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Special Article

Perioperative Quality Initiative consensus statement on intraoperative blood pressure, risk and outcomes for elective surgery

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Abstract

Background: Intraoperative mortality is now rare, but death within 30 days of surgery remains surprisingly common. Perioperative myocardial infarction is associated with a remarkably high mortality. There are strong associations between hypotension and myocardial injury, myocardial infarction, renal injury, and death. Perioperative arterial blood pressure management was thus the basis of a Perioperative Quality Initiative consensus-building conference held in London in July 2017.

Methods: The meeting featured a modified Delphi process in which groups addressed various aspects of perioperative arterial pressure.

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Results: Three consensus statements on intraoperative blood pressure were established. 1) Intraoperative mean arterial pressures below 60–70 mm Hg are associated with myocardial injury, acute kidney injury, and death. Injury is a function of hypotension severity and duration. 2) For adult non-cardiac surgical patients, there is insufficient evidence to recommend a general upper limit of arterial pressure at which therapy should be initiated, although pressures above 160 mm Hg have been associated with myocardial injury and infarction. 3) During cardiac surgery, intraoperative systolic arterial pressure above 140 mm Hg is associated with increased 30 day mortality. Injury is a function of arterial pressure severity and duration.
Conclusions: There is increasing evidence that even brief durations of systolic arterial pressure <100 mm Hg and mean arterial pressure <60–70 mm Hg are harmful during non-cardiac surgery.

Keywords: anaesthesia; arterial pressure; hypotension; mortality; myocardial injury; postoperative outcome; renal injury; surgery

Editor's key points

- The relationship between intraoperative arterial blood pressure and serious complications is of critical importance in perioperative medicine.
- An expert consensus meeting reviewed the relationships between intraoperative arterial pressure and major adverse postoperative outcomes using a modified Delphi approach to create recommendations.
- There are strong associations between intraoperative hypotension and myocardial injury, kidney injury, and death.
- Maintaining systolic arterial pressure above 100 mm Hg and mean arterial pressure above 60–70 mm Hg may reduce risk.

Death from anaesthesia is now rare.[1] In contrast, although there has been some improvement in recent decades, one in 50 surgical inpatients still die within 30 days after adult non-cardiac surgery.[2] Blood pressure changes may signal morbid events during anaesthesia; a decrease heralding an occult haemorrhage is an obvious example. But what constitutes an intolerable arterial pressure excursion during various clinical scenarios remains poorly understood.[3]

Both hypotension and hypertensive emergencies can be defined differently during surgery than in non-operative settings. For example, moderately high intraoperative pressures often demand immediate treatment, although the same pressure might otherwise be acceptable in a non-operative ambulatory setting. Thus, acceptable intraoperative arterial pressure depends on the clinical context (Supplementary Table S1). The equipment required to measure arterial pressure is almost universally available even when more invasive measures of cardiovascular performance are not.[4]

Much of the evidence presented here refers to outcomes in large patient populations. The challenge for anaesthesia providers is how best to apply population data to individuals in specific clinical contexts such that complications related to unacceptable intraoperative arterial pressures are minimised.

Methods

The Perioperative Quality Initiative (POQI) is an international, multidisciplinary non-profit organisation that organises consensus conferences on clinical topics related to perioperative medicine. Each conference assembles a collaborative group of diverse international experts from multiple healthcare disciplines who are tasked with using a modified Delphi technique to develop consensus-based recommendations in perioperative medicine.[5–9] The participants in the POQI consensus meeting were recruited based on their expertise in perioperative medicine and blood pressure management (see Appendix and Supplementary File 1). Conference participants were divided into four work groups: Group 1 reviewed the physiology and measurement of blood pressure with relevance to the perioperative setting[5]; Groups 2, 3, and 4 were focused on preoperative,[6] intraoperative (this paper), and postoperative[7] arterial pressure, respectively. The POQI process is based on an established modified Delphi process used in the Acute Dialysis Quality Initiative (ADQI) conferences[10] and includes the following iterative steps before (steps 1 and 2) and during (step 3) the conference: 1) building consensus around the most important questions related to the topic, 2) a literature review of the topic raised by each question, 3) sequential steps of content development and refinement until agreement is achieved and a consensus document is produced; see Ackland and colleagues[5] for detailed methods. Groups indicated the strength of evidence underlying practice recommendations using a structure consistent with UK National Institute for Health and Care Excellence (NICE) guidance.

This workgroup of the POQI-3 consensus meeting reviewed what is known of the systemic effects of low and high intraoperative blood pressure. Intraoperative blood pressure values that have been associated with harm were identified. Before the meeting a literature search was conducted in PubMed (1952–2017) using the following terms: intraoperative, hypotension, deliberate hypotension, controlled hypotension, induced hypotension, perioperative, blood pressure, outcomes, definitions, diastolic blood pressure, systolic blood pressure, MAP, pulse pressure, duration, magnitude, acute kidney injury, stroke, myocardial infarction, cognitive dysfunction, retrospective, prospective, tolerance of hypotension, and hypotensive anaesthesia. In the next section, we present each consensus statement, along with their rationales.

Results

Consensus statements

Consensus statement 1: *Intraoperative mean arterial blood pressures below 60–70 mm Hg are associated with myocardial injury, acute kidney injury, and death. Systolic arterial pressures below 100 mm Hg are associated with myocardial injury and death. Injury is a function of hypotension severity and duration.*

Intraoperative hypotension lacks a clear definition. A 2007 systematic review identified 140 different definitions from 130 studies.[11] Frequently used definitions include systolic arterial pressure <80 mm Hg, a decrease in systolic pressure to 20% below baseline, and a combination definition consisting of an absolute systolic pressure <100 mm Hg, 30% below baseline, or both. Lack of standard definitions for hypotension results in reported incidences between 5% and 99% depending on which definition is used and which blood pressure components are considered.[11] It is important to consider this variation when observational cohort studies report relationships between hypotension and adverse outcomes. Although some clinicians might argue that blood pressure is tightly controlled during surgery, there is evidence that arterial pressure management practices vary widely and that intraoperative hypotension remains common.[12]

There is a wealth of literature relating to deliberate hypotension, some of which is summarised in Supplementary Table S2. Much of this work pertains to small historical studies rather than definitive RCTs. These early studies provided signal for the relationship between hypotension and adverse effects on vital organs. However, many generalise poorly because they were conducted in limited populations, usually failed to quantify myocardial injury with routine troponin screening, and were not powered for the most important outcomes. A consequence is that early studies provide little guidance for current surgical patients.

Recently, several large observational cohort analyses have addressed the relationship between intraoperative blood pressure and myocardial injury, renal injury, and death. The collective data shown in Table 1 generally show that patients who maintain intraoperative MAP exceeding 60–70 mm Hg may be less likely to experience acute kidney injury (AKI) and myocardial injury[13,14] which are both associated with higher 30 day postoperative mortality.[14] In contrast to mean arterial blood pressure, blood pressure variability is only weakly associated with adverse outcomes in non-cardiac surgical patients.[13] Organ-specific injury is a strong function of the duration of hypotension[16] (Supplementary Fig. S1).

Both absolute thresholds (e.g. mean pressure <65 mm Hg) and relative thresholds (e.g. ≤30% reduction from baseline) predict myocardial and renal injury. However, absolute pressures appear to be as predictive as relative reductions over a wide range of clinic-obtained baseline pressures (Fig. 1).[13] Either is thus an acceptable approach to guiding intraoperative arterial pressure management, but absolute values are usually easier to work with, especially as reliable baseline pressures are often unavailable.[17] Hypotension is also strongly associated with 30 day mortality (Fig. 2).[13]

Remarkably, one-third of all intraoperative hypotensive episodes at one major institution occurred between anaesthetic induction and surgical incision; furthermore, pre- and post-incision hypotension were comparably associated with myocardial and kidney injury.[18] Pre-incision hypotension is caused by anaesthetic drugs (or rarely patient positioning) and cannot be blamed on surgeons; presumably it is also largely preventable. Avoiding angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) on the day of surgery helps prevent intraoperative hypotension.[19] In contrast to arterial pressure, intraoperative tachycardia up to 100 beats min^{-1} is not associated with myocardial injury[20] although heart rates exceeding 100 beats min^{-1} sustained for more than 30 min may be harmful.[21] Treating tachycardia with drugs that cause hypotension is therefore probably a poor clinical strategy.

A limitation of all studies of intraoperative arterial pressure is that unacceptably low postoperative arterial pressure is also associated with organ injury,[22] and is possibly more important than intraoperative pressure. For example, 94% of myocardial infarctions within 30 days after surgery occur in the initial 48 postoperative hours.[15] The difficulty, of course, is that intra- and postoperative arterial pressures are not independent and many patients who develop postoperative hypotension also had hypotension during surgery, making it difficult to distinguish when organ damage actually occurred.

In a recent multicentre French trial of tight *vs* minimal intraoperative blood pressure control (n=298), high-risk patients were randomised to minimal arterial pressure control (ephedrine for systolic pressure <80 mm Hg or <40% below baseline) *vs* norepinephrine to maintain systolic pressure within 10% of baseline values.[23] Arterial pressure was controlled during surgery and for 4 postoperative hours. The primary outcome was a composite of systemic inflammatory response syndrome, at least one organ failure, or both. The primary outcome occurred in 56/147 subjects in the norepinephrine group *vs* 75/145 subjects in the minimal control group: relative risk=0.73 (95% confidence interval [CI], 0.56–0.94). Secondary outcomes included fewer sepsis cases and shorter duration of hospitalisation with tight blood pressure control. This trial conducted by Futier and colleagues[23] provides the first evidence that previously identified associations between intraoperative hypotension and major complications are causally mediated. There are nonetheless aspects of the trial worth considering. For example, the intervention threshold in the minimal control group was a systolic pressure of 80 mmHg. Most anaesthetists intervene well before systolic pressure reaches 80 mm Hg.[24] Had a higher intervention pressure been used, the observed 25% risk reduction would presumably have been smaller. The actual difference in mean pressure was small, just 6.5 mm Hg. The investigators did not report the magnitude of hypotension below critical thresholds, which is probably when harm occurs.

Patients who were assigned to the individualised treatment group experienced significantly lower rates of organ-specific morbidity such as renal dysfunction. Renal injury is understandable as the threshold for AKI appears to be higher than for myocardial injury, about 75 mm Hg rather than 65 mm Hg. It is also consistent with previous trial evidence for an association between blood pressure control and AKI.[25] It is likewise curious that there was only one myocardial infarction identified in nearly 300 high-risk patients despite routine troponin screening. Based on the VISION (Vascular events In noncardiac Surgery patIents cOhort evaluatioN) cohort,[15] many more would be expected. In a secondary analysis of VISION trial data, even brief periods of systolic hypotension (systolic pressure <100 mm Hg) in patients having non-cardiac surgery were associated with myocardial injury and increased mortality.[15]

Consensus Statement 1 is restricted to adults having non-cardiac surgery. There is currently little evidence to guide blood pressure management in paediatric surgical patients. However, de Graaff and colleagues[26] recently described a range of paediatric blood pressures after anaesthetic induction and surgical incision in a cohort of 116 000 anaesthetised children. The 50th percentile of the MAP during anaesthesia varied from 33 mm Hg at birth to 67 mm Hg by age 18 yr. The lower cut-off, defined as 2 standard deviations below the 50th percentile, varied from 17 mm Hg at birth to 47 mm Hg by age 18 yr, with values being comparable in boys and girls. These data provide the first reference range of blood pressures for

Table 1 Recent cohort studies linking intraoperative hypotension with perioperative outcomes

Year, authors	Study type	Outcomes	Conclusions
2013, Walsh and colleagues[14]	Large cohort retrospective cohort study. Non-cardiac surgery—33 330 patients single centre. MAP 55–75 mm Hg used to determine the threshold at which the risk of AKI and myocardial injury increased. Relationship between duration of MAP and outcomes was assessed.	Risk of acute kidney injury (AKI) and myocardial injury	AKI and myocardial injury developed in 2478 (7.4%) and 770 (2.3%) surgeries, respectively. The MAP threshold where the risk for both outcomes increased was <55 mm Hg. Compared with never developing a MAP <55 mm Hg, those with a MAP less than 55 mm Hg for 1–5, 6–10, 11–20, and >20 min had graded increases in their risk of the two outcomes. 'We found that time spent with a MAP <55 mm Hg during non-cardiac surgery is independently associated with an increased risk of AKI and myocardial injury. Notably, any amount of time at a MAP <55 mm Hg was associated with adverse outcomes'. Even short durations of an intraoperative MAP <55 mm Hg are associated with AKI and myocardial injury.
2015, Mascha and colleagues[13]	Retrospective cohort analysis of 104 401 non-cardiac surgical patients. Patients were excluded when they had missing BP data or procedures <60 min.	The authors evaluated associations between 30 day mortality and both time-weighted average intraoperative mean arterial pressure (TWA-MAP) and measures of intraoperative MAP variability—including generalised average real variability of MAP (ARV-MAP) and SD of MAP (SD-MAP).	Although low MAP is strongly associated with mortality, low intraoperative blood pressure *variability* is only mildly associated with postoperative mortality after non-cardiac surgery. Anaesthesiologists should pay attention to MAP level rather than minute-to-minute fluctuations. MAP <75 mm Hg represents an inflection point at which hypotension begins to increase 30 day mortality.
2015, Monk and colleagues[31]	Retrospective cohort study of 18 756 patients. Combined intraoperative blood pressure data from six Veterans Affairs medical centres.	30 day outcomes to determine the risk-adjusted associations between intraoperative blood pressure and 30 day mortality. Deviations in blood pressure were assessed using three methods: 1) population thresholds (individual patient sum of area under threshold [AUT] or area over threshold 2 SD from the mean of the population intraoperative blood pressure values); 2) absolute thresholds; and 3) percent change from baseline blood pressure.	Approximate conversions of AUT into its separate components of pressure and time were: SBP <67 mm Hg for more than 8.2 min; MAP <49 mm Hg for more than 3.9 min; DBP <33 mm Hg for >4.4 min. Absolute thresholds: SBP <70 mm Hg for ≥5 min (odds ratio [OR]=2.9; 95% confidence interval [CI], 1.7–4.9); MAP <49 mm Hg for more than or equal to 5 min (2.4; 1.3–4.6); DBP <30 mm Hg for ≥5 min (3.2; 1.8–5.5). Percent change: MAP decreases to >50% from baseline for ≥5 min (2.7; 1.5–5.0). Intraoperative hypotension, but not hypertension, is associated with increased 30 day operative mortality. 'When our results are combined with the findings of Walsh and colleagues,[14] we believe that there is strong evidence that intraoperative hypotension, namely SBP <70 mm Hg, MAP <50 mm Hg, and DBP <30 mm Hg, is associated with excess operative morbidity and mortality'.
2015, Sun and colleagues[41]	Retrospective cohort study of 5127 inpatients, average age 60 yr, who had non-cardiac surgery between 2009 and 2012	The primary outcome was AKI (50% or 0.3 mg/dl increase in creatinine) during the first 2 postoperative days.	AKI occurred in 324 (6.3%) patients and was associated with MAP <60 mm Hg for 11–20 min and MAP <55 mm Hg for >10 min in a graded

Continued

Table 1 Continued

Year, authors	Study type	Outcomes	Conclusions
	with invasive MAP monitoring. The authors investigated the association between varying periods of intraoperative hypotension (IOH) with MAP less than 55, less than 60, and less than 65 mm Hg with AKI.	Multivariable logistic regression was used to model the exposure–outcome relationship.	fashion. For MAP <60 mm Hg, the adjusted OR for AKI was 1.84 (1.11–3.06) for 11–20 min exposure. Postoperative AKI was associated with sustained intraoperative periods of MAP <55 and <60 mm Hg. There was no association between pre-existing hypertension and intraoperative hypotension. The authors conclude that the magnitude and duration of intraoperative hypotension are both important risk factors for both stage I and II AKI.
2016, van Waes and colleagues[28]	Prospective cohort study included 890 consecutive patients, average age 73 yr, having vascular surgery from two university centres. The investigators considered two absolute MAP thresholds (MAP <50 mm Hg and MAP <60 mm Hg) and two thresholds relative to the pre-induction MAP (a decrease of 30% or more and a decrease of 40% or more). For each patient, the cumulative duration of hypotension was calculated, defined as the total number of minutes that the MAP was below the threshold during the surgical procedure. To account for severity of the hypotension, the total area under the curve (AUC) of IOH was calculated.	The occurrence of myocardial injury was assessed by troponin measurements as part of a postoperative care protocol.	Depending on the definition used, IOH occurred in 12–81% of the patients. Postoperative myocardial injury occurred in 131 (29%) patients with IOH as de fined by a MAP <60 mm Hg, compared with 87 (20%) patients without IOH (P=0.001). After adjustment for potential confounding factors including mean heart rates, a 40% decrease from the pre-induction mean arterial blood pressure with a cumulative duration of more than 30 min was associated with postoperative myocardial injury (relative risk, 1.8; 99% CI, 1.2–2.6, P<0.001). Shorter cumulative durations (<30 min) were not associated with myocardial injury. Postoperative myocardial infarction and death within 30 days occurred in 26 (6%) and 17 (4%) patients with IOH as defined by a MAP <60 mm Hg, compared with 12 (3%; P=0.08) and 15 (3%; P=0.77) patients without IOH, respectively.
2017, Salmasi and colleagues[17]	Retrospective cohort analysis of 53 315 non-cardiac surgical patients. Baseline MAP was defined as the average of all MAP readings over the 6 months before surgery. The authors characterised hypotension by the lowest MAP below various absolute and relative thresholds for cumulative 1, 3, 5, or 10 min and also time-weighted average below various absolute or relative MAP thresholds. The authors modelled each relationship using logistic regression.	The authors further evaluated whether the relationships between intraoperative hypotension and either myocardial or kidney injury depended on baseline MAP. The authors compared the strength of associations between absolute and relative thresholds on myocardial and kidney injury using C statistics. The goal of this study was to determine the relationship between intraoperative MAP <55–75 mm Hg and postoperative AKI, myocardial injury, or both.	MAP below absolute thresholds of 65 mm Hg or relative thresholds of 30% were progressively related to both myocardial and kidney injury. At any given threshold, prolonged exposure was associated with increased odds. The associations based on relative thresholds were no stronger than those based on absolute thresholds. Anaesthetic management can thus generally be based on intraoperative pressures without regard to preoperative pressure.
2018, Abbott and colleagues[15]	Secondary analysis of the Vascular Events in Noncardiac Surgery Cohort Evaluation (VISION) study, a prospective international cohort study of non-cardiac surgical patients.	Multivariable logistic regression analysis tested for associations between intraoperative HR and/or SBP and myocardial injury after non-cardiac surgery (MINS), defined by an elevated serum troponin T adjudicated as caused by an ischaemic aetiology within 30 days after surgery. Predefined thresholds for intraoperative HR and SBP	The highest heart rate decile (>96 beats min^{-1}) was independently associated with MINS (OR=1.48; 95% CI, 1.23–1.77), MI (OR=1.71; 95% CI, 1.34–2.18), and mortality (OR=3.16; 95% CI, 2.45–4.07). Intraoperative tachycardia, hypertension, and hypotension were associated with MINS.

Continued

Table 1 Continued

Year, authors	Study type	Outcomes	Conclusions
		were: maximum HR >100 beats or minimum HR <55 beats min^{-1}; maximum SBP >160 mm Hg or minimum SBP <100 mm Hg. Secondary outcomes were myocardial infarction and mortality within 30 days after surgery.	
2017, Futier and colleagues[23]	Multicentre, randomised, parallel-group clinical trial conducted in nine French university and non-university hospitals. The study enrolled 298 high-risk adults having major surgery lasting ≥2 h with general anaesthesia.	The primary outcome was a composite of systemic inflammatory response syndrome and dysfunction of at least 1 organ system of the renal, respiratory, cardiovascular, coagulation, and neurological systems by day 7 after surgery. Secondary outcomes included the individual components of the primary outcome, durations of ICU and hospital stay, adverse events, and all-cause mortality at 30 days after surgery.	Among patients predominantly undergoing abdominal surgery who were at increased postoperative risk, management targeting an individualised systolic blood pressure (within 10% of baseline), compared with standard management (a 40% decrease from baseline or an SBP of 80 mm Hg), reduced the risk of postoperative organ dysfunction by about a quarter.

healthy children and those with minimal morbidity undergoing anaesthesia.[26]

Best available evidence suggests that duration and magnitude of systolic arterial pressure below 100 mm Hg and mean arterial blood pressures below 60–70 mm Hg during non-cardiac surgery in adults are associated with organ injury. There is evidence that hypotension in association with tachycardia (heart rate >100 beats min^{-1}) enhances organ-specific risk.[15,27,28]

Consensus statement 2: *For adults having non-cardiac surgery, there is insufficient evidence to recommend a general upper limit of blood pressure at which therapy should be initiated.*

Just as there is no consistent definition for intraoperative hypotension, there is no generally accepted definition of intraoperative hypertension. In non-operative situations, the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure defined diagnostic thresholds for hypertension, hypertensive urgency, and

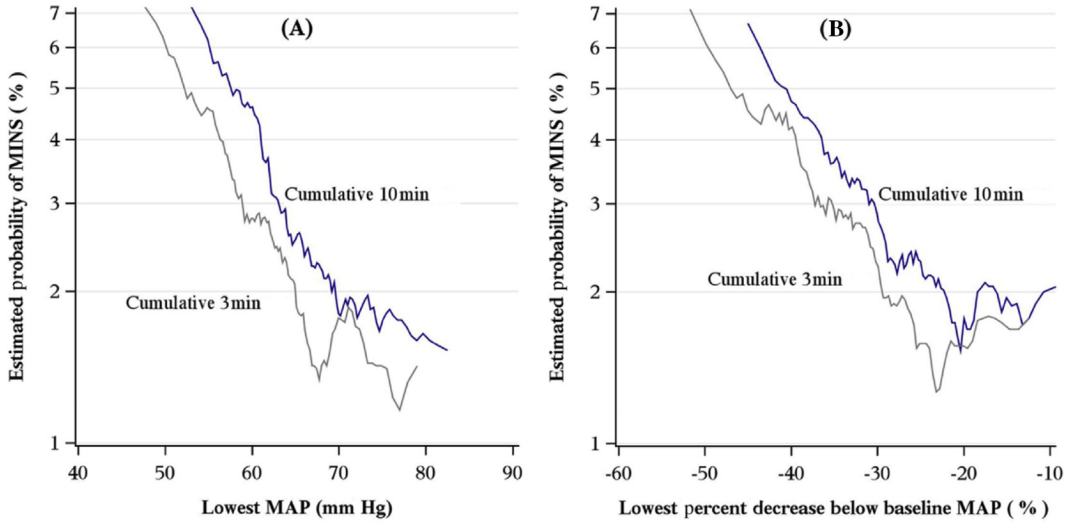

Fig 1. Relationship between the lowest cumulative absolute mean arterial pressure (MAP) maintained for 3 and 10 min and myocardial injury (left). Relationship between the lowest cumulative relative MAP maintained for 3 and 10 min and myocardial injury (right). Both were highly predictive, but relative thresholds were not more predictive than absolute thresholds which are easier to use. The relationships were generally similar for acute kidney injury (not shown). MINS, myocardial injury after non-cardiac surgery. Reproduced with permission from Salmasi and colleagues.[17]

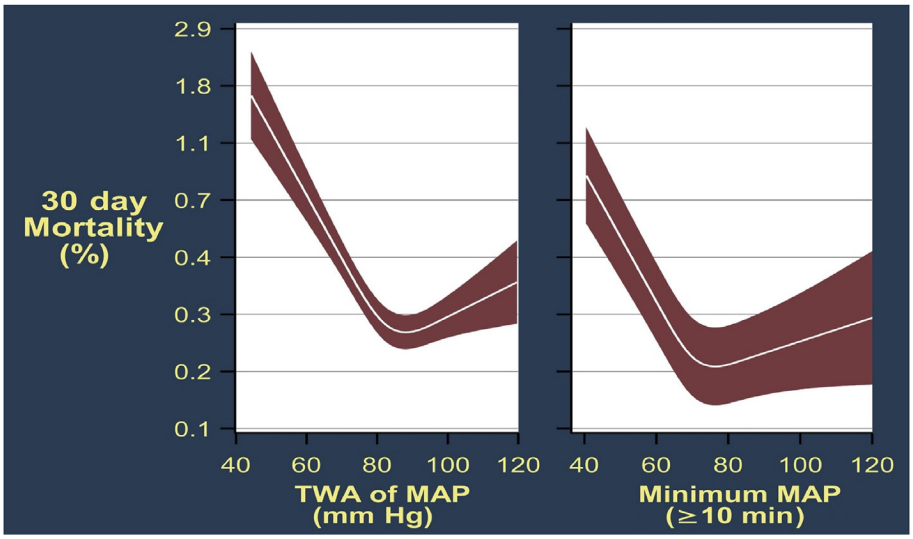

Fig 2. Relationship between average and lowest intraoperative mean arterila pressure (MAP) and 30 day postoperative mortality. High average or minimum MAP had relatively little effect on mortality. Note that the Y axis is logit; therefore, the increase in mortality from 80 to 40 mm Hg was more than six times greater than the small increase from 80 to 120 mm Hg. TWA, time-weighted average. Reproduced with permission from Mascha and colleagues.[13]

hypertensive emergency.[29] However, these guidelines for ambulatory medical patients do not apply to the dynamic nature of the perioperative period, and especially not to the intraoperative period where substantial blood pressure variation is common, expected, and situational. The Joint National Committee guidelines also failed to address or recognise the need to achieve acceptable targets and provide little guidance for intraoperative arterial blood pressure management.

The few available studies have used various definitions for intraoperative hypertension and adverse outcomes. They were also conducted in various surgical populations, evaluated different outcomes, and used heterogeneous study designs (Table 2). Except for a few specific situations, there is little evidence that elevations in intraoperative MAP are associated with increased post-surgical morbidity in non-cardiac surgical patients. For example, Charlson and colleagues[30] described two intraoperative haemodynamic patterns that were associated with post-surgical complications in an observational study of just 254 patients: MAP more than 20 mm Hg below baseline for ≥60 min, and MAP more than 20 mm Hg above baseline for ≥15 min. They also reported that the sensitivity, specificity, and prediction of complications were similar for 20% changes in MAP and absolute 20 mm Hg changes. Finally, this study showed an association between an absolute MAP of ≥120 mm Hg and adverse outcomes—although neither the range of pressures exceeding 120 mm Hg nor duration were specified.

Mascha and colleagues[13] extracted data from 104 401 adults having non-cardiac surgery lasting ≥1 h between 2015 and 2012 at the Cleveland Clinic. MAPs from 75 to 120 mm Hg sustained for ≥10 min were only slightly associated with increased odds of death. In contrast, mortality increased substantially when MAPs were sustained even briefly at lower pressures.

The evidence is inconclusive that elevations in intraoperative systolic or diastolic arterial pressure are associated with increased post-surgical morbidity. In 2002, Reich and colleagues[21] evaluated 797 patients who had prolonged (>220 min) general, orthopaedic, vascular, or gynaecologic surgery. They observed that systolic arterial pressures >160 mm Hg were associated with an odds ratio (OR) of 2.7 (P=0.01) for the risk of 'negative surgical outcomes', defined as a hospital length of stay >10 days with a morbid condition or death. Curiously, the investigators did not report the duration of systolic pressure >160 mm Hg although duration presumably influences outcome.

In contrast, Monk and colleagues[31] evaluated a cohort of 18,756 patients and reported that systolic arterial pressures >180 mm Hg for >5 min or diastolic pressures >120 mm Hg for >5 min were not associated with increased 30 day mortality. Furthermore, systolic pressures >50% above baseline for >5 min, or diastolic pressures >50% above baseline for >5 min also were not associated with 30 day mortality.

In specific cases, such as endovascular repair for acute stroke, keeping systolic arterial pressure greater than 140 mm Hg is associated with better neurological outcomes.[32] For example, Basali and colleagues[33] compared 69 craniotomy patients with matched controls and reported that intraoperative blood pressures exceeding 160/90 mm Hg were associated with post-surgical intracranial haemorrhage with an OR of 8. When pressures exceeded this threshold during emergence, the OR for postoperative intracranial haemorrhage was 3.4.

Given the paucity and heterogeneity of the published evidence, a general upper limit of blood pressure at which therapy should be initiated remains to be defined. Although data available from a secondary analysis of the VISION trial suggest that intraoperative systolic arterial pressures >160 mm Hg are associated with myocardial injury and infarction, a large retrospective analysis of >52 000 adult non-cardiac surgical patients reported that those patients with MAP >120 mm Hg did not exhibit complications within the perioperative period.[34]

Table 2 Studies of intraoperative elevated blood pressure and post-surgical outcomes. SBP, systolic blood pressure; SAP, systolic arterial pressure; DBP, diastolic blood pressure; HTN, hypertension

Study	Date	Design	Number of participants	Intraoperative hypertension definition	Population	Outcome	Comment
Charlson and colleagues[30]	1990	Prospective	254	>20 mm Hg increase relative to preoperative MAP	Essential HTN and diabetes. Elective general and vascular surgery patients.	>15 min was associated with increased renal and cardiac complications.	The actual number of patients in this category was small. *>20% increase in MAP was equivalent to 20 mm Hg increase.
Reich and colleagues[21]	2002	Retrospective	797	>160 mm Hg systolic arterial pressure	Major orthopaedic, vascular, and gynaecology.	Odds ratio (OR) of 2.0 ($P<0.009$) for negative outcome in procedures lasting >220 min	The actual duration of HTN during 220 min was not described. Causation cannot be assessed by a retrospective study.
Basali and colleagues[33]	2000	Retrospective	69	Two consecutive reads of >160/90 Sensitivity analysis 180/100 or 150/90 was not different than 160/90	Craniotomy all causes.	Two consecutive readings of HTN was associated with an OR of 8 for postoperative intracranial bleed	Causation cannot be assessed by a retrospective study.
Davis and colleagues[32]	2012	Retrospective	96	>140 mm Hg SBP	Endovascular therapy for stroke.	SBP <140 mm Hg was associated with poor neurological outcome.	Causation cannot be assessed by a Retrospective study. Not time-weighted.
Heyer and colleagues[42]	2014	Prospective	183	>20% of baseline MAP during cross clamp	Carotid endarterectomy without shunt.	Patients managed 1–10% below baseline had greater postoperative cognitive dysfunction. Patients managed 20–30% above had less cognitive dysfunction.	Single-centre, non-standardised haemodynamic management. Six patients had >40% above baseline and there was increased postoperative cognitive dysfunction.
Monk and colleagues[31]	2015	Retrospective	18,756	Absolute SBP >180 mm Hg for >5 min MAP >130 mm Hg for >5 min DBP >120 mm Hg for >5 min Relative to Baseline SBP increase ≥50% for >5 min MBP increase >50% for >5 min DBP increase >50% for >5 min	General, vascular, thoracic, urology, orthopaedic, and neurosurgical.	Hypertension was not associated with 30 day mortality.	Morbidity was not defined *per se*, causation cannot be assessed by a retrospective study
Levin and colleagues[34]	2015	Retrospective	52,919		Adult non-cardiac procedures.	Intraoperative arterial blood pressure lability occurs more often in hypertensive patients. Contrary to common belief, increased lability was associated with decreased 30 day mortality. No adverse events were observed in patients with MAP >120 mm Hg	
Abbott and colleagues[15]	2018	Prospective	15, 087	SBP >160 mm Hg (duration not specified)	Non-cardiac surgery in adults older than 45 yr.	Intraoperative BP >160 mm Hg was associated with increased OR of MINS [1.16] and MI [1.34] within 30 days after surgery. Unexpectedly, BP >160 mm Hg was associated with reduced OR of 30 day mortality [0.75].	

Overall, available data suggest that elevated intraoperative blood pressures are not as strongly associated with postoperative morbidity as hypotension. That said, intraoperative arterial pressure management should be individualised in consideration of underlying organ function and the surgical procedure being performed.

Consensus statement 3: *During cardiac surgery, intraoperative systolic blood pressure greater than 140 mm Hg is associated with increased 30 day mortality. Injury is a function of severity and duration.*

Intraoperative MAP below a defined threshold is associated with increased risk of postoperative myocardial ischaemia, stroke, neurocognitive dysfunction, and AKI in patients having non-cardiac surgery (see Consensus Statement 1). Moreover, the duration of hypotension and area under thresholds predicts myocardial infarction and AKI. For cardiac surgery, the magnitude of the excursion above and below a threshold intraoperative systolic pressure predicts 30 day mortality.[35] The relationship between intraoperative systolic arterial pressure and 30 day mortality was derived in 5038 patients and validated in 2466 others. The mean duration of systolic pressure excursion (outside a range of 105–130 mm Hg) was most predictive (OR =1.03 per min; 95% CI, 1.02–1.39; $P<0.0001$). The OR of 1.03 is *per min* of systolic arterial pressure excursion and thus is clearly clinically important (Fig. 3).

The association between systolic arterial pressure excursions above or below threshold values and 30 day mortality was also shown in the ECLIPSE trial that evaluated 1512 patients.[36] Systolic pressures <75 and >135 mm Hg intraoperatively and <85 and >145 mm Hg before and after operation were associated with 30 day mortality (OR=1.16 [95% CI, 1.04–1.30] for 30 day mortality per incremental systolic arterial pressure excursion of 60 mm Hg min h^{-1}). Based on these two independent studies, we conclude that intraoperative systolic arterial pressure excursion (duration times magnitude) above 140 mm Hg is associated with increased 30 day mortality after cardiac surgery.

There is compelling evidence that preoperative pulse pressure, as a surrogate of vascular ageing and health, is a good predictor of complications and poor long-term survival after coronary artery bypass surgery. Specifically, preoperative pulse pressure >70–80 mm Hg has been associated with stroke and death from cardiac complications in both retrospective[37,38] and prospective studies.[39,40]

Recommendations for research

There have been numerous reports on the physiology of blood pressure, blood pressure measurements, and the implications of ambulatory high and low blood pressures on long-term health.[5] However, the definitions and the implications of hypertension and hypotension in the perioperative period remain poorly characterised. Moreover, the threshold for intervention of hypotension and hypertension during the perioperative period and outcomes after intervention remain largely unknown. We consider the following topics to be research priorities.

Do organ specific thresholds for autoregulation exist, and, if so, how are they altered by factors within the perioperative period?

The most commonly used surrogate for organ perfusion within the perioperative period is systemic arterial pressure. Given that organ perfusion occurs within a normal range of pressures, defining how perioperative modifiers of autoregulation relate to patient outcomes is critical. As organ-specific thresholds for autoregulation likely differ, identifying how they differ and how these thresholds are affected by anaesthesia and surgery will be an important step in our understanding of the relationship between perioperative arterial pressure maintenance and organ-specific outcomes, and will better inform management strategies.

Which component/components of intraoperative arterial pressure best predict adverse outcomes?

Hypertension and hypotension beyond a certain threshold are associated with poor outcomes and mortality.[12,13,33] However, it is unclear whether systolic, diastolic, or MAP is the major

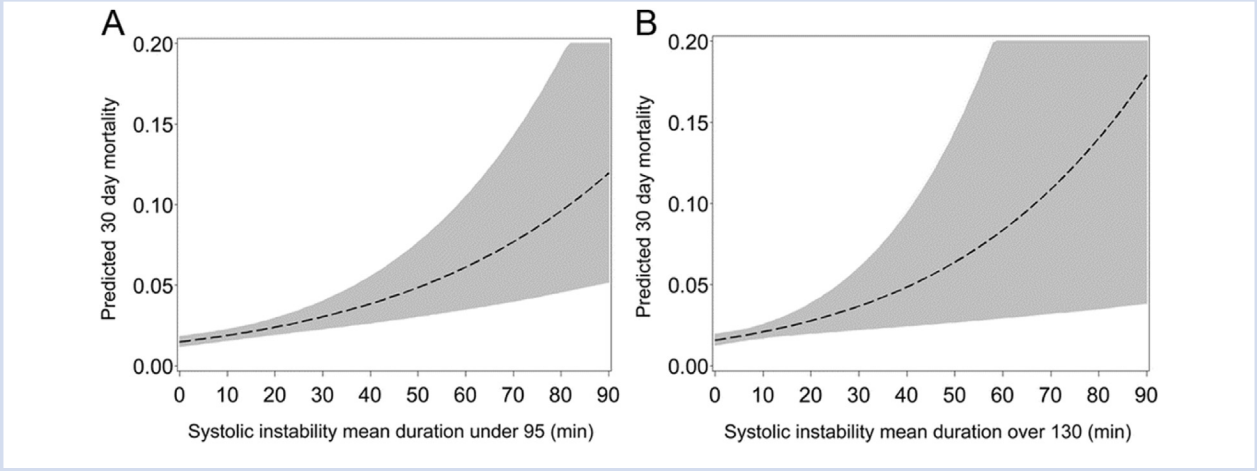

Fig 3. (a) Predicted association of mean duration per incursion (min) below the threshold 95 mm Hg and 30 day mortality in the combined sample (n=7504). *Shaded area* represents the 95% confidence intervals for the predicted values. (b) Predicted association of mean duration per incursion (min) above the threshold 130 mm Hg and 30 day mortality in the combined sample (n=7504). *Shaded area* represents the 95% confidence intervals for the predicted values. Reproduced with permission from Aronson and colleagues.[35]

determinant. It is also unknown to what extent pulse pressure might be predictive. The interactions among various arterial pressure components are also unknown. Findings that demonstrate poor outcomes from prolonged periods of haemodynamic perturbation, in particular prolonged hypotension, has been largely gleaned from association studies using large databases. But associations may not imply causal relationships as there are many confounding factors that may provide alternative explanations.

The recent trial conducted by Futier and colleagues[23] randomised patients to a systolic arterial pressure within 10% of baseline or to standard management defined as treating systolic pressure <80 mm Hg or <40% from the reference value during and for 4 h after surgery. They found that management targeting an individualised systolic pressure reduced the risk of postoperative organ dysfunction. This important, but small, trial suggests that about a quarter of the observed associations are causal rather than simply predictive. Considerable additional work is needed.

Do different monitoring techniques result in different associations between threshold arterial pressure values and adverse outcomes?

Arterial pressures are routinely measured using direct and indirect methods. However, it remains unknown whether different monitoring techniques result in different associations between threshold values and adverse outcomes.[5] Also, it remains unknown whether continuous arterial pressure monitoring allows clinicians to reduce exposure to harmful pressures. It is also unknown if the sites of arterial pressure measurement are important determinants. For example, are direct measurements of arterial pressures at the radial artery different from brachial or femoral arteries as a function of adverse outcomes? Are finger cuff measurements of indirect blood pressure as sensitive as brachial cuff measurements? The answers to these questions may be addressed in observational studies.

Does targeted blood pressure management affect outcome?

Association studies on blood pressure have taught us that hypertension and hypotension beyond certain thresholds are associated with adverse events.[12,13,33] However, Futier and colleagues[23] have demonstrated that maintaining tight blood pressure control both intraoperatively and for a specified time after operation, reduced the risk of postoperative organ dysfunction, but that no difference was observed at 30 days. How critical is maintaining blood pressure within predefined ranges and for how long after surgery? Ethical concerns limit the ability to define target limits at which hypotension or hypertension may cause harm which will invariably make conducting trials challenging.

Do various causes of alterations in blood pressure affect the association with treatment and outcome?

Pre-existing hypertension and hypotension may be caused by different disease processes, and intraoperative blood pressure perturbations have various causes. For example, hypotension may be a result of heart failure, hypovolaemia, or vasodilation. In contrast, hypertension may result from arteriolar constriction or from constriction at larger arterial vessels. Presumably, these various causes have different prognostic importance at given pressure levels. The interactions between heart rate and hypertension and hypotension are also largely unknown. Several perioperative observational studies are ongoing investigating how blood loss, blood pressure, and heart rate interact to affect outcomes. We hope that these results will guide development of haemodynamic management strategies that are pragmatic and generalisable.

What are the best therapies for specific causes of blood pressure alterations?

The choice of therapeutic option for the management of unacceptable blood pressure is a subject of continuing debate. For example, should an alpha agonist be used to restore blood pressure, or is it preferable to use an agonist that acts on both alpha and beta receptors? There are at least strong theoretical concerns about using pure alpha agonists that increase blood pressure at the expense of tissue perfusion—which is the real issue. Should calcium be used to increase ventricular contraction or a direct beta agonist? Although published studies have examined the haemodynamic effects of various pharmacological agents, it remains unclear which affect substantive outcomes. Large randomised studies could potentially answer some of these important clinical questions.

We believe that studies of targeted blood pressure management should be given priority. We already have ample data from association studies that demonstrate harm after even brief periods of hypotension. However, we need far better evidence to determine whether preventing hypotension, or at least rapidly restoring acceptable blood pressures, improves clinically important outcomes. It would also be helpful to determine whether the routine use of continuous measurements of blood pressure monitoring improves post-surgical outcomes. Several relevant studies have appeared since POQI 3 was conducted that are relevant to these issues.

Strengths and limitations

POQI uses an established modified Delphi process which has been used in more than 25 ADQI and POQI conferences in the past 20 yr. The combination of a literature review with expert opinion aims to produce a practical consensus statement focusing on areas of clinical uncertainty. This methodology does not incorporate a formal systematic review or meta-analysis. However, as this process is based partly on expert opinion, there remains some risk of bias. Areas of uncertainty have been clearly signposted in the discussions accompanying each statement.

Conclusions

During adult non-cardiac surgery there is increasing evidence that brief durations of systolic arterial pressure <100 mm Hg and MAPs <60–70 mm Hg are associated with organ injury. Intraoperative hypertension is not as strongly associated with morbidity as hypotension, and there is insufficient evidence to recommend a general upper limit of blood pressure at which therapy should be initiated. During adult cardiac surgery, intraoperative systolic arterial pressures >140 mm Hg are associated with increased 30 day mortality. Further research is warranted to define safe thresholds and durations of both intraoperative hypotension and hypertension, the role and

management of perioperative pulse pressure as it relates to morbidity and mortality, and finally, the best therapies for specific alterations in blood pressure.

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Appendix A. Supplementary data

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