Perioperative Cardiovascular Complications

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Some 230 million noncardiac surgeries are done annually, about 10 million of which are complicated by major cardiovascular events, including myocardial infarction (MI), within 30 days of surgery.

Thirty years ago, preventable anesthetic-related mortality was about 1 in 10 000 patients. Now, according to Daniel I. Sessler, MD, Cleveland Clinic, Cleveland, Ohio, USA, it is < 1 in 100 000 patients. Despite this significant improvement, mortality remains high after patients leave the operating theater. The majority of 1-year postoperative deaths are typically due to preexisting cancer, and the mortality rate remains at about 5% overall and 10% in patients > 65 years old. In contrast, 30-day postoperative mortality is 2% for American inpatients aged ≥ 45 years and is largely due to MI and subsequent complications, with 80% of the deaths occurring during the initial hospitalization. If the postoperative period was regarded as a disease, it would rank as the third-leading cause of death in the United States [Bartels K et al. *Anesthesiology*. 2013].

The majority of postoperative MIs are clinically silent. In the international prospective VISION cohort study of > 15 000 patients undergoing surgery, most postoperative MIs were detected only by elevated troponin (Table 1) [Devereaux PJ et al. *JAMA*. 2012; Botto F et al. *Anesthesiology*. 2014].

Troponin elevations > 0.3 ng/mL also increase the risk of nonfatal cardiac arrest, congestive heart failure, stoke, and death. According to an expert consensus document from the European Society of Cardiology, American College of Cardiology Foundation, American Heart Association, and World Heart Federation, routine monitoring of cardiac biomarkers such as troponin after major surgery has been recommended [Thygeson K et al. *Circulation*. 2012]. While it is tempting to think that silent troponin elevation is less serious than symptomatic infarctions, the mortality is identical with silent and symptomatic troponin elevations; therefore, each event needs to be taken seriously.

If the majority of postoperative MIs are clinically silent, can they be prevented? The first intervention that the investigators evaluated for general anesthesia was avoidance nitrous oxide. However, results from the 7000-patient ENIGMA-II trial clearly indicate that nitrous oxide does not worsen risk of cardiovascular complications after noncardiac surgery [Myles PS et al. *Lancet*. 2014]. A previous study, the 8351-patient POISE-1 trial, showed that β-blockers reduced perioperative MI risk but at the cost of an increased risk of stroke [POISE Study Group. *Lancet*. 2008].

Table 1. Troponin T Predicts Mortality[a]

Peak Troponin, ng/mL	30-Day Mortality, %	Time to Death, d
< 0.01	1	—
0.02	4	13
0.03-0.29	9	9
≥ 0.3	17	6

[a]"Prognosis defines diagnosis." Even slight troponin elevations predict death. Population-attributable risk = 34%.

Source: Devereaux PJ et al. *JAMA*. 2012.

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Table 2. 30-Day Primary, Secondary, and Tertiary Outcomes for Aspirin

Outcome	Aspirin (N=4998)	Placebo (N=5012)	Hazard Ratio (95% CI)†	P Value
	no. (%)			
Primary composite outcome: death or nonfatal myocardial infarction	351 (7.0)	355 (7.1)	0.99 (0.86–1.15)	0.92
Secondary outcomes				
Death, nonfatal myocardial infarction, or nonfatal stroke	362 (7.2)	370 (7.4)	0.98 (0.85–1.13)	0.80
Death, nonfatal myocardial infarction, cardiac revascularization, nonfatal pulmonary embolism, or nonfatal deep venous thrombosis	402 (8.0)	407 (8.1)	0.99 (0.86–1.14)	0.90
Tertiary outcomes — no. (%)				
Death from any cause	65 (1.3)	62 (1.2)	1.05 (0.74–1.49)	0.78
Death from cardiovascular cause	35 (0.7)	35 (0.7)	1.00 (0.63–1.60)	0.99
Myocardial infarction	309 (6.2)	315 (6.3)	0.98 (0.84–1.15)	0.85
Nonfatal cardiac arrest	9 (0.2)	12 (0.2)	0.75 (0.32–1.79)	0.52
Cardiac revascularization	13 (0.3)	17 (0.3)	0.77 (0.37–1.58)	0.47
Pulmonary embolism	33 (0.7)	31 (0.6)	1.07 (0.65–1.74)	0.79
Deep-vein thrombosis	25 (0.5)	35 (0.7)	0.72 (0.43–1.20)	0.20
New clinically important atrial fibrillation	109 (2.2)	94 (1.9)	1.16 (0.88–1.53)	0.28
Peripheral arterial thrombosis	13 (0.3)	15 (0.3)	0.87 (0.41–1.83)	0.71
Amputation	10 (0.2)	13 (0.3)	0.77 (0.34–1.76)	0.54
Rehospitalization for cardiovascular reasons	70 (1.4)	54 (1.1)	1.30 (0.91–1.86)	0.15
Acute kidney injury with receipt of dialysis‡	33 (0.7)	19 (0.4)	1.75 (1.00–3.09)	0.05
Safety outcomes				
Life-threatening bleeding	87 (1.7)	73 (1.5)	1.19 (0.88–1.63)	0.26
Major bleeding	230 (4.6)	188 (3.8)	1.23 (1.01–1.49)	0.04
Clinically important hypotension	2143 (42.9)	2096 (41.8)	1.03 (0.97–1.09)	0.37
Stroke	16 (0.3)	19 (0.4)	0.84 (0.43–1.64)	0.62
Congestive heart failure	44 (0.9)	38 (0.8)	1.16 (0.75–1.79)	0.50
Infection	488 (9.8)	495 (9.9)	0.99 (0.87–1.12)	0.86
Sepsis	243 (4.9)	258 (5.2)	0.94 (0.79–1.13)	0.52

Percentages were calculated with the use of the Kaplan–Meier method.

† Hazard ratios are for the aspirin group, as compared with the placebo group.

‡ For this outcome, an odds ratio is provided instead of a hazard ratio, because the date that patients first started dialysis was not known.

Platelet activation and the resulting thrombosis may be the reason for perioperative MI, according to Philip J. Devereaux, MD, PhD, McMaster University, Hamilton, Ontario, Canada, who discussed the follow-up POISE-2 trial in more detail [Devereaux PJ et al. *New Engl J Med*. 2014]. The randomized 2 × 2 factorial design trial evaluated the use of aspirin and/or clonidine to reduce perioperative cardiovascular events after noncardiac surgery. It involved more than 10 000 patients undergoing noncardiac surgery (orthopedic, 39%; general, 27%; urologic/gynecologic, 17%; vascular/other, 15%) at risk of vascular complications. Of the 10 010 randomized patients, 5628 were aspirin naïve, and 4382 were chronic aspirin users. The latter halted aspirin use at a median of 7 days prior to surgery. Patients were randomized to receive aspirin or placebo just prior to surgery and then daily postoperatively—30 days for aspirin-naïve patients and 7 days for chronic aspirin users. Clonidine/placebo was initiated and continued 72 hours postoperatively. Regular aspirin therapy resumed after study treatment in chronic aspirin users [Devereaux PJ et al. *New Engl J Med*. 2014].

No differences were evident in primary or secondary outcomes between aspirin- and placebo-treated patients (Table 2). There was an increased risk of acute kidney injury requiring dialysis in the aspirin- vs placebo-treated patients (HR, 1.75; 95% CI, 1.00 to 3.09). The risk of major bleeding was increased with the use of aspirin over placebo (HR, 1.23; 95% CI, 0.04), with the risk decreasing over time. Life-threatening bleeding and stroke were not significantly different in the aspirin and placebo groups. Primary outcomes were similar between the aspirin-naïve patients and chronic aspirin patients (HR, 0.99; 95% CI, 0.81 to 1.21; vs HR, 1.00; 95% CI, 0.81 to 1.23; $P_{\text{Interaction}} = .96$). Life-threatening bleeding and major bleeding independently predicted perioperative MI (HR, 1.82; 95% CI, 1.40 to 2.36; $P < .001$).

While aspirin to prevent MI following noncardiac surgery appears groundless, a preventive role prior to surgery—when the risk of bleeding is lower and the risk of thrombosis is higher—may still have merit. Withholding aspirin in patients having noncardiac surgery to reduce perioperative complications may be helpful, with patients suffering perioperative MI perhaps benefiting from aspirin in both the short and long term.

As discussed by Pablo Alonso-Coello, MD, Institute of Biomedical Research, Barcelona, Spain, paroxysmal atrial fibrillation (AF) is the most common perioperative arrhythmia.

The incidence of perioperative AF is >25% in cardiac surgeries and is particularly common following cardiac bypass and valvular surgery. The incidence is lower in noncardiac surgeries, but the magnitude of the problem is larger given the higher number of patients undergoing these procedures. While spontaneous conversion to normal rhythm usually occurs, postoperative AF can result in thromboembolic events.

In the POISE-1 trial [POISE Study Group. *Lancet*. 2008], perioperative AF was associated with increased 30-day postoperative risk of MI (HR, 5.34; 95% CI, 3.94 to 7.23), stroke (HR, 4.35; 95% CI, 1.87 to 10.12), congestive heart failure (HR, 6.55; 95% CI, 4.73 to 9.07), cardiac arrest (HR, 8.43; 95% CI, 3.73 to 19.05), and death (HR, 3.63; 95% CI, 2.27 to 5.81).

At 1 year after hospitalization, stroke due to perioperative AF is the major complication of noncardiac surgery (HR, 2147; 95% CI, 1.24 to 1.75) and cardiac surgery (HR, 0.99; 95% CI, 0.81 to 1.20) [Gialdini G et al. *JAMA*. 2014].

Prevention of AF in noncardiac surgery involves avoidance of triggers such as hypoxia and cardiac ischemia [Fauchier L et al. *Curr Opin Cardiol*. 2013; Imazio M et al. *Circulation*. 2011; POISE Study Group. *Lancet*. 2008]. Preventive factors in cardiac surgery include perioperative β-blockers, calcium channel blockers, amiodarone, and statins [*Cochrane Database Syst Rev*. 2013; Echahidi N et al. *J Am Coll Cardiol*. 2008].

Management strategies of perioperative AF involve treatment of an identifiable precipitant, electrical/pharmacologic cardioversion, and, for persistent AF, control of heart rate. Antithrombotic therapy can be considered for AF persistent over 48 hours, with attention paid to the risks of stroke and bleeding [Devereaux PJ et al. *New Engl J Med*. 2014; Whitlock R et al. *Can Med Assoc J*. 2014]. Long-term consequences of paroxysmal perioperative AF remain unclear.