Impact of Intraoperative Blood Pressure Management on Postoperative Outcomes

Solomon Aronson, MD, MBA

INTRODUCTION

Death due to anesthesia has become rare. Worldwide, the mortality due to general anesthesia is now estimated in the range 0.5 to 28 per 10,000 anesthetics, with the highest mortality rates reported by clinical investigators from developing countries (Anaesthesia 56:1141-1153, 2001). By contrast, morbid events related to anesthetic care are more prevalent and difficult to classify. Hemodynamic changes may signal morbid events during anesthesia. A decrease in blood pressure (BP), enabling detection of occult hemorrhage, is an obvious example of how hemodynamic monitoring contributes to the diagnosis of a morbid state; however, monitoring for BP variability outside acceptable target thresholds, because it may contribute to postoperative 30-day mortality, is a much more subtle example. It is estimated that 500 million surgeries will be performed worldwide annually by the year 2050, with approximately 2% of these in patients at high risk for the development of cardiovascular complications. In the United States alone, 30 million noncardiac surgical procedures are performed annually (N Engl J Med 335:1713-1720, 1996) and 2.5% to 10% of these procedures are associated with perioperative cardiovascular morbidity and mortality.

What do we mean by ‘Blood Pressure?’ Are we referring to systolic, diastolic, mean, ambulatory, intraoperative, postoperative? What about white coat hypertension? “Hypertension” accounts for 14% of cardiovascular deaths worldwide, and yet nearly one third of the population in the United States (70 million) has some form of the disease. In general, among the hypertensive population, approximately 25% are not treated, 50% are poorly treated, and 25% are undiagnosed. Data from NHANES/NCHS 2005–2006 showed that of those with hypertension ≥20 years of age, 78.7% were aware of their condition, 69.1% were under current treatment, 45.4% had it under control, and 54.6% did not have it controlled.7 According to several estimates, 90% of people in the United States will be diagnosed with hypertensive disease by their sixth to seventh decade of life, which coincidentally is the group constituting the fastest growing segment of the general population.

It has been estimated that the annual cost of hypertension management is nearly 70 billion dollars per year in the United States alone and that intensive blood pressure (BP) control saves approximately $2000 per quality-adjusted life year. Cardiovascular disease, a cause and consequence of hypertension, accounts for ~30% of all deaths worldwide and is expected to remain the most serious public health challenge in the decades to come. It is estimated that there are as many deaths and hospital readmissions attributable to acute BP crises (8.8% and 37.2%, respectively) as to acute coronary syndromes (ACS; 5%–7% and 21%, respectively) and congestive heart failure (CHF; 8.5% and 25.7%, respectively). Taking into account the fact that up to 64 million people per year in the United States have surgery requiring anesthesia, and that hypertension is an established risk factor for adverse outcome following surgery, it should come as no surprise that poorly controlled hypertension remains one of the most common medical indications for deferring elective surgery.

Prevalence of high blood pressure (BP) in adults aged ≥20 years by age and sex (NHANES: 2005 to 2006). Hypertension is defined as systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg, taking antihypertensive medication, or being told twice by a physician or other professional that one has hypertension. While some investigators have suggested acceptable ranges for MAP (55 to 100 mm Hg), and SBP (80 to 160 mm Hg) in surgical patients, there are few data to support such recommendations, and only recently have studies focused on the association and relationship between hemodynamic targets and outcomes.

Preexisting hypertension exists in over two-thirds of all patients undergoing cardiac surgery. None the less a target threshold for perioperative blood pressure is not clearly defined and optimal blood pressure management strategy in high-risk patients is even less well understood. Preexisting hypertension introduces further challenges, as it has been shown that the autoregulatory capacity of the brain and kidney, is impaired, potentially influencing end-organ tolerance of high or low blood pressures. As a result, the therapeutic window of acceptable blood pressure is narrowed and shifted to the right in these patients.
Classification of Hypertension Subtypes

Physiologic stress associated with surgical procedures may be associated with adverse perioperative cardiovascular events (ie, cardiac death, nonfatal MI, nonfatal cardiac arrest) (CMAJ 173:627-634, 2005). These events both cause and are precipitated by decreased fibrinolytic activity, hypercoagulability, decreased vasomotor reactivity, vulnerable plaque rupture, catecholamine surges, decreased coronary perfusion, shorter diastolic intervals, tachycardia, and a heightened inflammatory state (Am J Med 122:222-229, 2009, Pharmacotherapy 18:911-914, 1998). Hypertension represents a major risk factor for coronary artery disease (CAD), dyslipidemia, CHF, renal dysfunction, cerebral dysfunction, dementia and diabetes. Studies have established that cardiovascular morbidity and mortality risk increases continuously with increasing BP at levels well below thresholds for standard definitions of hypertension. The higher the BP, the higher the risk, such that between the ages of 40 and 69 years, for each 20-mm Hg increase in systolic BP (SBP) or 10-mm Hg increase in diastolic BP (DBP), the chance of developing cardiovascular disease doubles across the BP range of 115/75 to 185/115.

Isolated systolic hypertension (ISH) increases in prevalence with age and as the prevalence of isolated diastolic hypertension (IDH) decreases. Combined ISH and IDH also decreases with age. Evidence also indicates that adverse ischemic cardiac and cerebral vascular disease increase with age-adjusted increasing SBP. Systolic hypertension is more prevalent than diastolic hypertension, particularly in individuals aged ≥60 years, and is associated with greater risk of both fatal and nonfatal outcomes, including cerebral and cardiac dysfunction. Evidence now indicates that the specific BP subtype also conveys an independent risk to perioperative outcome. Mean arterial pressure (MAP) has also been extensively evaluated as an intraoperative index of perioperative risk during non-cardiac and cardiac surgery involving cardiopulmonary bypass (CPB). It has been reported that high-risk patients who experience a drop in MAP >20 mm Hg for more than 1 hour or the same in addition to an increase in MAP >20 mm Hg for more than 15 minutes from baseline while undergoing elective non-cardiac surgery had the greatest risk of complications. Additionally, a drop in MAP in patients undergoing cardiac surgery from baseline during CPB has been reported to be associated with an increased risk of cognitive dysfunction and bilateral watershed strokes. Data on the relationship of preoperative ISH to perioperative outcome have been reported in cardiac and noncardiac surgery. It was concluded that ISH was associated with a 40% increase in perioperative cardiovascular morbidity following coronary artery bypass graft. Interestingly, this risk remained, regardless of preoperative antihypertension medication, anesthetic techniques, or other perioperative cardiovascular risk factors.

Among patients undergoing cardiac surgery, the mean PP was greater in those patients who suffered a stroke (81 vs 65 mm Hg) with each additional 10 mm Hg contributing additive risk (odds ratio [OR], 1.35; confidence interval [CI], 1.13–1.62; \( P=0.001 \)). It was also noted in an independent observation that death from cardiac and cerebral causes was directly associated to preoperative PP among this patient population. Stroke after cardiac surgery is proportionate to pulse pressure.

Pathophysiology of Acute Hypertension

BP consists of a steady component (MAP) and a pulsatile component (PP). The fluid-pressure dynamic of BP is determined by different parameters depending on its component subtype; for example, the determinants of MAP are left ventricular (LV) ejection and peripheral vascular resistance (PVR), whereas the determinants of SBP are stroke volume, LV ejection, distensibility, and wave reflection. The determinants of PP are LV ejection, viscoelasticity, and wave reflection. The actual observed pulse contour that is displayed on a monitor is a summation of forward and returning pressure waves.

Adaptive changes in the vessel wall are dependent on BP load. The lumen to wall ratio is decreased in diastolic hypertension with inward (eutrophic) remodeling in small vessels. Vascular remodeling, characterized by outward hypertrophy, on the other hand occurs with PP hypertension, a disease of large conduit vessels (eg, aorta).

The conditions that cause an acute change in systemic hemodynamics during surgery are common and include acute changes in systemic vascular resistance due to anesthesia depth, surgical stimulation, aortic occlusive clamping and unclamping, fluid shifts, hemorrhage, secondary drug effects, and many other examples. These changes commonly occur in the setting of insufficient intravascular volume and likely effect patients differently, depending on their
underlying vascular physiology and compliance. Arterial compliance relates to the change in volume (stroke volume) and inversely to the ensuing change in pressure. PP, the difference between SBP and DBP, is an index of conduit vessel stiffness and the rate of pressure wave propagation within the arterial tree. When stiffening of the aorta occurs, propagated and reflected waves within the arterial tree travel much more rapidly, resulting in an early return of the propagated wave to the central aorta during late systole as opposed to early diastole. This augmented systolic component thereby effectively increases afterload, and the ensuing loss of DBP augmentation may decrease organ perfusion, including coronary, cerebral, and renal perfusion pressure.

There is a tight relationship between aging, long-standing arterial hypertension, vascular disease, and PP—all acting in concert to limit organ flow and reserve. The combination of such preexisting vasculopathy and aortic-wall injury from surgical manipulation (aortic clamping/declamping, cannulation and decannulation), as well as the inflammatory response associated with CPB, provide a compelling pathophysiologic basis for the increased postoperative vascular complications observed in patients with noncompliant arteries manifested by increased PP undergoing cardiac or major vascular surgery. Stiff vessels have altered vascular smooth muscle cell phenotypes with arterial remodeling of the blood vessels in vital organs. It is possible that the autoregulatory range is distinctly different across individuals with different vascular properties and with different types of superimposed surgery and anesthesia. An altered autoregulatory range might lead to organ hypoperfusion in some individuals, despite what may be deemed to be a “clinically acceptable” BP. Moreover, an increased systolic load, along with a lower diastolic perfusion pressure combined with relative intravascular volume depletion, may set up a unique pathophysiologic basis for perioperative vascular injury. It has been postulated that changes in strain and shear stress on the endothelial wall in the setting of endothelial plaque may contribute to inflammation and the destabilization of vulnerable plaque. This procoagulation effect may be further enhanced by low and oscillatory shear stress forces that are exacerbated in noncompliant arteries. Importantly, the pulsatile stress that conduit vessels are exposed to may cause the elastic elements in the vessel wall to break down, thereby producing further vessel dilation and stiffening. As the vessel dilates, the stress on the wall worsens. Remodeling changes lead to vessel-wall medial necrosis, stiffening, increased vascular resistance, and reduced organ perfusion. Whereas the effects of laminar shear stress in normal vessels are atheroprotective, the effects of oscillatory and low shear stress promote atherosclerosis and plaque rupture.

**Hypertension and Cardiovascular Surgery**

The behavior to actively manage high BP during cardiovascular surgery is a frequent occurrence (88% of all cases). Perhaps this behavior reflects that poorly controlled BP during surgery is not tolerated in part because of easily recognized safety concerns related to ischemia modulation, the need for aortovascular stress-strain modulation (eg, clamping, unclamping), maintaining adequate perfusion conditions during CPB, and balancing these pressure-perfusion requirements with surgical bleeding concerns throughout surgery. This is especially true during the postoperative period, when requirements for weaning from mechanical ventilation and analgesia are additional stresses for poor BP control. It is well understood that perioperative hypertension increases myocardial oxygen consumption and left ventricular end-diastolic pressure and contributes to sub-endocardial hypoperfusion and myocardial ischemia. It also increases the risk of stroke, neuron-cognitive dysfunction, and renal dysfunction and contributes to surgical bleeding from anastomotic sites. In addition, it is now understood that poorly controlled BP during surgery can trigger hyper-inflammatory and procoagulation conditions, including platelet activation, which may compromise microvascular blood flow.

**BP Control and Outcomes**

Defining goals for BP control should depend on patient factors such as the presence of preexisting hypertensive disease, the specific acute-care situation that is being managed, and the vulnerable end organ. Specific BP goals need to be defined for each patient in each instance, recognizing the *situation* (type of surgery, CHF, stroke, etc), the type of hypertension (ie, phenotype: DBP, SBP, MAP, PP), and the *condition* (treatment effectiveness). As few data support an association between blood pressure variability and clinical outcomes during cardiac surgery we tested the hypothesis that intraoperative systolic blood pressure variability outside a targeted blood pressure range predicts 30-day mortality in patients undergoing cardiac surgery. 3.1 million intraoperative blood pressure evaluations were analyzed. Systolic blood pressure variability was derived in 5038 patients and validated in 2466 patients. It was observed that mean duration of systolic excursion [outside a range of 105-130mmHg] was most predictive of 30 day mortality (OR =1.03 per minute, 95% CI [1.02-1.39], P<0.0001). Hence it was concluded that intra-operative blood pressure variability is associated with 30 day post-operative mortality in patients undergoing
aortocoronary bypass surgery. Although an odds ratio of 1.03 represents a modest effect; it is important a) to realize that this effect size is a per minute effect; such that for every minute outside the 105-130mmHg range, the odds ratio for 30 day mortality increases by 0.03 and b) intraoperative blood pressure is a modifiable risk factor.

The percent change of intraoperative systolic BP below baseline BP is associated with the percent increase change from baseline in creatinine observed following cardiac surgery. 7,247 patients were evaluated from Sept. 1996 to Dec. 2005 with systolic blood pressure variability determined for each patient and characterized by frequency, magnitude (mmHg), duration (min), area under curve (mmHg*min), and % change from baseline. The study sample was randomly divided into a development cohort (2/3) and a validation cohort (1/3). Each of these was evaluated separately in a linear regression model predicting % delta creatinine, adjusting for covariates (aprotinin use, age, chf, previous mi, baseline creatinine, bypass time, diabetes, weight, valve surgery, gender, and pulse pressure). The measure most highly associated with % delta creatinine based on model r^2 value in the developmental sample was % change from baseline SBP to the lowest SBP, p< 0.006 (model r^2 value =0.005). Multivariable linear regression demonstrated an association between % change in SBP below baseline to % delta creatinine (p< 0.0016) in the validation data set.

**BP Control and Outcomes in non cardiac surgery**

Bijker et al (Anesthesiology: 2012 - Volume 116 - Issue 3 - p 658–664) investigated the incidence of stroke in 48,241 pts who underwent non-cardiac & non-neurosurgical procedures (2002 to 2009). They found 42 ischemic strokes (0.09%) within 10 days after surgery (matched to 252 control pts) and concluded that the duration intraoperative MAP was decreased > 30% from baseline was assoc with postop stroke. They concluded that although, the most widely proposed mechanism of a postoperative stroke is arterial embolism, hypotension can also influence the evolution of a postoperative stroke by compromising (collateral) blood flow to ischemic areas. In this context, hypotension is best defined as a decrease in mean blood pressure relative to a preoperative baseline, rather than an absolute low blood pressure value. In another study Davis et al (Anesthesiology: 2012 ;116 , 396–405) reviewed 120 charts and found that independent predictors for good neurologic following non cardiac surgeryoutcome were local anesthesia, systolic BP >140 mmHg, and low baseline stroke scores.

**SUMMARY**

Pre-op HTN subclass predicts (postop) risk in patients undergoing cardiac surgery. Intra-op SBP variability predicts (postop) risk in patients undergoing cardiac surgery. BP goals remain an area for further investigation and depend on the patient, situation & condition. There is much to be learned about integrating observational data for individual patients in specific situations with specific conditions when establishing BP management strategies.

**Bibliography**


