th percentile) in 18% of included patients. Patients in the group with undetectable hs-cTnT were younger, more likely to be female, and less likely to have diabetes, prior MI, stroke, or congestive heart failure (Table 1).

Table 1. Patient Characteristics

		hs-cTnT Level (ng/L)		
	All Patients	**<5**	**5 to 14**	**>14**
Number of patients	14,636	8907	3150	2579
Percentage of cohort	100	61	21	18
Age (years)	55	47	63	71
Females (%)	48	53	41	37
Diabetes (%)	10	5	14	21
Prior MI (%)	9	4	14	39
Prior stroke (%)	5	2	7	13
Prior CHF (%)	6	1	8	22

CHF=congestive heart failure; hs-cTnT=high-sensitivity cardiac troponin T; MI=myocardial infarction.

MI was defined according to recent guidelines [Thygesen K et al. *J Am Coll Cardiol* 2012]. Among the patients with undetectable hs-cTnT and no ischemia on the presenting ECG, there were 15 MIs within 30 days (negative predictive value [NPV], 99.8%; 95% CI, 99.7 to 99.9). In comparison, within 30 days there were 97 MIs in the group with hs-cTnT levels of 5 to 14 ng/L (NPV, 96.9%; 95% CI, 96.3 to 97.5) and 676 recurrent MIs in those with hs-cTnT levels >14 ng/L at the index presentation (NPV, 73.8%; 95% CI, 72.1 to 75.5; Table 2).

There were two deaths within 30 days among patients with undetectable hs-cTnT (NPV, 100%; 95% CI, 99.9 to 100). At 1 year, there were 38 deaths in this group, of which 32 were caused by cancer and two were due to cardiovascular disease.

The admission rate for patients with an undetectable first hs-cTnT was 21%. Most patients (89%) had a second hs-cTnT measured and of these, 90% remained undetectable. The authors acknowledge that there may have been patients discharged without a second hs-cTnT measured who would have had an elevated hs-cTnT consistent with an MI if it had been checked; however, they imply that the equivalent 1-year mortality rate in the admitted and discharged populations argues against significant, unrecognized MIs.

Table 2. Absolute Risk and Negative Predictive Value for MI at 30 and 365 Days After ED Discharge

	hs-cTnT Level (ng/L)		
	<5	**5 to 14**	**>14**
Number of patients	8883*	3150	2579
30 Days			
Number of events	15	97	676
Absolute risk % (95% CI)	0.17 (0.09–0.27)	3.08 (2.48–3.68)	26.2 (24.5–27.9)
NPV % (95% CI)	99.8 (99.7–99.9)	96.9 (96.3–97.5)	73.8 (72.1–75.5)
365 Days			
Number of events	54	134	753
Absolute risk % (95% CI)	0.61 (0.45–0.78)	4.25 (3.55–4.96)	29.2 (27.4–31.0)
NPV % (95% CI)	99.4 (99.2–99.5)	95.7 (95.0–96.5)	70.8 (69.0–72.6)

*24 patients with a first hs-cTnT level of <5 ng/L were excluded because they had ECG changes suggestive of MI.

ECG=electrocardiogram; ED=emergency department; hs-cTnT=high-sensitivity cardiac troponin T; MI=myocardial infarction; NPV=negative predictive value.

Overall, the results of this study demonstrated that a first undetectable hs-cTnT level (<5 ng/L) and no signs of ischemia on ECG in patients presenting to the ED with chest pain ruled out MI with a high degree of accuracy, regardless of duration of symptoms, timing of hs-cTnT measurement, prior disease, age, sex, or other risk factors for MI. Dr. Bandstein concluded that use of a single hs-cTnT may prevent unnecessary hospital admissions and shorten ED stays leading to a reduction in ED overcrowding.

Perioperative Aspirin Does Not Reduce Cardiovascular Events in Noncardiac Surgery (POISE-2)

Written by **Brian Hoyle**

Acetylsalicylic acid (aspirin) is ineffective in reducing perioperative heart attacks and death in noncardiac surgery, but increases the risk of bleeding. Results from the Perioperative Ischemic Evaluation-2 trial [POISE-2; Devereaux PJ et al. *N Engl J Med* 2014] were presented by Philip J. Devereaux, MD, PhD, McMaster University, Hamilton, Ontario, Canada.

Patients aged ≥45 years undergoing noncardiac surgery who were at risk of vascular complications were eligible for the Phase 3, randomized, controlled, POISE-2 trial. Exclusion criteria were recent stent implantation (bare-metal stent within 6 weeks or drug-eluting stent within 1 year) and use of aspirin within 72 hours prior to surgery. The

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).