BJA

British Journal of Anaesthesia, 122 (5): 542–551 (2019)

doi: 10.1016/j.bja.2019.01.011
Advance Access Publication Date: 14 February 2019
Special Article

SPECIAL ARTICLES

Perioperative Quality Initiative consensus statement on the physiology of arterial blood pressure control in perioperative medicine

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This article is accompanied by an editorial: Consensus Statements and Expert Guidance: Interpret with Care by S.J. Howell, *Br J Anaesth* 2019:122, doi: https://doi.org/10.1016/j.bja.2019.03.013.

Abstract

Background: Perioperative arterial blood pressure management is a physiologically complex challenge influenced by multiple factors.
Methods: A multidisciplinary, international working subgroup of the Third Perioperative Quality Initiative (POQI) consensus meeting reviewed the (patho)physiology and measurement of arterial pressure as applied to perioperative medicine. We addressed predefined questions by undertaking a modified Delphi analysis, in which primary clinical

Editorial decision: 2 January 2019; **Accepted:** 2 January 2019

research and review articles were identified using MEDLINE. Strength of recommendations, where applicable, were graded by National Institute for Health and Care Excellence (NICE) guidelines.
Results: Multiple physiological factors contribute to the perioperative physiological importance of arterial pressure: (i) arterial pressure is the input pressure to organ blood flow, but is not the sole determinant of perfusion pressure; (ii) blood flow is often independent of changes in perfusion pressure because of autoregulatory changes in vascular resistance; (iii) microvascular dysfunction uncouples microvascular blood flow from arterial pressure (haemodynamic incoherence). From a practical clinical perspective, we identified that: (i) ambulatory measurement is the optimal method to establish baseline arterial pressure; (ii) automated and invasive arterial pressure measurements have inherent physiological and technical limitations; (iii) individualised arterial pressure targets may change over time, especially in the perioperative period. There remains a need for research in non-invasive, continuous arterial pressure measurements, macro- and micro-circulatory control, regional perfusion pressure measurement, and the development of sensitive, specific, and continuous measures of cellular function to evaluate blood pressure management in a physiologically coherent manner.
Conclusion: The multivariable, complex physiology contributing to dynamic changes in perioperative arterial pressure may be underappreciated clinically. The frequently unrecognised dissociation between arterial pressure, organ blood flow, and microvascular and cellular function requires further research to develop a more refined, contextualised clinical approach to this routine perioperative measurement.

Keywords: arterial pressure; blood pressure monitoring; haemodynamics; micro-circulation; perioperative care; perioperative medicine

Editor's key points

- Measurement of arterial pressure is fundamental to perioperative medicine, but has recognised limitations.
- An expert consensus meeting reviewed the physiology and measurement of arterial pressure in the perioperative period using a modified Delphi approach to create recommendations.
- Multiple interacting factors contribute to dynamic changes in perioperative arterial pressure that may be underappreciated clinically.
- Further research is needed to refine our understanding and management of arterial pressure in the perioperative period.

The measurement of arterial blood pressure is a fundamental tenet of modern perioperative practice, yet the limitations of using blood pressure to guide clinical management have long been recognised.[1] With the increasing complexity of clinical interventions and cardiorespiratory comorbidity, the interpretation of this measurement has become increasingly challenging and scrutinised. The development of novel monitoring technologies,[2] coupled with recent trials demonstrating the need for a reappraisal of chronic arterial hypertension management,[3] further demand a re-evaluation of applied bedside physiology to everyday perioperative practice. Here, we summarise the key aspects of arterial blood pressure physiology relevant to the perioperative period by focusing on applied physiological principles to guide the rational interpretation of this common, but frequently over-simplified, clinical measure. We also provide tractable clinical examples that highlight the need for the constant re-evaluation of perioperative blood pressure regulation.

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.

The POQI-3 consensus conference on perioperative blood pressure management took place in London, UK, from July 1 to 3, 2017. The objective of POQI-3 was to produce consensus statements and practice recommendations pertaining to the definition and management of perioperative arterial blood pressure, and to identify research priorities. The participants in the POQI consensus meeting were recruited based on their expertise in perioperative medicine and blood pressure management (Supplementary material, Appendix 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 (this paper), whereas Groups 2, 3, and 4 were focused on preoperative,[4] intraoperative,[5] and postoperative[6] blood pressure, respectively.

The POQI process is based on an established modified Delphi process used in the Acute Dialysis Quality Initiative (ADQI) conferences[7] that 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, and (3) sequential steps of content development and refinement until agreement is achieved and a consensus document is produced. This final step of content development and refinement involves a modified Delphi process of alternating breakout and plenary sessions. In the breakout sessions, work groups addressed the issues in their assigned topic area and formulated consensus statements and practice recommendations. In the plenary sessions, the findings and deliberations of each work group are presented, debated, and refined. Consensus on some statements and recommendations may be achieved in the first plenary session. Other statements and recommendation required further refinement by the work groups before re-presentation to the plenary group in the next cycle. At the end of the conference, plenary group members vote to signal either formal agreement with the final statements/recommendations, or signal their

disagreement. In the latter case, a statement of disagreement would be included in the manuscript. All recommendations were unanimously approved, unless stated otherwise.

This workgroup of the POQI-3 consensus meeting reviewed the (patho)physiology and measurement of arterial blood pressure as applied to perioperative medicine. Before the meeting, a literature search was conducted in Medline based on predefined questions (Supplementary material, Appendix 2).

Results

Consensus statements

Consensus statement 1: *Different measures and values of arterial blood pressure reflect multivariable, complex physiology that are not interchangeable.*

Blood pressure is a composite measurement comprising several values with differing physiological roles and origins

Arterial blood pressure is determined by the interaction between left ventricular cardiac contraction, the hydraulic load of the arterial system, and extravascular, intra-thoracic, and intra-abdominal mechanical forces.[8]

Common measures of arterial blood pressure include systolic, diastolic, mean arterial, and pulse pressure

These different measures are not constant and reflect fundamentally different components shaping the physiology of blood pressure regulation (Fig 1).[9] Systolic pressure is the maximal aortic pressure achieved after the left ventricle has ejected blood into the aorta. During left ventricular relaxation and refilling, aortic pressure declines to a nadir, termed the diastolic blood pressure. Pulse pressure represents the difference between systolic and diastolic pressures, representing the interaction between stroke volume and arterial tone.[10]

Systolic pressure is determined by the pattern and duration of left ventricular ejection (stroke volume), the compliance (distensibility) of the arterial vessels, the velocity of the pressure wave in large arteries and vasomotor tone in peripheral arteries, which regulates the magnitude of reflection of pressure waves.[8] Increased transmission velocity of both the forward and reflected pressure waves leads to arrival of the reflected wave in the central aorta during systole, augmenting systolic pressure.[11] Hypertension, the prevalence of which increases with age, has a multifactorial aetiology including loss of elasticity in central arteries.[12] Hence, arterial stiffening augments systolic and pulse pressures. In essence, this means that central aortic pressure serves as a surrogate of ventricular wall tension, and is the most accurate measure of afterload.

Systolic pressure increases progressively towards the peripheral arterial tree through augmentation of the arterial pulse wave. As systolic pressure increases, diastolic pressure decreases slightly, because of branching vessels reflecting pressure waves in combination with the decreased arterial compliance of the distributing arteries.[9] As a result of increased resistance and reduced compliance in smaller arteries and arterioles, the amplitude of pulsation decreases until becoming minimal in the capillaries.[13] The capacitive ('reservoir') function is determined by the compliance of the aorta and large elastic arteries and largely determines the morphology of the pulse waveform.[14] The arterial reservoir declines with age as compliance decreases, leading to changes in the aortic pressure waveform.

Diastolic pressure depends on arterial compliance (stiffness), heart rate, and the resistance and distribution of the vascular network, which is arranged in series and parallel. As humans age, diastolic pressure increases until ~50 yr of age and then typically declines thereafter. Laminar and turbulent flow characteristics, as well as blood viscosity, also influence systolic and diastolic pressures. Taken together, changes in vascular tone and viscosity associated with pathology affect both the amplitude and timing of the reflected waves, meaning that measured peripheral pressures rarely equate to central arterial pressure. Therefore, when tone, viscosity, or contractility varies rapidly, organ input pressure is unlikely to reflect central pressure. This, in part, explains the inconsistent and variable threshold values of blood pressure associated with pathophysiology.

The clinical importance of calculating MAP

MAP is the average pressure value during the arterial pulse pressure cycle. As there is relatively low resistance in the arterial tree down to the smaller arteries, MAP declines by only a small degree as the aortic pressure pulse travels away from the aorta and to the distributing arteries. By analogy to Ohm's law, MAP is a function of cardiac output and arterial resistance with

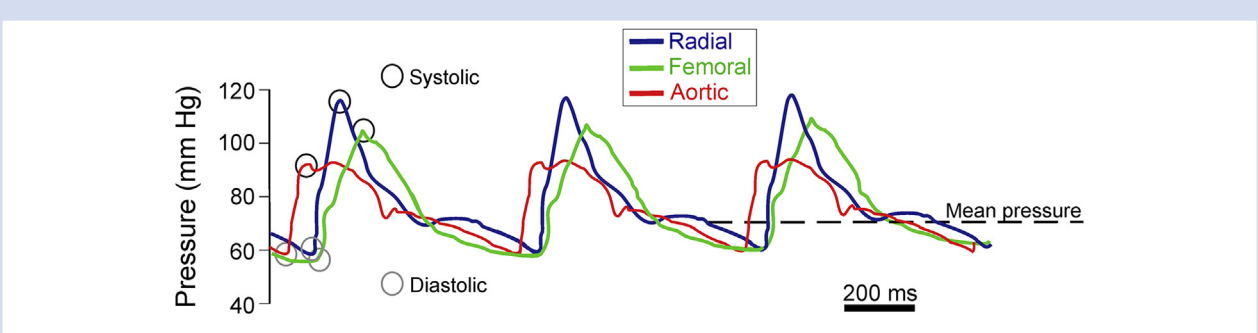

Figure 1. Variation in arterial pressure by site of measurement. Simultaneously measured arterial pressure waveforms from the radial artery, femoral artery and ascending aorta. Although diastolic and mean arterial pressures are similar regardless of the site at which arterial pressure is measured, systolic pressure increases as the monitoring site is further away from the ascending aorta. Figure reused with the permission of the Perioperative Quality Initiative (POQI).

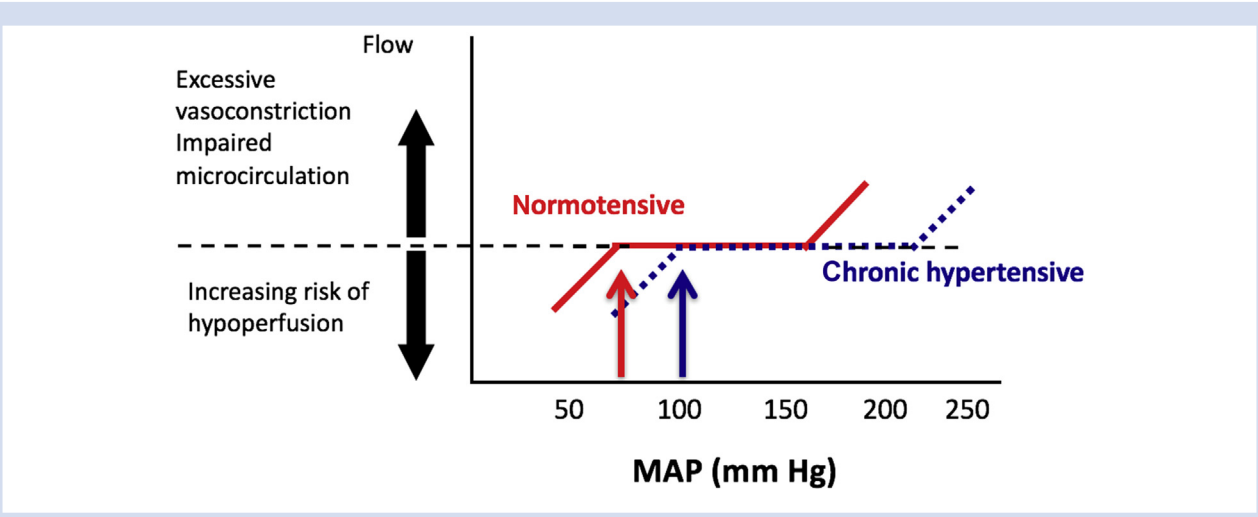

Figure 2. Autoregulation of blood flow. Schematic diagram showing altered relationship between flow and arterial pressure in normotensive and hypertensive individuals. Autoregulation allows optimal blood flow to be maintained for a wide range of pressure values. Autoregulation is present also in hypertensive individuals, but the lower pressure limit is higher and the curve is shifted to the right compared with healthy subjects. Blood flow outside the autoregulation areas leads to either excessive vasoconstriction and impaired microcirculation, or to low blood flow and hypoperfusion. Figure reused with the permission of the Perioperative Quality Initiative (POQI).

the arterial resistance determined primarily in the downstream small arteries and arterioles. This also means that MAP can be used as a reference value along the entire central arterial system to estimate organ input pressure. However, MAP does not accurately reflect left ventricular afterload because the hydraulic impedance encountered by the left ventricle comprises static (total peripheral resistance) and pulsatile elements more accurately quantified by the combination of hydraulic pressure, arterial elastance, and compliance.

Arterial blood pressure may be dissociated from intact autoregulation mechanisms

Across different organs, maintenance of tissue perfusion requires autoregulatory mechanisms that counteract extreme variations in arterial pressure (Fig 2).[15,16] Autoregulation in the cerebral circulation, for example, involves myogenic, neurogenic, and metabolic feedback mechanisms to optimise brain perfusion.[17] However, interactions between these three regulatory mechanisms are poorly understood, particularly under anaesthesia, in the presence of systemic inflammation, or both. Experimental data suggest that neurogenic (sympathetic autonomic) control is a key player in rapid cerebral autoregulatory adjustments during acute changes in arterial pressure.[18] In hypertension, autoregulation is impaired, at least in part because of impaired neurovascular responses to carbon dioxide compared with normotensive subjects.[19] Impairment of cerebral autoregulation in hypertension may extend beyond a rightward shift, with a marked narrowing, or complete loss, of the plateau range of pressure over which constant flow is ensured.[20]

Circadian and neural/hormonal changes influence blood pressure over time

Circadian rhythms regulate cardiovascular physiology through alterations in metabolism, feeding, sleep, and wakefulness, coupled with coordinated neurohormonal secretion.[21] The master circadian clock situated in the suprachiasmatic nuclei of the hypothalamus is synchronised to the external environment primarily by signals from the visual system, providing information about light–dark cycles. Interoceptive stressors similarly shape circadian signalling. Beyond the brain, peripheral circadian clocks also regulate circadian oscillations.[21]

Arterial pressure is substantially lower during sleep in healthy individuals.[22] Loss of central diurnal rhythms, peripheral diurnal rhythms, or both, that alter activity, metabolism, and hence neurohormonal release, profoundly influence blood pressure and other cardiovascular functions that contribute to the development of cardiometabolic disease.[23] Many (hypertensive) individuals fail to show such marked declines in blood pressure at night,[24] a feature associated with end-organ damage and a higher incidence of cardiovascular complications.[25] Acute inflammation and anaesthetic drugs are additional potent triggers for disrupting normal circadian regulation of arterial pressure.[26]

Essential hypertension is a complex, multi-organ disease

The complexity of blood pressure regulation is amplified in an estimated 25% of adults with essential hypertension.[27] The uncoupling of mechanisms regulating blood volume, ventricular function, central and peripheral autonomic control, neurohormonal activation via the renin–angiotensin–aldosterone system, and endothelial release of nitric oxide disrupts blood pressure, blood pressure variability, or both. The role of salt sensitivity in hypertensive individuals highlights the potential impact of increased sodium administration, which is a crucial regulator of blood volume.[28] Chronic systemic inflammation driven by perturbations in innate and adaptive immune cells acting at both vascular and non-vascular substrates further contribute to the multifaceted pathophysiology of hypertension.[29] There are limited clinical data on how perioperative interventions are affected by, or impact on, various pathophysiological drivers of hypertension.

Perioperative implications of consensus statement 1

The contribution of arterial pressure measurement to clinical management is dependent on the context within which that measurement occurs. A single measurement divorced from both acute and chronic clinical contexts is highly unlikely to provide clinically useful information.

Consensus statement 2: *Arterial blood pressure is necessary to ensure adequate blood flow to meet cellular metabolic demands.*

Adequate blood flow that meets the metabolic demands of tissues is usually reflected by pulse pressure (reflecting stroke volume) and MAP (reflecting cardiac output) remaining within a population-defined normal range. Recent trials suggest that end-organ damage in chronic hypertension occurs at lower than previously accepted arterial pressure thresholds,[3,30] and that preoperative elevated pulse pressure is associated with perioperative myocardial injury.[31] Moreover, within organs, significant heterogeneity in intra-organ blood flow occurs as a result of intrinsic variability in local microvascular resistance that is likely to be chiefly determined by regional and local metabolic requirements. Micro-circulatory perfusion is frequently perturbed by acute hypotension for prolonged periods, even after brief episodes, resulting in metabolically compromised, dysoxic, or hypoxic tissues.[32] Despite evidence for cellular dysfunction after tissue hypoperfusion in vulnerable tissues, such as the gastric mucosa during controlled haemorrhage in healthy conscious volunteers, arterial pressure may remain within its normal range during significant hypovolaemia.[32] Thus, the physiological response to hypovolaemia maintains arterial pressure, which is dissociated from cardiac output for a variable length of time.[33] Attempts to reverse hypotension may therefore not be effective in restoring micro-circulatory perfusion.[34] Loss of haemodynamic coherence between the macro-circulation and the micro-circulation occurs when either spontaneously, or through clinical intervention, systemic arterial pressure is restored yet deficiencies in micro-circulatory perfusion and oxygen delivery persist.[35] Macro- and micro-circulatory incoherence is likely to promote therapeutic measures targeted towards macrovascular variables that potentially cause harm, such as the inappropriate administration of fluids, vasopressor drugs, or both. This may explain why correcting macrovascular haemodynamic variables to normalise, or supranormalise, systemic oxygen delivery may be ineffective once systemic inflammation is established.[36,37] Thus, even though macrovascular (systemic arterial pressure) parameters may appear to be adequate in both acute and chronic pathological states, this does not necessarily reflect intra-organ microvascular blood flow. In other words, adequate arterial pressure is necessary to ensure adequate blood flow to meet cellular metabolic demands, but is not sufficient to guarantee such flow.

Perioperative implications of consensus statement 2

Arterial blood pressure measurement alone cannot ensure that adequate blood flow meets cellular metabolic demands. Therefore, confirmatory measures are required to establish whether a particular clinical arterial pressure target is adequate. Confirmatory measures may require simple measures (e.g. central–peripheral temperature gradient), additional sophisticated measures, or both (e.g. lactate, mixed venous oxygen saturation).

Consensus statement 3: *Blood flow is often independent of changes in perfusion pressure as a consequence of autoregulatory changes in vascular resistance.*

Within a broad range of organ-specific perfusion pressures, autoregulatory mechanisms ensure that flow is preserved (Fig 2). Pharmacological (e.g. anaesthetic agents) and pathological (e.g. sepsis) perturbation of autoregulatory control renders organ blood flow pressure dependent.[38] These observations partly explain why perioperative complications are frequently observed in organs (kidney, heart, brain) that require highly autoregulated, yet individualised, control of arterial pressure. Extremes of arterial pressure (hypotension, hypertension) are associated with perioperative injury in these organs.[39]

Perioperative implications of consensus statement 3

An arterial blood pressure reading deemed 'normal' for any individual may lead to the erroneous conclusion that this accurately reflects normovolaemia, adequate cardiac output, or both. For example, progressive haemorrhage in surgical patients often fails to manifest as a decline in arterial pressure when compensatory mechanisms are intact. Moreover, in the presence of concomitant pain or exogenous catecholamine infusion, arterial pressure measurements may mask an injurious decline in organ perfusion.

Consensus statement 4: *Arterial blood pressure is the input pressure to organ blood flow, but is not the sole determinant of perfusion pressure.*

Total systemic vascular resistance has long been defined by electrical circuit theory, which assumes that a constant pressure decrease from input to output sites exists. However, laboratory and human studies demonstrate that two separate pressure gradients are likely to exist, enabled by the presence of Starling resistors residing within arteriolar or precapillary loci. The arterial gradient is generated from the central arterial circuit to the critical closing pressure, whereas a venous pressure gradient exists between mean systemic pressure and central venous pressure (Fig 3). The input pressure to an organ is determined by the difference between the central arterial pressure and organ-specific arterial critical closing pressure, the pressure threshold that coincides with cessation of blood flow at an inflow pressure higher than outflow venous pressure.[40] Perfusion pressure to an organ is determined by the input pressure minus the outflow pressure, which in turn is determined by the surrounding organ pressure (e.g. interstitial pressure) and right atrial pressure. Input pressure thresholds and outflow pressure vary significantly between organs, highlighting the importance of arterial and venous resistances which determine a 'vascular waterfall' that ensures organ perfusion even in low-flow conditions.[41] The presence of two separate, but in-series, vascular resistances ensures that a pressure gradient within an organ (i.e. critical closing pressure > mean systemic pressure) is maintained for a finite length of time even during profound hypotension (when MAP decreases to the critical closing pressure). These data suggest that common perioperative scenarios such as hypotension—characterised by a short-lasting dissociation between MAP and cardiac output—are unlikely to be rationally addressed by conventional clinical intervention(s) (Fig 3).

Perioperative implications of consensus statement 4

Raised local intra-abdominal organ pressure (e.g. insufflation during laparoscopy, intra-abdominal organ oedema) may

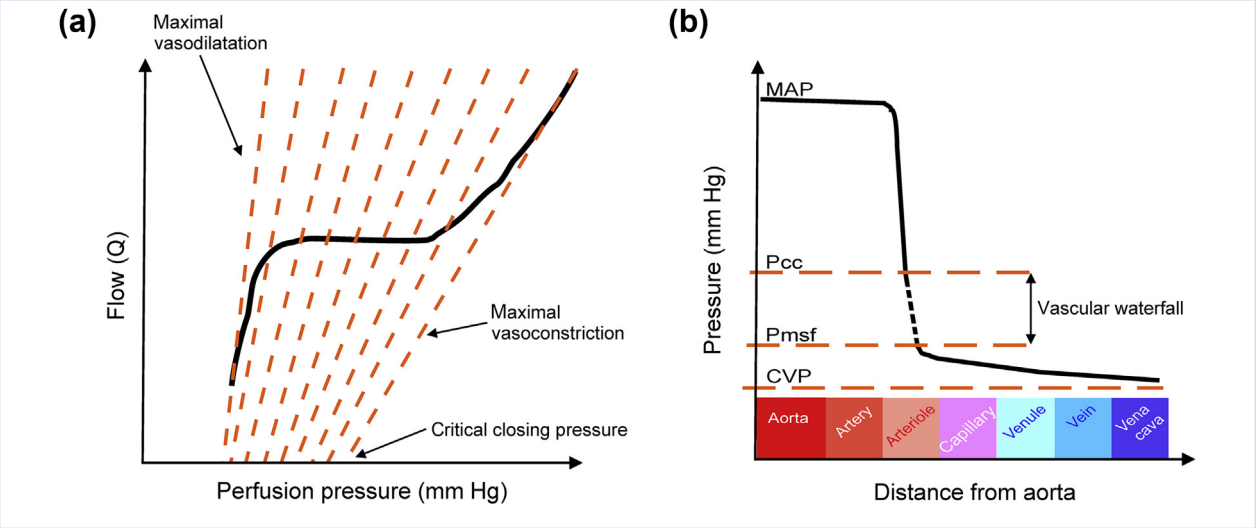

Figure 3. Arterial input pressure and flow. (a) Theoretical relationship between pressure and flow (black line) showing the autoregulation of vascular tone to sustain a constant blood flow despite varying arterial input pressures. The orange dashed lines illustrate how changes in vascular tone alter the relationship between instantaneous arterial input pressure and blood flow subject to autoregulation. The point at which arterioles spontaneously collapse (zero blood flow) limiting arterial pressure decrease is referred to as the critical closing pressure (Pcc), which also varies with changes in vasomotor tone. (b) Theoretical vascular pressure profile throughout the circulatory tree. MAP is constant for most of the arterial tree because larger arteries serve mainly as vascular capacitors holding stored blood under pressure. By contrast, vascular pressure decreases rapidly once blood reaches smaller arteries that branch into arterioles and precapillary sphincters. The vascular waterfall is approximated by the critical closing pressure (Pcc) mirroring how water flowing over a waterfall is unaffected by how far it falls once over the edge. Thus, the decline in pressure from arterioles to venules, or changes in downstream venous pressure, does not influence either arterial pressure or blood flow. Mean systemic filling pressure (Pmsf) represents the upstream pressure driving venous return against downstream central venous pressure (CVP). Figure reused with the permission of the Perioperative Quality Initiative (POQI).

result in inappropriate systemic arterial pressure targets aimed at maintaining regional organ perfusion.

Consensus statement 5: *Measurement of arterial blood pressure has inherent limitations because of inaccurate values, interpretation, or both.*

On physiological and sampling frequency grounds alone,[42] gold-standard measurement of arterial pressure necessitates an intra-arterial catheter,[43] taking into account several well-established factors including the site of catheter placement, waveform damping, and catheter dimensions. Manual mercury sphygmomanometry remains the gold standard to assess the accuracy of automated oscillometric devices, the most widely used technique in the perioperative setting to measure arterial blood pressure. Manually measured blood pressures often differ from those obtained using automated devices, and this adversely influences correct blood pressure classification. Although easy to use, two key inaccuracies are likely to contribute to the variability in measurement of cuff pressure.[44] First, fixed deflation rates (typically 2 mm Hg s^{-1}) set a limit of resolution that is dependent on incident heart rate. Second, measurement of the maximal rate of pressure increase during arterial pressure oscillation throughout the cardiac cycle is imprecise. The pressure level at which the rate of increase is maximal defines MAP; a proprietary algorithm uses this value to estimate systolic and diastolic blood pressure.[45] Absolute arterial pressure, differences in arterial pressure between left and right arms, variability between different devices/manufacturers, cuff size, posture, environment, and ambient temperature may all adversely affect accuracy.[45] Failing to take these limitations into account may lead to iatrogenic harm when single or intermittent measurements shape clinical decisions.

Perioperative implications of consensus statement 5

The site and mode of arterial blood pressure management yield different values. Accordingly, clinical management (including blood transfusion and vasopressor use) may differ depending on the method used, as suggested by observational database studies.[46]

Consensus statement 6: *Ambulatory arterial blood pressure measurement is the optimal method to establish baseline values.*

Guidelines from multiple international bodies recommend that adults with elevated arterial pressure in a clinical setting should undergo ambulatory measurements to exclude white coat hypertension before diagnosis.[47–50] Ambulatory blood pressure measurements are a stronger predictor of all-cause and cardiovascular mortality than one-off blood pressure measurements made in clinics. However, masked hypertension[51] is associated with higher mortality than overt hypertension.[52] Ambulatory blood pressure measurement also reduces the risk of misdiagnosing hypertension, which occurs in up to 18% of the general population when clinic or home-based measurements are made.[53] Inappropriate treatment of apparent white coat hypertension after a clinic-based measurement has been associated with adverse outcomes, chiefly through hypotension.[54,55] A further ~15–30% patients exhibit

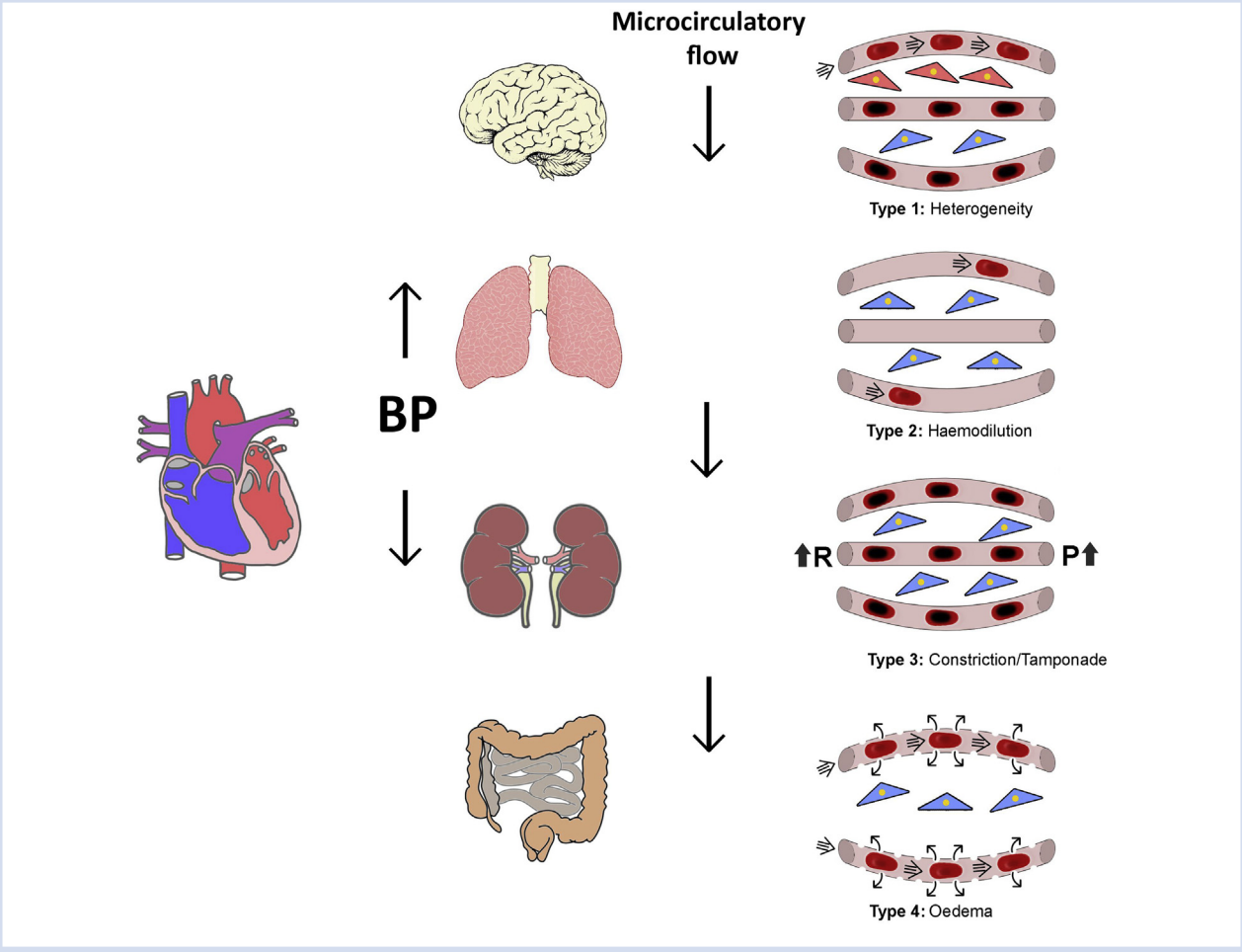

Figure 4. Microcirculation and arterial pressure. Microcirculatory conditions where control of arterial blood pressure under conditions of hypotension or hypertension impairing tissue perfusion are not effective in improving microcirculatory perfusion. Such conditions occur when there is a loss of haemodynamic coherence characterised by normalised systemic haemodynamic variables but persistent microcirculatory dysfunction leading to a lack of oxygen availability in tissue (as indicated by blue cells). Four distinct aetiologies of haemodynamic incoherence leading to microcirculatory shock include. Type 1: heterogeneous perfusion of the microcirculation as seen in septic patients with obstructed capillaries next to perfused capillaries resulting in heterogeneous oxygenation of tissue cells. Type 2: haemodilution of microcirculatory blood resulting in the loss of erythrocyte-filled capillaries and increasing diffusion distance between erythrocytes in capillaries and tissue cells. Type 3: stasis of microcirculatory erythrocyte flow induced by altered systemic variables (e.g. increased arterial vascular resistance (R) and or increased venous pressures caused by tamponade). Type 4: alterations involve oedema caused by capillary leak syndrome which results in increased diffusion distances from erythrocytes to tissues and reduced ability of the oxygen to reach tissue cells. Figure reused with the permission of the Perioperative Quality Initiative (POQI).

masked hypertension, where clinic measurements are normal but breach hypertension thresholds outside the clinical setting.[56] The Ambulatory Blood Pressure Collaboration in Patients With Hypertension meta-analysis found that both a blunted nocturnal decline (dipping) in arterial pressure and more extreme dipping in untreated hypertensives were associated with excess cardiovascular morbidity and mortality, independent of ambulatory blood pressure measurements averaged over 24 h.

Perioperative implications of consensus statement 6

Intraoperative arterial pressure management is frequently based on a very limited number of preoperative readings that are unlikely to be a true representation of an individual's long-term blood pressure control. The hypertension literature implies that a non-representative preoperative, one-off, clinic-based value is likely to be misleading in >30% of patients.

Consensus statement 7: *Arterial pressure targets may change over time for any individual patient.*

With advancing age, a U-shaped association develops between systolic arterial pressure and all-cause mortality.[57] These observational data challenge the findings of the Systolic Blood Pressure Intervention Trial (SPRINT), reinforcing the view that lower targets may require a more personalised approach.[58] Lower systolic pressure appears to be associated with mortality linked to non-cardiovascular causes,[57] which may reflect subclinical cardiac failure/deconditioning.[59,60] In the acute setting, the perioperative period is characterised by

heterogenous metabolic demands across disease states and different organs.[61] Fixed arterial pressure targets may lead to unintended adverse effects of interventions, as they are likely to be incompatible with maintaining a state of haemodynamic coherence, where macro- and micro-circulatory flow are matched.[35] Additionally, the arterial baroreflex plays an important role in long-term control of arterial pressure.[62] Impaired responses through loss of baroreflex sensitivity, a key autonomic regulatory mechanism, are associated with poorer perioperative outcomes[63] and linked mechanistically with organ injury.[64,65] The loss of haemodynamic coherence may occur in a highly heterogeneous, organ-specific pattern (Fig 4).

Perioperative implications of consensus statement 7

Dynamic perioperative alterations in arterial pressure regulation require repeated evaluation of clinical targets. Therefore, arterial pressure management requires repeated, contextualised assessment of systemic targets in conjunction with other clinical haemodynamic parameters (e.g. cardiac output monitoring) and markers of organ perfusion, including metabolites (e.g. lactate), enzyme function (hepatic transferases), and biomarkers for injury (e.g. troponin, B-type natriuretic peptide).

Recommendations for research

From the consensus points developed above, we recommend that further research relevant to the perioperative period should include:

1. Methods for non-invasive, continuous arterial pressure measurements.
2. Impact of perioperative arterial pressure therapies on autoregulatory, micro-circulatory, and autonomic control.
3. Methods to evaluate regional perfusion pressures to enable the assessment of individualised organ responses to alterations in arterial pressure control.
4. Identify sensitive, specific and continuous measures of cellular function that enable a more refined evaluation of arterial pressure management.

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. We acknowledge that by primarily focusing on perioperative issues, many complex areas of blood pressure (patho)physiology have been considered briefly. 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

Changes in the optimal management of perioperative arterial pressure are very likely given the shifting clinical landscape in diagnosis and management of chronic changes in arterial pressure. However, there is a current lack of evidence linking the latest international guidelines on chronic management of arterial pressure with targets for perioperative practice. Inevitably, this has major implications for perioperative medicine, and reinforces the need to refine our understanding and management of this complex physiological measure in the perioperative period.

Authors' contributions

Drafting of the first version of the manuscript: GLA, CSB, MC, CI, MGI, JL, MRP.
Review and editing of revised manuscript: GLA, CSB, MC, CI, MGI, JL, MRP, MPWG, MGM, MRE, TEM.
Participation in the conference: GLA, CSB, MC, CI, MGI, JL, MRP, MPWG, MGM, MRE, TEM.
Submission of the manuscript: MPWG, MGM, MRE, TEM.
Chair of the physiology group: GLA.
Member of the physiology group: CSB, MC, CI, MGI, JL, MRP.
POQI conference organiser: MPWG, MGM, MRE, TEM.

Declarations of interest

GLA: Editor, *British Journal of Anaesthesia*. Research supported by the British Oxygen Company Research Chair grant, British Heart Foundation Programme grant (RG/14/4/30736), Royal College of Anaesthetists/British Journal of Anaesthesia Basic Science Career Development Award. Consultancy work undertaken for GlaxoSmithKline, unrelated to this work. Editorial advisory board, *Intensive Care Medicine Experimental*. CSB: speaker and member of advisory boards for Grifols, Hospira/Pfizer, and Orion. MC: has received honoraria for speaking at symposia, financial support for educational programs and honoraria for advisory board from Edwards Lifesciences, LiDCO, Deltex, Massimo, Bmeye, Cheetah and Imacor. CI: runs an Internet site microcirculationacademy.org that offers services (e.g. training, courses, analysis) related to clinical microcirculation. MGI: Editor of *Anaesthesia*. JL: no declarations. MRP: Research supported by US National Science Foundation and National Institutes of Health. MPWG: National Specialty Lead for Anaesthesia, Perioperative Medicine and Pain within the UK National Institute of Heath Research Clinical Research Network, an elected council member of the Royal College of Anaesthetists and president of the Critical Care Medicine section of the Royal Society of Medicine. MPWG serves on the board of ERAS UK, Oxygen Control Systems Ltd, the Evidence Based Perioperative Medicine (EBPOM) social enterprise and the medical advisory board of Sphere Medical Ltd and the international advisory board of the American Society of Enhanced Recovery (ASER). MPWG has received honoraria for speaking and/or travel expenses from Edwards Lifesciences, Fresenius-Kabi, BOC Medical (Linde Group), Eli Lilly Critical Care, and Cortex GmBH. MPWG is executive chair of the Xtreme-Everest Oxygen Research Consortium. MGM: University Chair Sponsored by Smiths; director, UCL Discovery Lab; co-director, Duke-UCL Morpheus Consortium; consultant for Edwards Lifesciences; director, Bloomsbury Innovation Group (BiG); shareholder and scientific advisor, Medical Defense Technologies LLC; shareholder and director, Clinical Hydration Solutions Ltd (Patent holder 'QUENCH'); editorial board, BJA; editorial board Critical Care; founding editor-in-chief of Perioperative Medicine; chair, Advisory Board American Society of Enhanced Recovery. MRE: has received an honorarium for lecturing for Edwards Lifesciences. He is deputy Chief Investigator for the OPTIMISE II trial, which is part-

funded by Edwards Lifesciences, although he does not receive financial support in this role. TEM: research funding and consultant for Edwards Lifesciences and consultant for Mallinckrodt.

Funding

The POQI-3 consensus conference was supported by an unrestricted educational grant from Edwards Lifesciences.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2019.01.011.

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Handling editor: H.C. Hemmings Jr

BJA

British Journal of Anaesthesia, 122 (5): 552–562 (2019)

doi: 10.1016/j.bja.2019.01.018
Advance Access Publication Date: 2 March 2019
Special Article

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

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This article is accompanied by an editorial: Consensus Statements and Expert Guidance: Interpret with Care by S.J. Howell, *Br J Anaesth* 2019:122, doi: https://doi.org/10.1016/j.bja.2019.03.013.

Abstract

Background: A multidisciplinary international working subgroup of the third Perioperative Quality Initiative consensus meeting appraised the evidence on the influence of preoperative arterial blood pressure and community cardiovascular medications on perioperative risk.

Methods: A modified Delphi technique was used, evaluating papers published in MEDLINE on associations between preoperative numerical arterial pressure values or cardiovascular medications and perioperative outcomes. The strength of the recommendations was graded by National Institute for Health and Care Excellence guidelines.

Editorial decision date: 1 January 2019; **Accepted:** 1 January 2019

Results: Significant heterogeneity in study design, including arterial pressure measures and perioperative outcomes, hampered the comparison of studies. Nonetheless, consensus recommendations were that (i) preoperative arterial pressure measures may be used to define targets for perioperative management; (ii) elective surgery should not be cancelled based solely upon a preoperative arterial pressure value; (iii) there is insufficient evidence to support lowering arterial pressure in the immediate preoperative period to minimise perioperative risk; and (iv) there is insufficient evidence that any one measure of arterial pressure (systolic, diastolic, mean, or pulse) is better than any other for risk prediction of adverse perioperative events.
Conclusions: Future research should define which preoperative arterial pressure values best correlate with adverse outcomes, and whether modifying arterial pressure in the preoperative setting will change the perioperative morbidity or mortality. Additional research should define optimum strategies for continuation or discontinuation of preoperative cardiovascular medications.

Keywords: arterial pressure; haemodynamics; perioperative care; preoperative blood pressure; surgical risk

Editor's key points

- Numerous studies have suggested that preoperative hypertension is associated with increased perioperative risk.
- An expert consensus meeting reviewed the relationships between preoperative arterial pressure, cardiovascular medications, and postoperative outcomes using a modified Delphi approach to create recommendations.
- There are insufficient data to suggest that monitoring of preoperative arterial pressure should alter decisions to proceed with surgery or not.
- Further studies are required to define optimal perioperative management of chronic cardiovascular medications.

Preoperative risk stratification involves synthesis of patient, anaesthetic, and operative factors to determine the optimal approach to patient care. Of patient factors, vital signs provide relevant physiological information and, appropriately, are widely monitored. However, the value of individual measurements is unclear. In this consensus paper, we consider the importance of preoperative arterial pressure values for risk stratification and planning perioperative management. Numerous studies have suggested that preoperative hypertension is associated with increased perioperative risk, although other reports suggest that this is not always the case. Reflecting this, different risk stratification tools either use (e.g. National Surgical Quality Improvement Program) or do not use (e.g. Revised Cardiac Risk Index) preoperative arterial pressure as a risk measure. In this context, 'risk' relates to different postoperative outcomes: a specific morbidity, a group of morbidities, or mortality. It may be that this variation in outcomes studied in part explains the predictive utility of arterial pressure measures. This complexity is compounded by the variability of the measure itself, both in terms of measurement error of the value and in terms of fluctuation in the measured values of resting arterial pressure. Despite these limitations, we consider it valuable to understand the relationships between preoperative arterial pressure and postoperative mortality and morbidity; in particular, whether these relationships are linear or non-linear (with potential for risk escalation at specific values) requires clarification.

The predictive value of arterial pressure may also be modulated by antihypertensive medications and the patient co-morbidities that may result from arterial pressure changes. Hence, consideration of the differential impact of cardiovascular medications and the interaction with co-morbidities on perioperative risk is also warranted. For example, if certain arterial pressures are associated with increased risk, it would be useful to know if treating arterial pressure before an operation improved perioperative risk, how long (if at all) treatment should occur, and whether surgery should be deferred or non-surgical options explored. Similarly, it would be useful to know if specific medications would be preferred in this context, and whether discontinuing certain medications may be helpful to reduce perioperative risk. Discontinuation of medications may also have consequences on arterial pressure important for consideration of perioperative risk. These issues are clearly complex, and hence, we sought to reach consensus on core statements, and practice and research recommendations, relating to preoperative blood pressure and the associations with risk and outcomes from elective surgery.

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.[1–5] The participants in the POQI consensus meeting were recruited based on their expertise in perioperative medicine and blood pressure management (Supplementary Appendix S1). Conference participants were divided into four work groups. Group 1 reviewed the physiology and measurement of blood pressure with relevance to the perioperative setting.[1] Groups 2–4 were focused on pre- (this paper), intra-,[2] and postoperative[3] arterial pressure, respectively; see Ackland and colleagues[1] for detailed methods. The groups indicated the strength of evidence underlying practice recommendations using a structure consistent with the UK National Institute for Health and Care Excellence guidance (Supplementary Appendix S2).

This workgroup of the POQI-3 consensus meeting reviewed the importance of preoperative arterial pressure thresholds in determining perioperative risk, and related to this primary aim, considered the potential effects of concomitant cardiovascular medications. We did not seek to evaluate whether diagnoses of hypertension *per se* were associated with

perioperative risk, but rather to evaluate the data based on numerical pressure values and their association with risk.

We focused *a priori* on the following questions: (i) what is the risk associated with different preoperative arterial pressure values?; (ii) what is the importance of community cardiovascular medications in influencing perioperative risk? If there are risks, are these arterial pressure dependent?; (iii) what is the evidence guiding whether surgery should be deferred in patients with specific arterial pressure values and, if surgery is deferred, how should risk be optimised?; and (iv) is there evidence to support the use of preoperative arterial pressure to inform perioperative management, including intraoperative arterial pressure?

Before the meeting, a literature search was conducted in PubMed from 1966 to June 2017 using the following terms: preoperative AND hypotension AND elective AND surgery AND mortality OR preoperative AND hypertension AND elective AND surgery AND mortality OR preoperative AND blood pressure AND threshold AND surgical AND mortality OR preoperative blood pressure AND elective AND surgery AND mortality OR preoperative blood pressure AND elective AND surgery AND myocardial infarction OR preoperative blood pressure AND elective AND surgery AND stroke OR preoperative blood pressure AND elective AND surgery AND renal failure. All were with the added filters: *Humans *Ages 19+. This literature search was supplemented by reading the relevant references of the papers identified. After our meeting in July 2017, the American College of Cardiology (ACC) and the American Heart Association (AHA) released updated hypertension guidelines that included perioperative recommendations.[6] Therefore, we sought to compare our recommendations with those of that body and with those from the Association of Anaesthetists of Great Britain and Ireland/British Hypertension Society (AAGBI/BHS) guidelines that were in existence at the time of the meeting.

Results

Consensus statements

Consensus statement 1: *Preoperative arterial pressure values may be used to define targets for perioperative management; however, these should ideally reflect the patient's usual preoperative blood pressure.*

Recent studies have evaluated the use of target arterial pressure thresholds based on preoperative values, and suggest that this approach may improve outcomes.[7–9] Results from a recent randomised controlled trial suggested that patients who were randomised to tight systolic arterial pressure control, aiming for maintenance within 10% of baseline, may be at reduced risk of brain dysfunction and infection.[7] Observational data support tight control of intraoperative arterial pressure based on preoperative risk thresholds (within 20%[8] or 50%[9] of mean arterial pressure), but it remains unclear whether this is superior to a specific mean arterial pressure threshold.[2] Nonetheless, it appears that, in many centres, setting intraoperative arterial pressure targets based upon preoperative arterial pressure is routine.

We propose that, when available, ambulatory (as opposed to single office or clinic reading) arterial pressure[10] should be used to establish the relevant preoperative arterial pressure to avoid white coat hypertension and inaccurate readings.[1] Acting on isolated clinic arterial pressure readings brings a substantial risk of either overdiagnosing hypertension, or missing—and undertreating—true hypertension.[11] Both scenarios are associated with adverse outcomes,[12] and multiple hypertension guidelines now recommend ambulatory arterial pressure readings before a diagnosis of hypertension is made.[13] An ambulatory value will typically be a daytime average of readings from an automated device measuring arterial pressure at repeated intervals through the day and night whilst the patient continues routine activities. In the absence of a recent ambulatory arterial pressure measurement, we propose that a clinic (or office) baseline measure should be obtained (ideally within 30 days) before the day of surgery to limit the effects of white coat hypertension.[14] These preoperative measures may be used for setting intraoperative arterial pressure targets. However, we acknowledge that the optimal preoperative measure is unclear, and we recommend further research to identify this metric (see research recommendations).

Consensus statement 2: *Although extremes of preoperative blood pressure may be associated with increased perioperative risk, there is insufficient evidence to recommend a specific threshold of blood pressure upon which to decide whether or not to proceed with surgery, unless the extreme arterial pressure is associated with a medical emergency.*

Data suggest that both preoperative hypo- and hypertension are associated with increased risk, although study findings on this are not consistent.[15–18] We emphasise that the following description is based on observational data, and therefore, causality is not established between the exposure (arterial pressure value) and clinical outcome. First, we consider mortality. In patients more than 65 yr of age undergoing non-cardiac surgery, Venkatesan and colleagues[15] found evidence that low preoperative arterial pressure is more strongly associated with increased postoperative risk of mortality than high pressure using primary care data. In this large study (n=251 567), increased mortality risk was identified in patients with a preoperative systolic arterial pressure <119 mm Hg, diastolic <63 mm Hg, and pulse pressure <37 mm Hg. The change in odds ratio was non-linear, demonstrating escalating risk as arterial pressure decreased. The apparent effect of low preoperative pulse pressure is consistent with a recent analysis of the prospective Vascular Events in Noncardiac Surgery Cohort Evaluation (VISION) cohort in non-cardiac surgery patients that suggested that low pulse pressure (<45 mm Hg) may be associated with increased mortality.[18] The influence of preoperative hypertension appears less clear. After risk adjustment for age and a range of co-morbidities, Venkatesan and colleagues[15] identified that high preoperative diastolic pressure was associated with increasing mortality risk. This indicates a J-shaped association between diastolic arterial pressure and mortality risk, with increasing risk at both extreme low and high values. The lack of relationship found between systolic hypertension and mortality may be explained by a number of factors. These include the presence of unmeasured confounders in observational studies, or the possibility that the secondary effects of systolic hypertension, which were included in the multivariable model, have a greater effect on perioperative risk. These and other data suggest that raised diastolic or pulse pressure may be more important than systolic hypertension in the non-cardiac perioperative period, although these findings should be confirmed in future studies.[19,20]

In contrast, in cardiac surgery, there are data to suggest that systolic hypertension and a high pulse pressure are associated with increased mortality.[21,22] It is possible that

methodological differences in risk adjustment and uncontrolled confounding contribute to this apparent inconsistency between cardiac and non-cardiac populations. Another explanation is that these patient cohorts have different levels of risk and undergo different types of injury. However, in these studies, no clear numerical risk threshold was identified limiting the clinical impact of the work.

Accumulating data from both cardiac and non-cardiac surgical studies suggest that preoperative high arterial pressure values are associated with increased cerebral, cardiac, and renal morbidities.[18,22–29] In seminal studies, Howell and colleagues[30,31] demonstrated relationships between systolic hypertension and postoperative cardiovascular morbidity, suggesting a linear relationship between preoperative systolic blood pressure and risk of ischaemic events after non-cardiac surgery.[26] Similar studies have been completed in cardiac surgery; for example, Wolman and colleagues[29] reported that systolic hypertension (>145 mm Hg) was a risk factor for a diverse group of postoperative cerebral adverse events. Fontes and colleagues[22] found that raised preoperative pulse pressure was associated with all-cause mortality and cerebral and cardiac events after cardiac surgery. Abbott and colleagues[18] found that raised preoperative pulse pressure was associated with increased risk of myocardial injury after non-cardiac surgery, even when systolic pressure was controlled for. However, they also found that intermediate pulse pressure (46–53 mm Hg) was associated with reduced risk of myocardial injury. This latter finding was also echoed by Venkatesan and colleagues,[15] who showed that pulse pressures from 42 to 58 mm Hg were associated with lower postoperative mortality. Ackland and colleagues[32] also found that a *low* preoperative pulse pressure was associated with increased postoperative morbidity, assessed by the PostOperative Morbidity Survey, in patients with low cardiopulmonary reserve undergoing non-cardiac surgery, consistent with the mortality findings.[15,18] It is plausible that the association of low pulse pressure with adverse outcomes involves heart failure events or pathophysiology, and high pulse pressure is associated with acute vascular events or pathophysiology. This requires further study.

No study has identified clear thresholds of arterial pressure (for hypotension or hypertension) beyond which risk rapidly escalates. Rather, whilst the (unadjusted) relationships between risk and blood pressure may be J shaped (Fig. 1), and thus, non-linear, there is no consensus on the threshold at which patients would be deemed at an increased risk, and hence, their surgery should be deferred. The ACC/AHA and AAGBI/BHS guidelines suggest that elective surgery in patients with arterial pressure >180/110 mm Hg may be deferred; however, this appears to be driven largely by expert opinion (Table 1). We were unable to identify consistent evidence that patients who underwent operations with preoperative arterial pressure above these values experienced increased harm. However, it is important to note that the data evaluated largely came from a period that was likely influenced by the expert opinion recommending deferral of surgery,[33] potentially resulting in a lack of operations in patients with very high preoperative arterial pressure and a resultant lack of evidence. In 1971, Prys-Roberts and colleagues[28] showed that patients with untreated hypertension, with mean arterial pressures of ~130 mm Hg, were associated with intraoperative hypotension, and five of seven of these patients sustained myocardial ischaemia associated with mean arterial pressure changes greater than 50% from baseline. This not only suggests that extremely high arterial pressure may be a perioperative risk factor, but also that the harm may be mediated by intraoperative pressure changes. Whether pre- or intraoperative treatment may modify this putative relationship remains unclear.

Consensus statement 3: *There is insufficient evidence to support lowering blood pressure in the immediate preoperative period to reduce perioperative risk.*

The only randomised trial of acute preoperative lowering of arterial pressure identified no difference in postoperative complications after non-cardiac surgery in patients at low cardiovascular risk with raised preoperative diastolic pressure (>110 mm Hg).[34] However, it is unclear whether a sufficient decrease in arterial pressure was achieved, or for long enough, to induce a change in outcome. A small subgroup analysis of another study found similar event rates for postoperative myocardial injury and death in hypertensive patients deferred for surgery compared with those not deferred.[35] Importantly, a reduction in arterial pressure was not achieved by deferring surgery. Consequently, there is currently no evidence that deferring patients for better arterial pressure control changes their risk unless they are manifesting acute pathological symptoms (defined as new onset end-organ damage) requiring urgent medical therapy (see ACC/AHA guidelines[6]). We acknowledge that, for specific surgeries, for example, neurosurgery or endocrine surgery, specific pressure parameters may be recommended; however, this was considered beyond the scope of these general guidelines.

Consensus statement 4: *There is insufficient evidence that any one measure of blood pressure (systolic pressure, diastolic pressure, MAP, or pulse pressure) is better than any other for risk prediction of adverse perioperative events.*

There are limited data comparing the utility of different preoperative arterial pressure measures for predicting perioperative risk.[15,18,22] Fontes and colleagues[22] found that raised preoperative pulse pressure was associated with all-cause mortality and cerebral and cardiac events after cardiac surgery. A comprehensive comparison with similar metrics from systolic and diastolic pressures was not conducted, making inference about the relative importance of all variables difficult. In particular, systolic and diastolic pressures were analysed as continuous variables, and pulse pressure was analysed in 10 mm Hg increments. Methodological differences, such as these, make direct comparison of the variables problematic. Nonetheless, Fontes and colleagues[22] did attempt to control for systolic and diastolic changes in their analyses, suggesting that pulse pressure may be predictive, independent of these other pressure metrics. Abbott and colleagues[18] also showed that the association of pulse pressure with myocardial injury was independent of systolic pressure in non-cardiac surgery. Venkatesan and colleagues[15] analysed all three variables as continuous data and found similar findings with each measure: low systolic, diastolic, and pulse pressures were each associated with increased postoperative mortality. In sum, these data show that arterial pressure can provide important prognostic information; however, the relative value of each measure has been inadequately explored. A thorough analysis of several data sets should be undertaken to rigorously compare the different metrics. Of course, interpretation of any arterial pressure value is dependent on the clinical context. It is also likely that the data sets investigated do not capture all of the relevant variables. Referral to the POQI-3 physiology report[1] is recommended for discussion of clinical context.

The consensus statements are summarised in Figure 2.

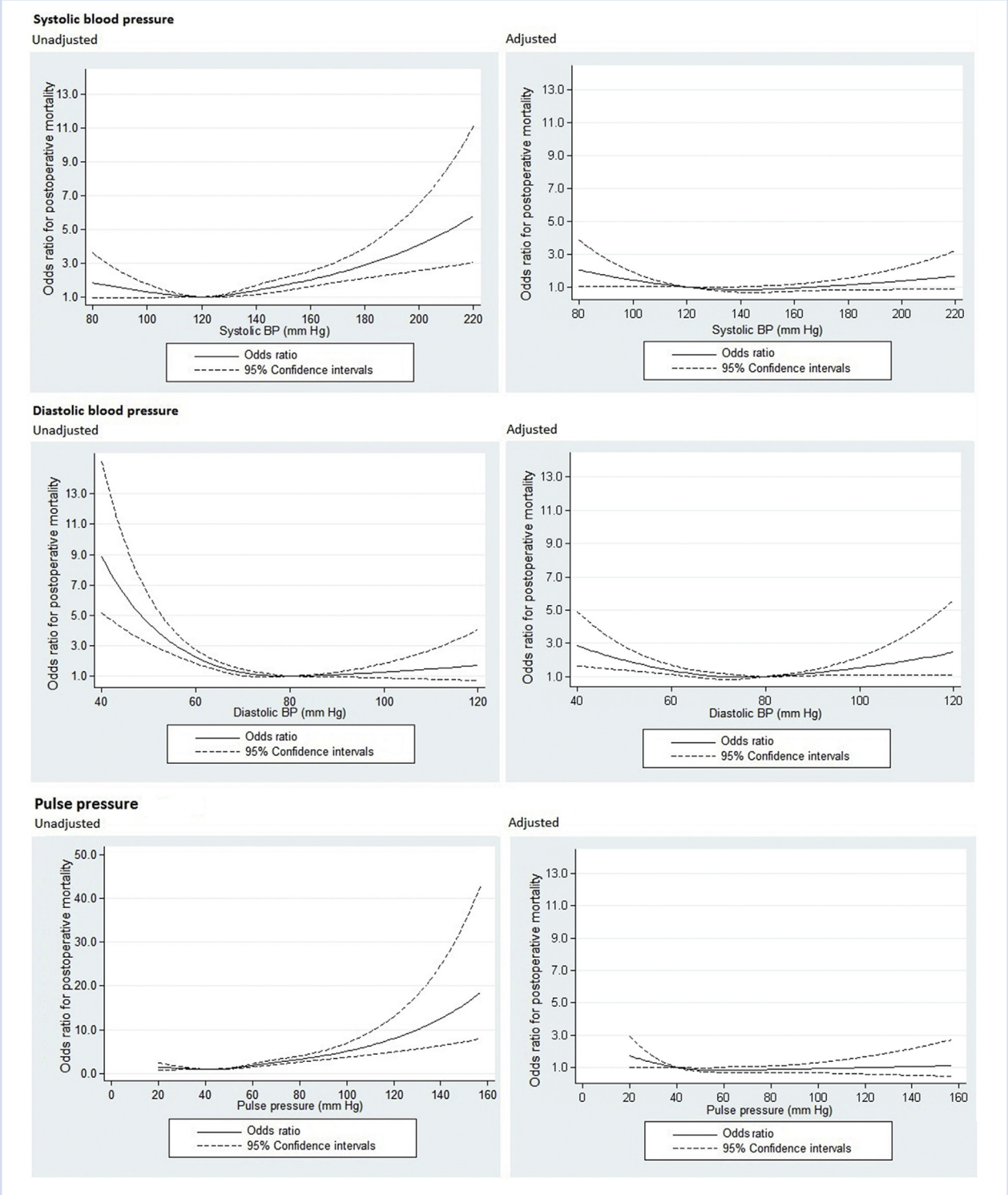

Fig 1. Examples of the association of preoperative arterial pressure and postoperative mortality. The unadjusted data on the left demonstrate the J-curve phenomenon for the association between preoperative systolic, diastolic, and pulse pressures, and postoperative mortality. On the right, the fully adjusted spline curves do not demonstrate the J-curve phenomenon clearly. Fully adjusted model adjusted for age; gender; atrial fibrillation; unstable angina; valvular heart disease; myocardial infarction; congestive heart failure; peripheral vascular disease; cerebrovascular disease; chronic obstructive pulmonary disease; liver disease; diabetes mellitus; renal disease; cancer; Charlson's comorbidity score; smoking; alcohol; surgical risk scale; socioeconomic status (Index of Multiple Deprivation 2010); number of arterial pressure measurements; and use of statins, beta blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors, alpha-2 agonists, loop diuretics, thiazide diuretics, aspirin, other antiplatelet drugs, and selective serotonin reuptake inhibitors. Reproduced from Venkatesan and colleagues[17] with permission.

Table 1 Contrast between two recent guidelines concerning preoperative blood pressure. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker

High blood pressure clinical practice guideline (Whelton and colleagues[6])			Perioperative quality Initiative[xx]	Discussion on discordance
COR	LOE	Statements	Statements	
I	B-NR	In patients with hypertension undergoing major surgery who have been on beta blockers chronically, beta blockers should be continued.	For patients on chronic beta blockade for high-risk indications (such as congestive heart failure or recent myocardial infarction within the last 2 yr), beta blockers should be continued.	Recent evidence suggests that beta blockers exert protective effects in patients with high-risk indications, but not for those patients solely taking beta blockers for hypertension. It remains unclear whether beta-blocker drug withdrawal is safe in patients with low-risk indications or not.
IIa	C-EO	In patients with hypertension undergoing planned elective major surgery, it is reasonable to continue medical therapy for hypertension until surgery.	Currently, there is limited evidence to withhold thiazide diuretics or calcium channel blockers in the preoperative period. Continuation or stopping of loop diuretics should be considered on a per-patient basis.	
IIb	B-NR	In patients with hypertension undergoing major surgery, discontinuation of ACEIs or ARBs perioperatively may be considered.	Unless clinically contraindicated, withhold ACEIs/ARBs 24 h before surgery with attention to restarting the medications within 48 h after operation where appropriate.	
IIb	C-LD	In patients with planned elective major surgery and SBP of 180 mm Hg or higher, or DBP of 110 mm Hg or higher, deferring surgery may be considered.	Unless associated with a medical emergency, there is insufficient evidence to recommend a specific threshold of blood pressure upon which to decide whether or not to proceed with surgery.	The limited data available do not suggest that deferring surgery for blood pressure control is effective or reduces risk. Unless there is a medical emergency, surgery need not be deferred based solely on the blood pressure value.
III: Harm	B-NR	For patients undergoing surgery, abrupt preoperative discontinuation of beta blockers or clonidine is potentially harmful.	For patients on chronic beta blockade for high-risk indications (such as congestive heart failure or recent myocardial infarction within the last 2 yr), beta blockers should be continued.	See above. Recent data have suggested there may be less morbidity with beta blocker withdrawal, but continue to show increased mortality. This discordance requires further investigation.
III: Harm	B-NR	Beta blockers should not be started on the day of surgery in beta-blocker-naïve patients.	Beta blockers should not be initiated in the preoperative period solely to reduce perioperative risk.	

COR, class of recommendation; LOE, level of evidence; B-NR, moderate quality of evidence from non-randomized studies; C-LD, evidence from randomized or non-randomized studies with limitations in design or execution.

Recommendations for practice

Based on the original questions, the consensus group discussed practice recommendations.

Practice recommendation 1: *Unless clinically contraindicated, withhold angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ACEIs/ARBs) 24 h before surgery with attention to restarting the medications within 48 h after operation where appropriate.*

A recent analysis of the VISION study of non-cardiac surgery suggested that withholding ACEIs/ARBs before surgery may reduce the risk of mortality, stroke, and myocardial injury,[36] supporting prior concerns that these drugs may be associated with intraoperative haemodynamic instability.[37] It is likely that these drugs should be restarted after operation as soon as is reasonable, as delayed or omitted reinstitution of ACEIs/ARBs has been associated with increased postoperative mortality.[38] We believe that a prospective randomised controlled trial is needed to confirm whether ACEI/ARB withdrawal improves outcomes, including attention to when the medications are restarted. However, based on the present

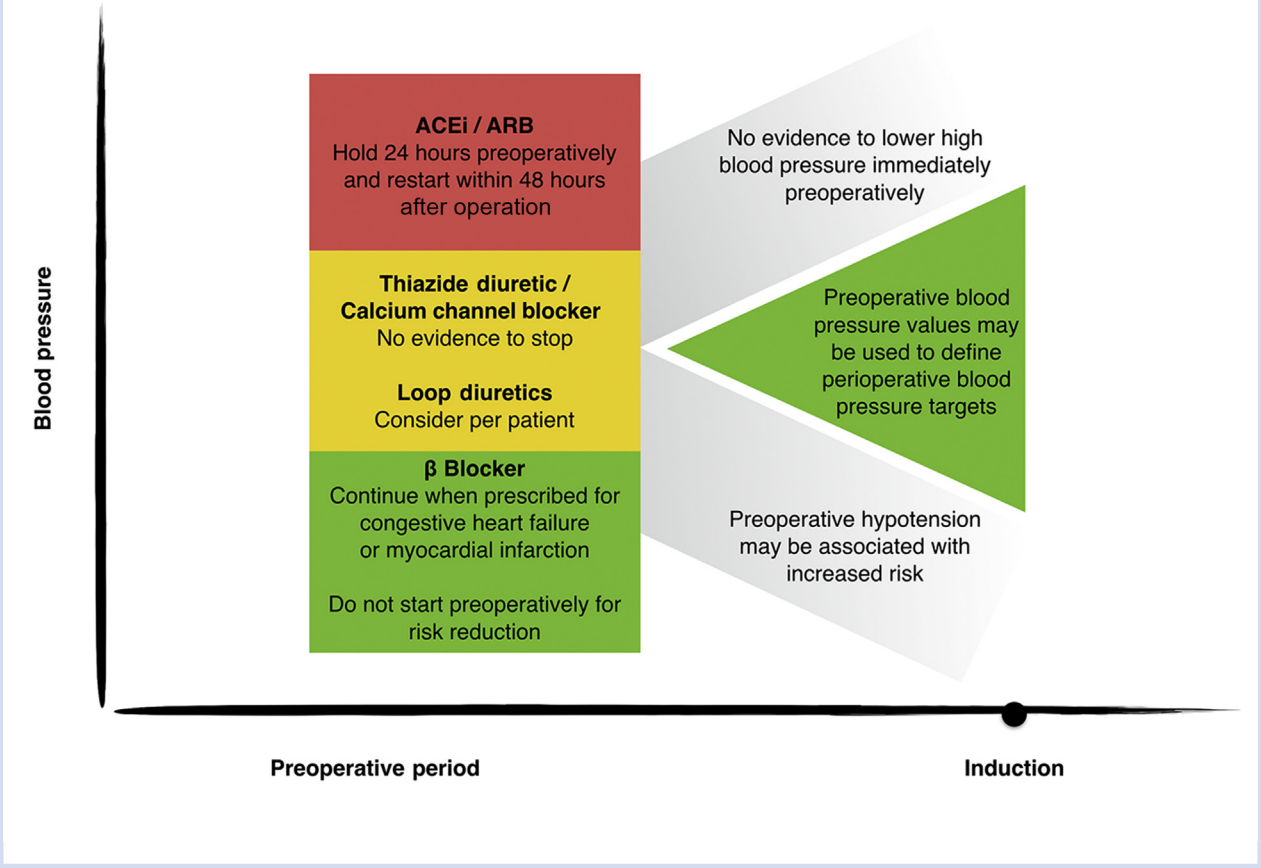

Fig 2. Infographic demonstrating the consensus recommendations. Figure reused with the permission of the Perioperative Quality Initiative (POQI). For permission requests, contact info@poqi.org.

data, our consensus was that withholding ACEIs/ARBs before surgery is reasonable, consistent with prior guidance.[6]

The data for cardiac surgery are less clear; whilst similar concerns over haemodynamic instability have been noted,[37] discontinuation of ACEIs/ARBs before surgery was associated with increased mortality.[39] Whether this represents failure to reinstitute therapy is unclear.

Practice recommendation 2: *Beta blockers should not be initiated in the preoperative period solely to reduce perioperative risk.*

Beta blockers have been associated with increased risk in the perioperative period, particularly increasing the risk of stroke and mortality when initiated just for surgery.[40–42] In line with present guidelines,[6,43] we conclude that there is limited evidence that *de novo* initiation in the perioperative period is warranted.

Practice recommendation 3: *For patients on chronic beta blockade for high-risk indications (such as congestive heart failure or recent myocardial infarction within the past 2 yr), beta blockers should be continued.*

Observational data suggest that beta blockers should not be withdrawn from these 'higher-risk' patients in the perioperative period.[44,45] Beta blockers may exert protective effects in those with congestive heart failure or recent myocardial infarction in particular,[46] but have been associated with increased harm in lower-risk individuals,[44,47] such as those on beta blockers for hypertension control[47] or ASA physical status 1–2.[44] This is in concordance with the present guidelines.[6,43]

Practice recommendation 4: Currently, there is limited evidence supporting withholding thiazide diuretics or calcium channel blockers in the preoperative period; continuation or stopping of loop diuretics should be considered on a per-patient basis.

There have been few studies of the effects of diuretics and calcium channel blockers on perioperative outcomes. For diuretics, thiazides have not been associated with harm,[47] and data from small randomised controlled trials suggest that calcium channel blockers may be associated with improved outcomes.[48,49] There are limited data to suggest these drugs are harmful in the perioperative period. Continuation or stopping of loop diuretics should be considered on a per-patient basis; definitive data that these drugs are harmful are lacking.[50]

Recommendations for research

Folllowing the consensus statements and practice recommendations, the group sought to identify important remaining research recommendations.

Research recommendation 1: *What is the best time and setting in which to measure blood pressure in the preoperative period? Studies addressing environment, technique, equipment, and reproducibility are required. The blood pressure measure that best predicts*

perioperative risk is unknown, and this question may be addressed via large-scale pragmatic observational and interventional trials.

Intraoperative relative reductions in arterial pressure of >20% of baseline are associated with increased risk of perioperative myocardial ischaemia, acute kidney injury, and stroke.[7,9] The definition of this baseline has not been formalised, and no single metric is consistently used (systolic, diastolic, mean, or pulse pressure). White coat hypertension in both the primary care setting and on the morning of surgery may yield falsely high baseline pressure measurements. The clinical significance of this is unknown, particularly when these measurements are used to set intraoperative arterial pressure targets.[14] Measurements taken in the primary care setting from 1 to 52 weeks before surgery have been found to be predictive of postoperative risk, with increased risk in patients with preoperative arterial pressure <119/63 mm Hg in one study.[15] However, it is unclear whether this is the best available measure. Whilst ambulatory monitoring may provide the best index for establishing baseline arterial pressure, it is unlikely this is feasible in every patient before operation. Prospective studies are required to investigate which method, and time point, of blood pressure measurement is both predictive of adverse perioperative outcomes and feasible.

Research recommendation 2: *Whether or not correction of preoperative hypo- or hypertension improves outcomes is unknown, and requires answering given the numbers of patients who have surgery deferred based on preoperative arterial pressure readings.*[43]

Outside the settings of shock or hypertensive emergency, the value and feasibility of preoperative arterial pressure optimisation are unknown. It is unclear whether deferring surgery for better control of arterial pressure leads to lower arterial pressure on the day of the rescheduled surgery. It is also unclear how long surgery should be deferred in order to reduce perioperative risk, if it does at all.

Research recommendation 3: *The effect of preoperative discontinuation of ACEIs and the relative effects of ACEIs vs ARBs need clarifying, with emphasis on time of withdrawal and reinstitution of therapy.*

Withholding ACEIs/ARBs 24 h before non-cardiac surgery was associated with reduced risk of all-cause mortality, myocardial injury, and stroke in an observational study[36]; however, this is yet to be shown in a randomised controlled trial. In cardiac surgery, the benefits of withholding ACEIs/ARBs are less clear.[39] Randomised controlled trials are required to assess the benefit of ACEI/ARB continuation or withdrawal, and the timing of withdrawal and reinstitution of therapy (e.g. ISRCTN17251494).

Research recommendation 4: *The role of beta blockers and alpha-2 agonists in the perioperative setting remains uncertain; further data are required on the perioperative withdrawal of beta blockers in low-risk patients.*

Observational data suggest that beta blockers may be harmful in low-risk patients.[44,47] However, epidemiological data often lack accurate recording of drug withdrawal and physiological data, and are insufficient to estimate whether beta blocker withdrawal may benefit some patients. A recent observational study found that beta blocker withdrawal was associated with increased mortality, but paradoxically shorter PACU stays and less vasopressor support.[51] The discordance in these findings needs to be resolved, especially as the reported mortality rates were very low in both groups. Despite the limitations of observational data, including selection bias for one group or another, before conducting a randomised controlled trial, we recommend a prospective cohort study to evaluate the potential benefit/harm of beta blocker withdrawal in patients at a low risk of cardiac mortality or morbidity.

Less commonly used antihypertensives have similarly not been studied on a suitable scale to fully define perioperative management. However, it should be noted that acute cessation of chronic alpha-2 agonists (e.g. clonidine) may cause acute rebound hypertension.[52] There are inadequate data to comment on the perioperative cessation/continuation of alpha-blockers (e.g. doxazosin).

Research recommendation 5: *Investigation of the potential benefit of loop diuretic withdrawal is required in the perioperative setting.*

Diuretics are often withheld on the day of surgery based on the rationale that their use is associated with a risk of intraoperative hypotension. The withdrawal of loop diuretics, in a relatively small randomised controlled trial of non-cardiac surgical patients, led to no reduction in the incidence of intraoperative hypotension and cardiac morbidity.[50] This study did show a small trend to increased harm from loop diuretic continuation that warrants evaluation in a large randomised controlled trial.

Research recommendation 6: *Evaluation of perioperative diltiazem use in a large randomised controlled trial.*

The use of non-dihydropyridine calcium channel blockers may reduce the risk of perioperative myocardial ischaemia and arrhythmias.[48,49] A meta-analysis of several small studies shows a reduction in myocardial ischaemia when diltiazem is administered perioperatively.[48,49] An adequately powered, well-designed randomised controlled trial investigating the effect of diltiazem on perioperative myocardial ischaemia and mortality should be undertaken.

Strengths and limitations

POQI uses an established modified Delphi process, which has been used in more than 25 Acute Dialysis Quality Initiative[53,54] and POQI conferences in the last 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. Although a formal strength of evidence scoring system was not used, the wording of statements and practice recommendations as defined here gives an indication of the group's opinion on the strength of evidence underlying those statements. Areas of uncertainty have been clearly signposted in the discussions accompanying each statement.

Conclusions

Despite widespread monitoring of preoperative arterial pressure, there are insufficient data to suggest that this should alter decisions to proceed with surgery or not. However, the use of preoperative arterial pressure to guide intraoperative management appears promising. Further observational studies and randomised controlled trials are required to define optimal perioperative management of chronic cardiovascular medications. Our consensus statements broadly agree with recent hypertension guidelines; however, there is some discordance, as summarised in Table 1. Ultimately, this topic requires investment in novel research approaches to resolve ambiguities in the evidence.

Authors' contributions

Writing first draft: RDS.
Infographic design: FH.
Final version approval: all authors.

Declarations of interest

AS: member of the Scientific Advisory Board, Edwards Lifesciences. MGM: University Chair Sponsored by Smiths; director, UCL Discovery Lab; co-director, Duke-UCL Morpheus Consortium; consultant for Edwards Lifesciences; director, Bloomsbury Innovation Group (BiG); shareholder and scientific advisor, Medical Defense Technologies LLC; shareholder and director, Clinical Hydration Solutions Ltd (Patent holder 'QUENCH'); editorial board, BJA; editorial board Critical Care; founding editor-in-chief of Perioperative Medicine; chair, Advisory Board American Society of Enhanced Recovery. TEM: research funding and consultant for Edwards Lifesciences and consultant for Mallinckrodt. MRE: has received an honorarium for lecturing for Edwards Lifesciences. He is deputy Chief Investigator for the OPTIMISE II trial, which is part-funded by Edwards Lifesciences, although he does not receive financial support in this role. MPWG: National Specialty Lead for Anaesthesia, Perioperative Medicine and Pain within the UK National Institute of Heath Research Clinical Research Network, an elected council member of the Royal College of Anaesthetists and president of the Critical Care Medicine section of the Royal Society of Medicine. MPWG serves on the board of ERAS UK, Oxygen Control Systems Ltd, the Evidence Based Perioperative Medicine (EBPOM) social enterprise and the medical advisory board of Sphere Medical Ltd and the international advisory board of the American Society of Enhanced Recovery (ASER). MPWG has received honoraria for speaking and/or travel expenses from Edwards Lifesciences, Fresenius-Kabi, BOC Medical (Linde Group), Eli Lilly Critical Care, and Cortex GmBH. MPWG is executive chair of the Xtreme-Everest Oxygen Research Consortium. RDS, FH, AT, AB, AH, DAW: none.

Funding

EBPOM CiC and Edwards Lifesciences (to Perioperative Quality Initiative-3).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2019.01.018.

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Handling editor: H.C. Hemmings Jr

BJA

British Journal of Anaesthesia, 122 (5): 563–574 (2019)

doi: 10.1016/j.bja.2019.01.013
Advance Access Publication Date: 27 February 2019
Special Article

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

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This article is accompanied by an editorial: Consensus Statements and Expert Guidance: Interpret with Care by S.J. Howell, *Br J Anaesth* 2019:122, doi: https://doi.org/10.1016/j.bja.2019.03.013.

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.

Editorial decision: 09 January 2019; **Accepted:** 9 January 2019

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

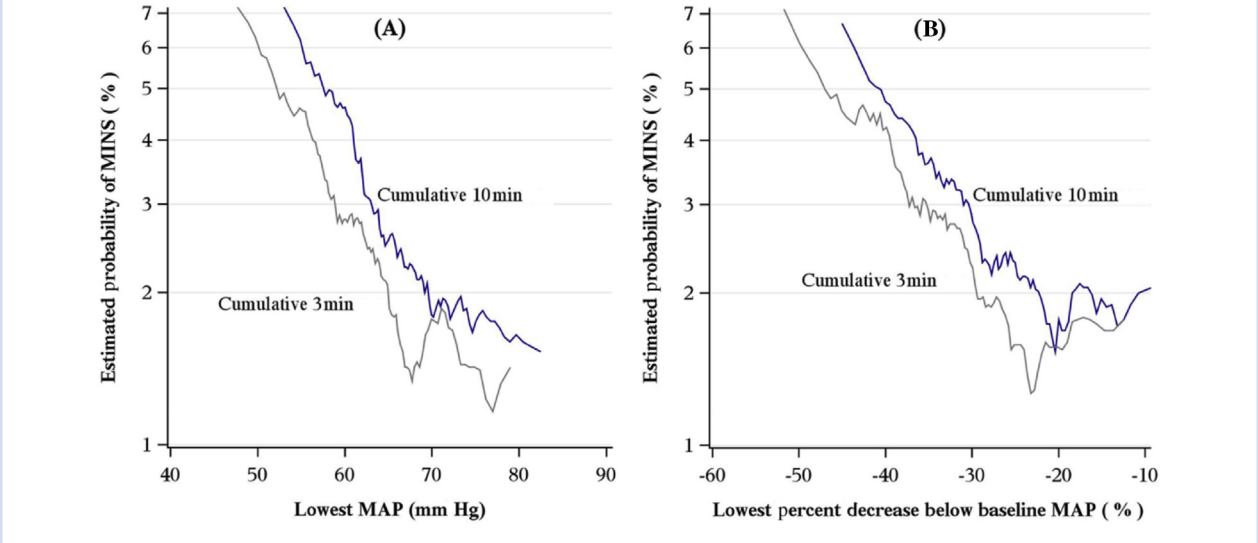

Fig 1. Relationship between the lowest cumulative absolute mean arterial pressure (MAP) maintained for 3 and 10 min and myocardial injury (left). Relationship between the lowest cumulative relative MAP maintained for 3 and 10 min and myocardial injury (right). Both were highly predictive, but relative 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]

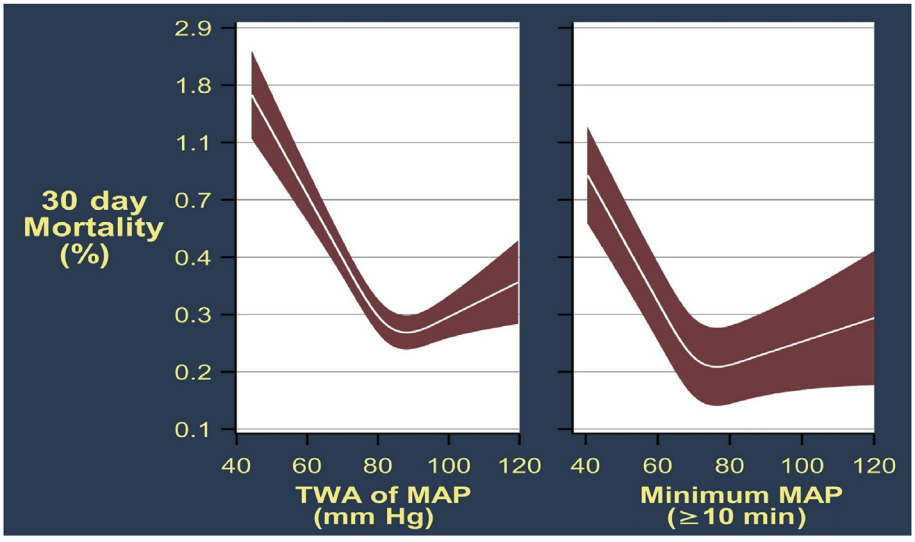

Fig 2. Relationship between average and lowest intraoperative mean arterila pressure (MAP) and 30 day postoperative mortality. High average or minimum MAP had relatively little effect on mortality. Note that the Y axis is logit; therefore, the increase in mortality from 80 to 40 mm Hg was more than six 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

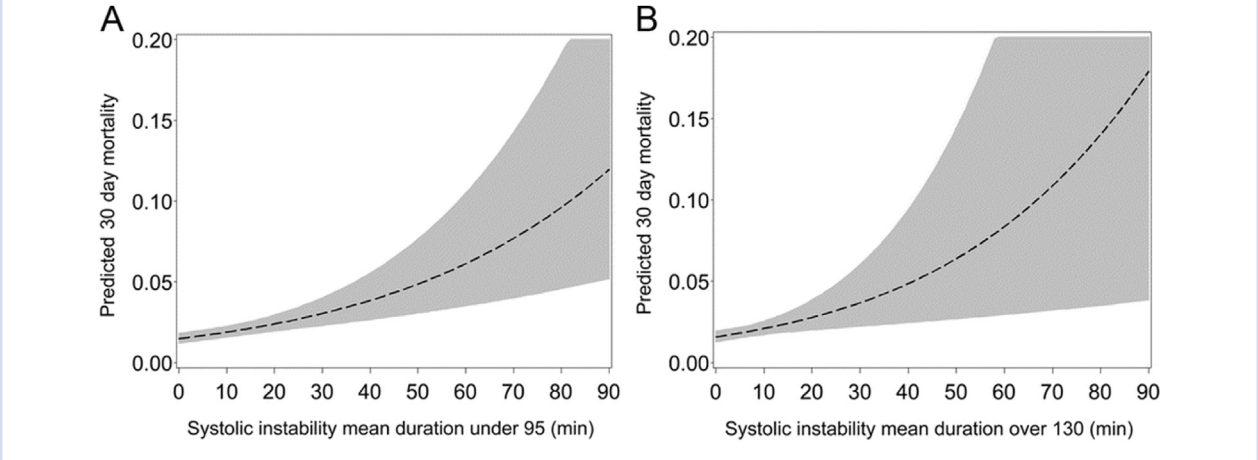

Fig 3. (a) Predicted association of mean duration per incursion (min) below the threshold 95 mm Hg and 30 day mortality in the combined sample (n=7504). *Shaded area* represents the 95% confidence intervals for the predicted values. (b) Predicted association of mean duration per incursion (min) above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

Authors' contributions

Consensus conferences participation: all authors.
Writing paper: all authors.
Revising paper: all authors.

Funding

Edwards Lifesciences (travel expenses only).

Declarations of interest

DIS: paid consultant for Edwards Lifesciences. SA: serves on the Executive Advisory Board for GeNO LLC, is the Chief Medical Advisor for Summus Global LLC, and is a paid consultant for Chiesi USA Inc. and Pfizer Inc. MGM: University Chair Sponsored by Smiths; director, UCL Discovery Lab; co-director, Duke-UCL Morpheus Consortium; consultant for Edwards Lifesciences; director, Bloomsbury Innovation Group (BiG); shareholder and scientific advisor, Medical Defense Technologies LLC; shareholder and director, Clinical Hydration Solutions Ltd (Patent holder 'QUENCH'); editorial board, BJA; editorial board Critical Care; founding editor-in-chief of Perioperative Medicine; chair, Advisory Board American Society of Enhanced Recovery. MPWG: National Specialty Lead for Anaesthesia, Perioperative Medicine and Pain within the UK National Institute of Heath Research Clinical Research Network, an elected council member of the Royal College of Anaesthetists and president of the Critical Care Medicine section of the Royal Society of Medicine. MPWG serves on the board of ERAS UK, Oxygen Control Systems Ltd, the Evidence Based Perioperative Medicine (EBPOM) social enterprise and the medical advisory board of Sphere Medical Ltd and the international advisory board of the American Society of Enhanced Recovery (ASER). MPWG has received honoraria for speaking and/or travel expenses from Edwards Lifesciences, Fresenius-Kabi, BOC Medical (Linde Group), Eli Lilly Critical Care, and Cortex GmBH. MPWG is executive chair of the Xtreme-Everest Oxygen Research Consortium. MRE: has received an honorarium for lecturing for Edwards Lifesciences. He is deputy Chief Investigator for the OPTIMISE II trial, which is part-funded by Edwards Lifesciences, although he does not receive financial support in this role. TEM: research funding and consultant for Edwards Lifesciences and consultant for Mallinckrodt. JAP, CB, TJG, JAK, AP: none.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2019.01.013.

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Handling editor: H.C. Hemmings Jr

BJA

British Journal of Anaesthesia, 122 (5): 575–586 (2019)

doi: 10.1016/j.bja.2019.01.019
Advance Access Publication Date: 2 March 2019
Special Article

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

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This article is accompanied by an editorial: Consensus Statements and Expert Guidance: Interpret with Care by S.J. Howell, *Br J Anaesth* 2019:122, doi: https://doi.org/10.1016/j.bja.2019.03.013.

Editorial decision: 03 January 2019; **Accepted:** 3 January 2019

Abstract

Background: Postoperative hypotension and hypertension are frequent events associated with increased risk of adverse outcomes. However, proper assessment and management is often poorly understood. As a part of the PeriOperative Quality Improvement (POQI) 3 workgroup meeting, we developed a consensus document addressing this topic. The target population includes adult, non-cardiac surgical patients in the postoperative phase outside of the ICU.

Methods: A modified Delphi technique was used, evaluating papers published in MEDLINE examining postoperative blood pressure monitoring, management, and outcomes. Practice recommendations were developed in line with National Institute for Health and Care Excellence guidelines.

Results: Consensus recommendations were that (i) there is evidence of harm associated with postoperative systolic arterial pressure <90 mm Hg; (ii) for patients with preoperative hypertension, the threshold at which harm occurs may be higher than a systolic arterial pressure of 90 mm Hg; (iii) there is insufficient evidence to precisely define the level of postoperative *hypertension* above which harm will occur; (iv) a greater frequency of postoperative blood pressure measurement is likely to identify risk of harm and clinical deterioration earlier; and (v) there is evidence of harm from withholding beta-blockers, angiotensin receptor blockers, and angiotensin-converting enzyme inhibitors in the postoperative period.

Conclusions: Despite evidence of associations with postoperative hypotension or hypertension with worse postoperative outcome, further research is needed to define the optimal levels at which intervention is beneficial, to identify the best methods and timing of postoperative blood pressure measurement, and to refine the management of long-term antihypertensive treatment in the postoperative phase.

Keywords: antihypertensive drugs; postoperative; hypotension; hypertension; blood pressure; outcomes; myocardial infarction; surgery

Editor's key points

- An expert consensus meeting reviewed the relationships between postoperative arterial pressure and postoperative outcomes using a modified Delphi approach to create recommendations.
- There is evidence of harm associated with postoperative systolic arterial pressure <90 mm Hg, and higher with preoperative hypertension.
- There is insufficient evidence to precisely define the level of postoperative hypertension above which harm will occur.
- Further studies are required to define the optimal thresholds for intervention, the best methods and timing of blood pressure measurement, and management antihypertensive drugs in the postoperative phase.

Postoperative blood pressure regulation is complex and can be affected by a variety of factors including patient, procedure, and perioperative care.[1] Postoperative hypotension and hypertension are frequent events and are associated with an increased risk of adverse outcomes.[2] However, the proper assessment and management of postoperative hypotension and hypertension is often poorly understood.[3] Accordingly, we present the latest data concerning risks associated with postoperative hypotension and hypertension and evidence for postoperative monitoring of vital signs. As this topic is both complex and important for patient outcomes, we sought to propose evidence-based consensus statements and practice and research recommendations relating to postoperative blood pressure and the associations with risk and outcomes after elective surgery.

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.[4–8] The participants in the POQI consensus meeting were recruited based on their expertise in perioperative medicine and blood pressure management (Supplementary material, Appendix 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,[4] whereas Groups 2, 3, and 4 were focused on preoperative,[5] intraoperative,[6] and postoperative blood pressure (this paper), respectively; see Ackland and colleagues[4] for detailed methods. The POQI process is based on an established modified Delphi process used in the Acute Dialysis Quality Initiative (ADQI) conferences.[9–11] Groups indicated the strength of evidence underlying practice recommendations using a structure consistent with UK National Institute for Health and Care Excellence (NICE) guidance (Supplementary Table S1).

This workgroup of POQI-3 meeting sought to develop a consensus document addressing postoperative blood pressure assessment and management. Our target population included adult, non-cardiac surgical patients in the postoperative phase who go through the PACU or high-dependency unit (HDU) and continue to the hospital ward. This consensus statement does not apply to ICU-based care of surgical patients or to postoperative cardiac surgery patients. We focused *a priori* on the following questions regarding adult postsurgical patients:

1. What arterial pressure readings should trigger a bedside assessment?
2. How should clinicians determine the *intensity* of postoperative blood pressure monitoring and *location* of postoperative care?
3. What treatment options are available for postoperative hypotension and when should an escalation of care be considered?
4. What treatment options are available for postoperative hypertension and when should an escalation of care be considered?
5. When should home antihypertensive medications be resumed in the postoperative period?

For content to be included in the paper, we searched PubMed from 1966 to June 2017 using the following search terms with the filters of 'human', 'age 18+', and 'published in English' selected: postoperative AND hypotension AND mortality OR postoperative AND hypertension AND mortality OR postoperative AND hypotension AND morbidity OR postoperative AND hypertension AND morbidity OR postoperative AND blood pressure AND outcomes OR postoperative AND blood pressure AND mortality OR postoperative AND blood pressure AND morbidity OR postoperative AND blood pressure AND threshold AND risk OR postoperative blood pressure AND myocardial infarction OR postoperative blood pressure AND myocardial injury OR postoperative blood pressure AND major adverse cardiac event OR postoperative blood pressure AND stroke OR postoperative blood pressure AND renal failure OR postoperative blood pressure AND acute kidney injury OR postoperative blood pressure AND delirium OR postoperative AND hypotension AND treatment OR postoperative AND hypertension AND treatment OR postoperative blood pressure AND treatment. Based on a review of the reference lists of papers, one citation was included from 1957. This literature search was supplemented by reading the relevant references of the journals identified.

Results

Consensus statements

Consensus statement 1: *There is evidence of harm associated with postoperative systolic arterial blood pressure <90 mm Hg. However, there is insufficient evidence to precisely define the levels of postoperative pressure below which harm will occur. The level of risk is increased with longer durations of hypotension.*

Consensus statement 2: *For patients with preoperative hypertension, the threshold at which harm occurs may be higher than a systolic pressure of 90 mm Hg.*

Postoperative hypotension is a common occurrence.[12,13] Roshanov and collegues[12] recently reported that 20% of the 14 687 patients in the VISION (Vascular events In noncardiac Surgery patIents cOhort evaluatioN) cohort experienced at least one episode of clinically significant hypotension in the perioperative period (systolic pressure <90 mm Hg with an intervention given to raise blood pressure), with 95% of those events occurring from postoperative day (POD) 0–3 and the largest percentage on POD1.[12] These events occurred in a patient population with an average baseline preoperative mean arterial pressure of 93 mm Hg, which corresponds to a blood pressure of about 120/80, so it is difficult to draw conclusions from these data about patients with significant preoperative hypertension. There is emerging evidence from the POISE-II (PeriOperative Ischemic Evaluation-2) cohort that systolic pressures of <90 mm Hg in the postoperative period are associated with increased risk of all-cause death, myocardial injury after non-cardiac surgery (MINS), and stroke.[13] This risk increased for each 10 min epoch of hypotension during the intraoperative period and POD0. Furthermore, the odds ratio of poor outcomes with hypotension was almost three times as high if it occurred on POD1–4, a time when extended periods of hypotension can occur, particularly if vital signs are only checked every 4–6 h on the surgical ward (Fig. 1). Thus, a systolic pressure <90 mm Hg or <30% below baseline is likely to put most patients at risk of end organ injury.

These findings are in line with the literature on intraoperative blood pressure control where recent reports have identified a mean arterial pressure <65 mm Hg as an independent risk factor for postoperative MINS and acute kidney injury (AKI). The risk of harm increased with the duration of hypotension (with increasing risk accruing with increasing time of hypotension).[14] Salmasi and colleagues[14] reported that mean arterial pressure reductions of 25–30% or more are associated with increased risk of harm. The effects of 20% reductions from baseline were less clear. This study is in keeping with previous literature reporting an association between intraoperative hypotension and postoperative renal and cardiac injury and 30 day mortality.[15–18] It also agrees with a systematic review that found avoidance of hypotension as a key strategy for reducing AKI.[19]

Beyond these data on surgical patients from the intraoperative period, the Modified Early Warning System (MEWS) provides further indirect support for the importance of postoperative blood pressure in determining surgical outcomes.[20–23] Blood pressure is an important element of the MEWS score with systolic arterial pressure <100 or <90 mm Hg equating to medium or high-risk scores, respectively. Although data are mixed concerning the effect of MEWS scoring in general ward patients,[20,21] postoperative MEWS scores are strongly associated with postoperative outcome.[22] Patients with high MEWS scores, or a trend of increasing MEWS scores, had an increased risk of complications. Conversely, low scores or a trend of decreasing scores were associated with favourable surgical outcomes. This corresponds with other studies that have further confirmed the importance of hypotension (defined as systolic arterial pressure <90 mm Hg) as an antecedent to adverse patient outcomes. In one study, systolic pressure <90 mm Hg was the most common cause (25%) for emergency team activation on the ward after orthopaedic or general surgery.[24] This is similar to the finding from the ACADEMIA study from 90 hospitals in the UK, Australia, and New Zealand in which a systolic arterial pressure <90 mm Hg was the most common antecedent event of patient deterioration in the inpatient setting.[25]

In order to interpret postoperative blood pressure, it is important to understand variations with circadian rhythm. Although the majority of patients experience a 10–20% reduction compared with their awake blood pressure when asleep, some do not show a decrease at all and some have increased blood pressure.[26] Consequently, tolerating prolonged periods of postoperative hypotension during sleep may not be appropriate and may put patients at risk unless it can be shown that they achieve these pressures when not in the hospital setting.

Although current evidence suggests that postoperative hypotension is associated with increased risk of patient harm, it is yet to be definitively shown that using postoperative arterial pressure as a therapeutic target improves outcome. The optimal strategy to achieve blood pressure targets is also

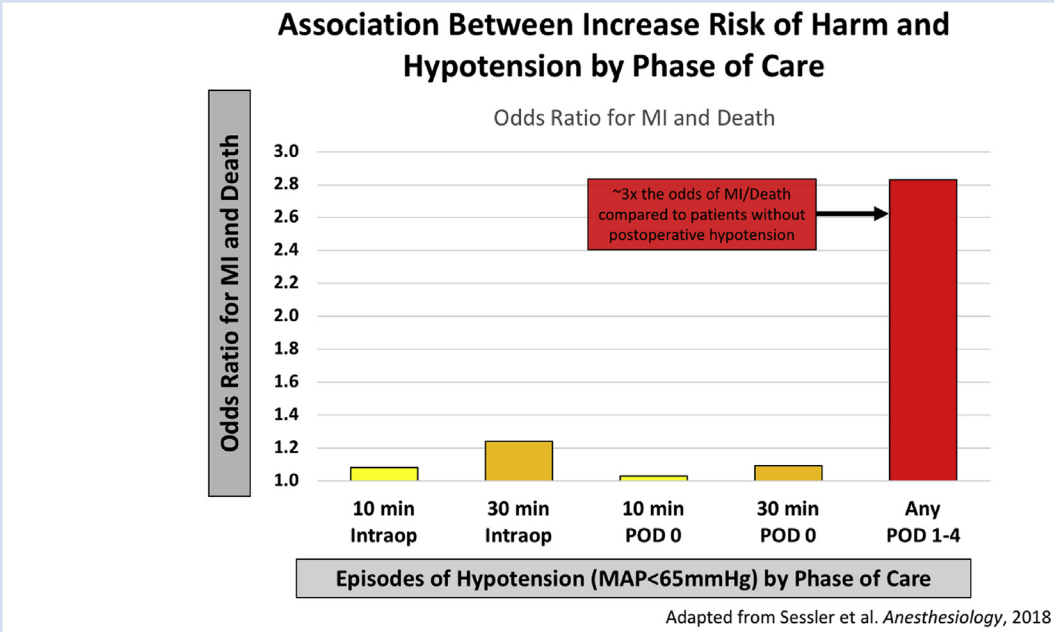

Fig 1. This figure demonstrates the association of perioperative hypotension with myocardial infarction (MI) and death, showing that each 10-minute episode of hypotension of postoperative day (POD) 0 is associated with a 3% increase in risk, and *any* episodes of hypotension on POD 1-4 are associated with almost a doubling or risk. The actual incidence of the composite outcome (MI and death) was 7.2%. [Adapted from Sessler DI, et al. Period-dependent Associations between Hypotension during and for Four Days after Noncardiac Surgery and a Composite of Myocardial Infarction and Death: A Substudy of the POISE-2 Trial. *Anesthesiology*, 2018 128:317-327.] Figure reused with the permission of the Perioperative Quality Initiative (POQI).

unclear. For instance, the INPRESS (Intraoperative Noradrenaline to Control Arterial Pressure) trial suggested that tight blood pressure control achieved using a norepinephrine infusion during and for 4 h after surgery improves outcome compared with standard care when used in addition to a stroke volume maximisation algorithm intraoperatively.[27] Although this trial further highlights the potential role for blood pressure control as a perioperative target, the relative contribution from the intra- and postoperative phases of treatment is not clear. Overall, it should be noted that relatively few studies have been performed in this arena, and none of the studies to date have *a priori* used postoperative blood pressure as a primary outcome. Non-standardisation in data collection methods and measurement bias surrounding blood pressure might impact the results of these studies. As such, although the association between postoperative hypotension and adverse patient outcomes has clinical plausibility and appears robust, further research is needed.

Consensus statement 3: *There is insufficient evidence to precisely define the level of postoperative hypertension above which harm will occur.*

Postoperative hypertension is common and independently associated with adverse events after non-cardiac surgery, including stroke, myocardial injury and infarction, and bleeding.[2,3,28,29] Its frequency varies in different types of surgery: carotid endarterectomy (9–58%),[30–35] abdominal aortic aneurysm surgery (25–85%),[36,37] intracranial neurosurgery (57–91%),[38,39] and elective non-cardiac surgery (5–20%).[40–42] The accepted definition of acute postoperative hypertension is 'a significant elevation in blood pressure during the immediate postoperative period that may lead to serious neurologic, cardiovascular, or surgical-site complications and that requires urgent management'.[43] However, a precise consensus definition of postoperative hypertension does not exist.[3,42,43] One source defined postoperative hypertension as a systolic pressure >190 mm Hg, diastolic pressure >100 mm Hg, or both on two consecutive readings after surgical intervention, whereas a recent publication that linked postoperative hypertension with cardiovascular complications used a cut-off of systolic pressure >180 mm Hg and diastolic pressure >110 mm Hg. The latter is in accord with the modified and national early warning systems (MEWS and NEWS, respectively), which have shown good validity and predictive ability.[21,22,43,44] It is worth noting that hypertension after carotid endarterectomy and intracranial neurosurgery have specific considerations not present with other cases. Specifically, post-carotid endarterectomy hypertension may be attributable to altered baroreceptor sensitivity and is associated with cerebral hyperaemia and poor neurologic outcomes.[45,46] Hypertension after intracranial neurosurgery with craniotomy is common and places the patient at risk of intracranial bleeding and worse neurologic outcomes.[47,48] Hypertension in these cases should be rapidly treated while considering whether surgical intervention to address haematoma or haemorrhage is required.

The timing of postoperative hypertension is also relevant. Many episodes occur in the first 20 min of the postoperative period and are relatively short-lived; however, resolution can require 3 h or longer.[41,42] Untreated postoperative hypertension increases the risk of myocardial ischaemia, myocardial

infarction, arrhythmia, pulmonary oedema, stroke, and surgical site bleeding.[42,43] Postoperative hypertension is characterised by sympathetic stimulation resulting in catecholamine release, vasoconstriction, tachycardia, and impaired baroreceptor sensitivity. Rose and colleagues[1] found that patients who had intraoperative hypertension, excessive pain, and inadequate ventilation had a higher risk of developing postoperative hypertension, and also noted that these patients had more critical care admissions and a higher risk of mortality. Accordingly, bedside evaluation of the patient with acute postoperative hypertension is important to address the adequacy of ventilation and analgesia before considering specific blood pressure therapy.

In addition to direct evidence of harm as summarised above, use of MEWS with a systolic pressure >180 mm Hg indicating high-risk has been validated in numerous acute care situations, including the emergency department, medical ward, and surgical patients.[20–22] This level of hypertension is predictive of end organ dysfunction and harm and should be immediately assessed and treated according to the underlying cause. Most of the studies of MEWS to date have been retrospective in nature; however, prospective studies related to implementing EWSs, including MEWS and NEWS, have shown that these systems can predict worse outcomes. It is not clear whether treatment regimens given in response to these systems are beneficial, or whether intervention for postoperative hypertension with systolic pressure <180 mm Hg would be of benefit.

Consensus statement 4: A *greater frequency of postoperative blood pressure measurement is likely to identify risk of harm and clinical deterioration earlier.*

There currently exists no direct evidence to specifically address the optimal intensity of postoperative blood pressure monitoring. The standard of care is typically to measure and record vital signs every 4 h, although studies show that it is often less frequent in clinical practice.[49–52] Audits of vital sign recording on postoperative general care wards display significant deficits in applying this standard in routine care.[53,54] Continuous monitoring of other vital signs reveals concerning trends that are not picked up with the current standard of care. Continuous monitoring of ventilatory frequency for the first 6 h on a general care ward after PACU discharge revealed that in patients ≥60 yr old who underwent elective intra-abdominal or orthopaedic surgery under general anaesthesia, almost 80% had at least one episode of bradypnoea (1–6 breaths min^{-1}) and almost 60% had at least one episode of apnoea (cessation of inspiratory flow for >60 s).[49] A recent trial of continuous monitoring of oxygen saturation on the postoperative general care ward revealed that 21% of patients had ≥10 min h^{-1} of SpO_2 readings <90%, 8% had ≥20 min h^{-1} <90%, and 8% had ≥5 min h^{-1} <85%.[50] Nursing records only documented hypoxaemia in 5% of patients, and 90% of hypoxaemic episodes (SpO_2 <90% for at least 1 h) were missed. In a randomised trial setting, continuous measurement of oxygen saturation significantly reduces the amount of hypoxaemia in the PACU.[55,56]

There is also evidence that vital sign disturbances in one phase of care can predict further perturbations or complications later in the perioperative course. For instance, hypoxaemia or bradypnoea in the PACU is strongly associated with similar events on the postoperative ward for elderly patients and for those with sleep apnoea.[49,57] For patients with sleep apnoea, respiratory events in the PACU are strongly associated with use of naloxone within 12 h after PACU discharge.[58] The Surgical Apgar score, a rapid scoring system based on intraoperative vital signs and blood loss, is highly predictive of postoperative complications and death after major surgery.[59–64]

Taken together, the evidence shows that disturbances in vital signs on the postoperative ward are common and often missed. Given that clinical deterioration is often preceded by changes in physiologic parameters, more frequent or continuous ward monitoring may improve patient care.[20,21,23,65] Given that disturbances in one phase of care can predict events in subsequent phases, clear guidelines for moving patients between levels of care and a structured assessment at those transition points may be of benefit (Fig. 2).

As noted above, NEWS[66] and MEWS[20] are validated patient screening systems that can predict deterioration in clinical status earlier than traditional means of assessment. These systems have a scoring algorithm that takes into account

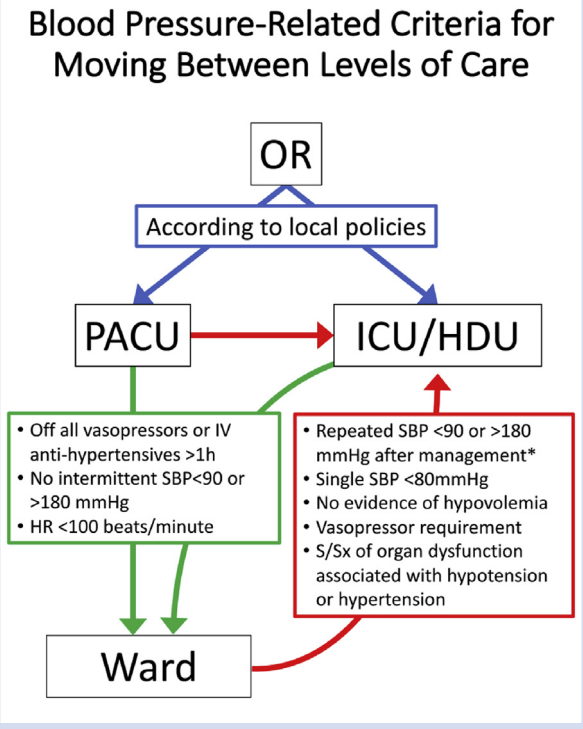

Fig 2. This figure represents structured criteria for moving patients between levels of care based upon postoperative blood pressure. If the patient meets all criteria in the green box, then they would be cleared to move from PACU or the ICU/HDU to the ward based upon blood pressure (other vital signs or care issues may prevent such change in level of care). If the patient meets criteria in the red box, then they should move from the ward to a higher level of care, such as ICU/HDU. Figure reused with the permission of the Perioperative Quality Initiative (POQI). *Of note, this algorithm assumes that the bedside assessment and initial management shown in Figure 4 has occurred and the patient remains hypotensive or hypertensive after appropriate initial therapies have been undertaken that are possible on the postoperative ward. [OR = operating room/theater; PACU = post-anesthesia care unit; ICU = intensive care unit; HDU = high-dependency unit; IV = intravenous; SBP = systolic blood pressure; HR = heart rate; S/Sx = signs and symptoms].

parameters such as systolic arterial pressure, heart rate, ventilatory frequency, oxygen saturation, temperature, and mental state.[21,44] Although composite scores from EWSs may perform better than single components,[66] the most common antecedent finding 15 min to 24 h before in-hospital death, cardiac arrest, or unanticipated ICU admissions was a systolic pressure ≤90 mm Hg, which was present in more than 30% of events.[25] Thus, increased frequency of arterial pressure monitoring is likely to improve detection of risk of harm. The significant resource implications of increased frequency of monitoring should be considered.[66] It is possible that new products (e.g. wearable and wireless sensors) designed specifically for ward monitoring will aid in providing continuous vital signs monitoring until the patient shows a sustained return to baseline cardiopulmonary physiologic status.[52,65,67,68]

Consensus statement 5: *There is evidence of harm from withholding beta-blockers, angiotensin receptor blockers (ARBs), and angiotensin-converting enzyme (ACE) inhibitors in the postoperative period.*

There is strong evidence that resuming beta-blockers after operation decreases morbidity and mortality. Wallace and colleagues[69] demonstrated that continuation of a beta-blocker decreases both short-term (30 days) and long-term (1 yr) mortality in the perioperative period. In a retrospective cohort analysis of more than 136 000 patients, London and colleagues[70] noted a two-fold increase in mortality when a patient was not continued on a beta-blocker after operation. In addition, Hoeks and colleagues[71] reported direct evidence that withdrawal of beta-blockers increased both in-hospital mortality and 1 yr mortality in vascular surgery patients as opposed to continuation of beta-blockers throughout the perioperative period. Although evidence has shown that prophylactic treatment with beta-blockade for -blocker naïve patients is not of benefit, it is clear that continuing beta-blockers throughout the perioperative period is of benefit for those on chronic therapy.[72,73]

We know from the POISE trial that fixed dosing of beta-blockers can be harmful, particularly in large doses.[72] Therefore, we urge caution when restarting a beta-blocker at the chronic preoperative dose. A smaller dose and titration to heart rate and blood pressure may be more appropriate in the perioperative setting to avoid hypotension. Beta-blockers should not be resumed in patients who develop an absolute contraindication (i.e. third-degree atrioventricular block without a pacemaker).[73] Therefore, we recommend that beta-blockers be resumed as soon as possible after operation with titration or holding if clinically indicated for hypotension or severe bradycardia.

The evidence surrounding cessation of ACE inhibitors/ARBs before surgery is presented in the POQI-3 paper from the Preoperative Blood Pressure Group.[ref - Sanders R, et al.][6] Failure to restart ACE inhibitor or ARB medications within 48 h after operation has been shown to increase all-cause 30 day mortality and the incidence of postoperative complications, with the largest effect on those <60 yr old.[74,75] Caution is warranted in patients with postoperative increases in creatinine or low/borderline low blood pressure.

There is little direct evidence on the resumption of calcium channel blockers after surgery. However, calcium channel blockers have been shown to reduce ischaemia and arrhythmias in patients undergoing non-cardiac surgery when patients take them throughout the perioperative setting.[76] In the cardiac surgery population, calcium channel blockers have been shown to reduce overall mortality, but it is unknown if this can be extrapolated to all perioperative patients.[77]

There is a lack of evidence about when to resume a chronic clonidine therapy, but withdrawal from clonidine is associated with rebound hypertension in non-surgical patients.[78]

At present, there is little evidence to guide reintroduction of diuretics in the postoperative period.

Practice recommendations

Practice recommendation 1: *Patient-specific postoperative blood pressure target ranges should be created based on baseline preoperative blood pressure measurements and clinical context.*

Practice recommendation 2: *A clinical assessment should be conducted in response to high or low postoperative blood pressure. Trigger blood pressure values should allow enough time for assessment in cases where blood pressure is trending downward or upward.*

Maintaining systolic pressure >90 and <160 mm Hg is a reasonable therapeutic target for a broad range of adult post-surgical patients with normal preoperative baseline blood pressure. These targets should be adapted for patients with abnormal baseline values (e.g. systolic pressure >140 or <100 mm Hg); observational data suggest that intraoperative systolic pressures >70% of preoperative baseline are associated with less harm.[14] Other targets may be chosen depending on other co-morbidities and clinical context, for example after vascular surgery or neurosurgery.

A narrower range of 'trigger' values should provide a safety margin in alerting clinicians to abnormal blood pressures. This provides an opportunity for assessment before pressures on a down- or upward trend reach levels associated with harm. Suggested trigger values for assessment are therefore systolic pressure <100 mm Hg (or <75% of baseline, whichever is higher) or >160 mm Hg (or >140% of baseline, whichever is lower). These trigger values may be further adapted to clinical context.

Practice recommendation 3: *The frequency of postoperative surveillance, including blood pressure monitoring, should be determined by the patient status and clinical context.*

We recommend that the frequency of postoperative blood pressure surveillance be determined by patient status and clinical context. Although routine current practice for many patients may be intermittent measurement of vital signs every 4–6 h, we recommend increased frequency of blood pressure monitoring in certain settings (Fig. 3), such as patients with a decreasing or increasing trend in blood pressure or those requiring tighter targets. Non-invasive continuous blood pressure monitoring is becoming a reality with volume clamp methods and application tonometry with devices designed for operating room and ICU use. Future products (e.g. wearable and wireless sensors) will be designed specifically for ward monitoring in ambulatory patients.[67]

We recommend that clinicians consider use of a structured alert system, including an individualised alert for hypotension for postoperative patients on the general care ward. Such early warning systems have been shown to identify postoperative patients at risk of deterioration earlier than standard monitoring and has correlated with improved mortality in one study.[20–22,79] More intensive monitoring—through novel technology, alert systems, or both—is likely to have resource implications and should undergo thorough evaluation before its routine use can be more strongly recommended.

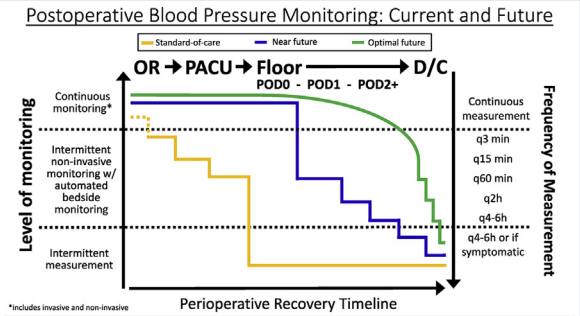

Fig 3. This figure illustrates the current standard of care for monitoring blood pressure in the perioperative period and also depicts how that may change in the near future based on available technologies and evolving evidence. Finally, we propose what may be present optimally in the future concerning the level of postoperative monitoring, anticipating that improved continuous monitoring in the first 48 hours after surgery may improve patient safety and reduce adverse events related to hypotension. Figure reused with the permission of the Perioperative Quality Initiative (POQI).

Practice recommendation 4: *A structured bedside assessment should be carried out in response to postoperative hypotension/hypertension in order to (a) determine aetiology, (b) select appropriate treatment if indicated, and (c) consider changing the intensity of future monitoring and care environment.*

A focused history and physical examination should be performed with an emphasis on characterising the hypotensive or hypertensive state as stable or unstable, as described in practice guidelines and recommendations (Fig. 4).[80–82] Unstable patients displaying signs and symptoms of end-organ dysfunction should be treated in a high acuity care setting (Fig. 2).

Hypotension

The most appropriate management for hypotensive, haemodynamically unstable patients is to perform a bedside assessment in order to define the cause and then treat accordingly as supported by a recent meta-analysis.[83] In that meta-analysis of 2260 patients, the mean prevalence of fluid responsiveness was 50%, and typical signs and symptoms of suspected hypovolaemia were not predictive of fluid responsiveness. However, an increase in cardiac output after passive leg raise (PLR) strongly predicted fluid responsiveness (positive likelihood ratio [LR]=11; 95% confidence interval [CI], 7.6–17; pooled specificity, 92%). No increase in cardiac output after PLR classified patients who most likely would not respond to fluid (negative LR=0.13; 95% CI, 0.07–0.22; pooled sensitivity, 88%).

To assess the situation of postoperative hypotension and better understand the most appropriate therapy, El Hadouti and colleagues[84] performed a prospective observational study on postsurgical patients with suspected hypovolaemia (systolic pressure <90 mm Hg, MAP <70 mm Hg, oliguria, or heart rate >100 beats min^{-1}) who were spontaneously breathing in the recovery room. The primary outcome was change in cardiac output before and after PLR and a 500 ml intravenous bolus of lactated Ringer's solution. Of the patients who met inclusion criteria for suspected hypovolaemia, only 54% responded to the fluid bolus. This suggests that the typical approach of correcting postoperative hypotension with intravenous fluid (preload correction) may be inappropriate ~50% of the time, with correction of vascular tone or inotropy being required in the remaining patients.

A PLR test should be considered for patients with postoperative hypotension.[83] Although the existing literature has specifically examined the effect of PLR on monitored cardiac output, it is likely to be useful in detecting whether inadequate preload is contributing to hypotension. If the PLR test does not correct hypotension, further management should focus on vascular tone and chronotropy/inotropy. In this setting, non-invasive cardiac output monitors and portable ultrasound devices may help in identifying the root cause of hypotension and hence in choosing the most appropriate treatment. Patient transfer to a higher level of care may be required in order to deliver appropriate therapies, dependent on local facilities and available resources.

Hypotension should be treated immediately in the symptomatic patient. For a positive PLR test, intravenous fluid would be appropriate in many instances.[83,84] If preload augmentation is not needed, vasopressor or inotropic support is indicated. The side-effect profile of drugs used in the treatment of hypotension must be taken into account. For example, phenylephrine is best used in situations where the hypotension is accompanied by tachycardia because phenylephrine can result in a reflex bradycardia, especially in the preload independent state.[85]

Hypertension

For treatment for hypertension in the PACU setting, therapy should be individualised with a focus on the choice of agent based on the specific clinical situation, patient characteristics, and care setting. In the absence of a hypertensive emergency, attempts should be made to determine if there is a reversible underlying cause of the hypertension.[41,86] Common non-pharmacological interventions can be used depending on aetiology, such as supplemental oxygen for hypoxaemia, forced air warmer for hypothermia, catheterisation for urinary retention, and verbal reassurance/family presence/anxiolytic for anxiety. For postoperative hypertension from withdrawal of long-term antihypertensive therapy, administering a home dose of the antihypertensive drug is appropriate after other causes have been ruled out. In situations where this is not possible, rapid acting analogues with the same mechanism of action as the chronic medications are appropriate.

Generally, the treatment goal should be based on preoperative blood pressure with a target of ~10% above the baseline (although a more aggressive approach may be necessary for patients at very high risk of bleeding or with severe heart failure who would benefit from afterload reduction).[2,3,41] Adequate monitoring of the response to the chosen therapy, and appropriate adjustments to the treatment itself, are paramount to safe and effective treatment of postoperative hypertension. In the days after surgery, a careful transition ought to be planned to an effective oral antihypertensive regimen to manage the long-term risks of hypertension.

The side-effects of drugs used in the treatment of hypertension must be taken into account before administration. For example, isolated hypertension with a low heart rate (<60 beats min^{-1}) should not be treated with a non-selective beta blocker. Similarly, calcium channel blockers should be used with caution in conditions where such agents can have

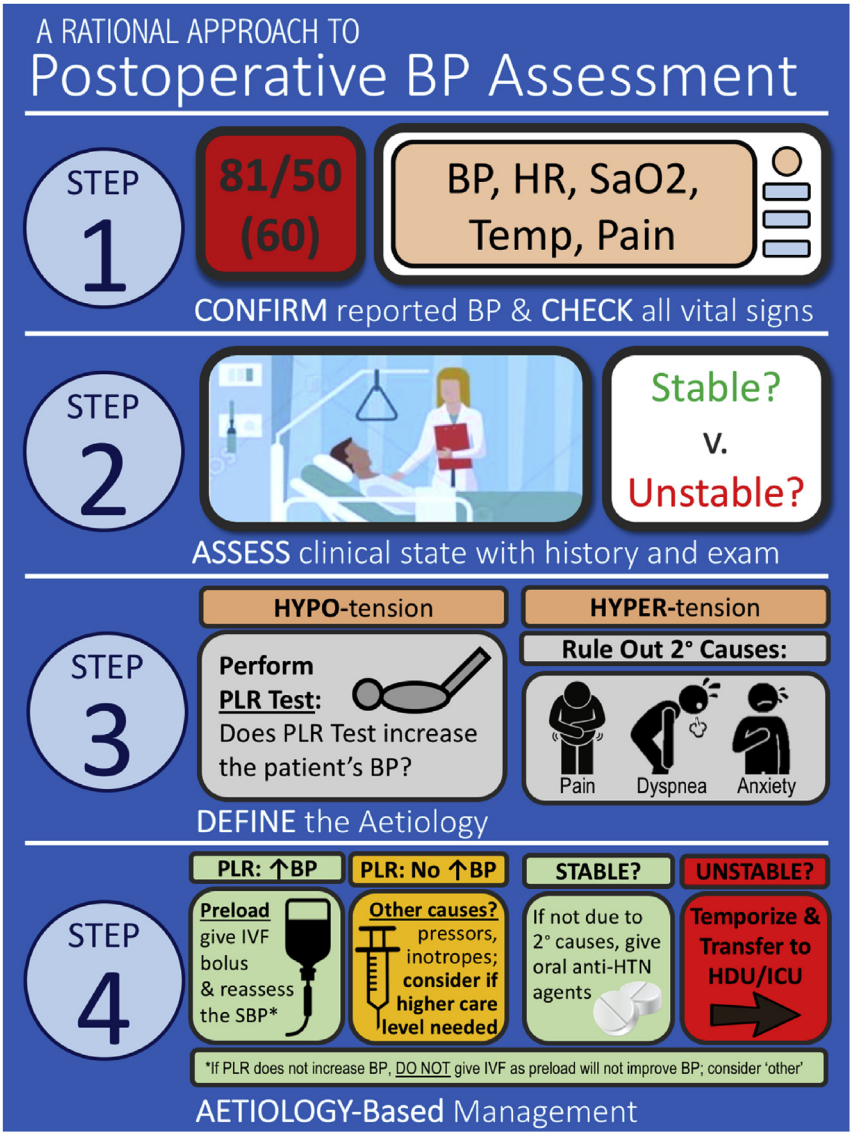

Fig 4. This figure illustrates our recommendations for a structured bedside assessment due to perturbations in postoperative blood pressure readings. *An unstable patient would be any patient who is displaying signs and symptoms of end organ dysfunction related to blood pressure (e.g. altered mental status, chest pain). [BP = blood pressure; PLR = passive leg raise; SV = stroke volume; TTE – transthoracic echocardiography; SVR = systemic vascular resistance; ECG = electrocardiogram; PACU = post-anesthesia care unit; HDU = high-dependency unit; ICU = intensive care unit] Figure reused with the permission of the Perioperative Quality Initiative (POQI).

harmful side-effects (i.e. Wolff–Parkinson–White syndrome). Drugs that lower blood pressure indirectly by anxiolysis and sedation must be used with caution in patients prone to rapid desaturation, such as those with obstructive sleep apnoea.

Practice recommendation 5: *Home antihypertensive medications should be restarted as soon as is appropriate in the clinical context.*

As noted in Consensus Statement 5 above, there is evidence of harm from withholding beta-blockers, ARBs, and ACE inhibitors in the postoperative period. Thus, beta-blockers should be continued in the postoperative period with specific criteria for withholding the drug to avoid hypotension and bradycardia.[69–71] ACE inhibitors or ARBs should be resumed within 48 h after surgery unless the patient has persistent hypotension or AKI.[75] Alpha-agonists can cause withdrawal hypertension, so we recommend resuming these after beta-blockers and ACE/ARBs if the patient is normotensive. We recommend resuming calcium channel blockers after the patient is on home doses of beta-blockers and ACE inhibitors/ARBs, although there is no direct evidence about the time of resumption after operation. Diuretics should be resumed based on the patient's volume status and the indication for the diuretic. All antihypertensive medications should be omitted if a patient is hypotensive.

Recommendations for research

The above consensus statements and practice recommendations concerning risks and outcomes associated with postoperative blood pressure regulation are based upon the latest evidence. However, the evidence base is far from conclusive and future research is needed to answer several important questions related to this topic.

First, large, observational studies are needed to identify the *relative* and *absolute* lower and upper limits of postoperative arterial blood pressure associated with optimal patient outcomes and risk of harm. Although current data demonstrate an association of harm with hypotension, the studies cited were not designed to evaluate postoperative blood pressure and patient outcomes specifically and thus further research is needed. Second, prospective studies are needed to identify a reliable reference blood pressure for postoperative management (i.e. ambulatory, immediately before surgery, PACU). Both absolute and relative changes in blood pressure have been associated with patient outcomes, so it is important to know the most reliable reference from which to build patient-specific postoperative management targets, especially for those with hypotension or hypertension who present for elective surgery. Third, prospective studies are needed to identify the best method and timing of postoperative blood pressure measurement, including use of continuous monitoring with wearable devices. Although more frequent measurement is likely to improve patient assessment and reduce the risk of unrecognised significant clinical deterioration and harm, the resource limitations that such a system would place upon nurses and other personnel are significant. Therefore, well-designed prospective studies need to be performed that include measurement of blood pressure and patient outcomes, provider workload, alarm fatigue, and related human factors. Fourth, research is needed to define the optimal treatment strategy for postoperative hypotension. Current evidence suggests that much postoperative hypotension is not caused by hypovolaemia, but treatment with a vasopressor or inotrope typically requires a high-intensity, monitored setting that has significant resource implications. Additionally, the optimal targets for blood pressure and how these are achieved is not yet known. Finally, prospective studies are needed to determine the optimal strategies of resuming chronic antihypertensive therapy. Although some studies suggest that continuing or quickly resuming some of these medications after surgery is associated with reduced risk of harm, it is important to know the optimal parameters for managing these medications.

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.[9,10] 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. Although a formal strength of evidence scoring system was not used, the wording of practice recommendations as defined here gives an indication of the group's opinion on the strength of evidence underlying those statements. Areas of uncertainty have been clearly signposted in the discussions accompanying each statement.

Conclusions

Perioperative blood pressure management has been an area of research for more than 70 yr.[87,88] Both hypotension and hypertension occur frequently in the postoperative period and both can place the patient at significant risk of complications and death. A clear definition is emerging for what defines postoperative hypotension and the risk associated with it. However, much remains to be done in terms of defining optimal blood pressure goals, monitoring strategies, and interventions to improve patient outcomes.

Authors' contributions

Conception and design of consensus document: all authors.
Analysis and interpretation of data in the literature: all authors.
Writing paper: all authors.

Declarations of interests

MDM: research funding from Edwards Lifesciences, Cheetah Medical, and the GE Foundation for projects unrelated to this work. RG: research funding from Merck unrelated to this work. AF: research funding from Oxypka Medical GmbH, travel support and speaking fees by Medac Ltd., Roche Pharmaceuticals unrelated to this work. FM: founder and managing director of MiCo, a Swiss consulting firm. DL: unrestricted educational grant from Pharmacosmos for a project unrelated to this work. MPWG: National Specialty Lead for Anaesthesia, Perioperative Medicine and Pain within the UK National Institute of Heath Research Clinical Research Network, an elected council member of the Royal College of Anaesthetists and president of the Critical Care Medicine section of the Royal Society of Medicine. MPWG serves on the board of ERAS UK, Oxygen Control Systems Ltd, the Evidence Based Perioperative Medicine (EBPOM) social enterprise and the medical advisory board of Sphere Medical Ltd and the international advisory board of the American Society of Enhanced Recovery (ASER). MPWG has received honoraria for speaking and/or travel expenses from Edwards Lifesciences, Fresenius-Kabi, BOC Medical (Linde Group), Eli Lilly Critical Care, and Cortex GmBH. MPWG is executive chair of the Xtreme-Everest Oxygen Research Consortium. MGM: University Chair Sponsored by Smiths; director, UCL Discovery Lab; co-director, Duke-UCL Morpheus Consortium; consultant for Edwards Lifesciences; director, Bloomsbury Innovation Group (BiG); shareholder and scientific advisor, Medical Defense Technologies LLC; shareholder and director, Clinical Hydration Solutions Ltd (Patent holder 'QUENCH'); editorial board, *BJA*; editorial board *Critical Care*; founding editor-in-chief of *Perioperative Medicine*; chair, Advisory Board American Society of Enhanced Recovery. TEM: research funding and consultant for Edwards Lifesciences and consultant for Mallinckrodt. MRE: has received an honorarium for lecturing for Edwards Lifesciences. He is deputy Chief Investigator for the OPTIMISE II trial, which is part-funded by Edwards Lifesciences, although he does not receive financial support in this role. EK, JKMT, MH: none.

Funding

EBPOM CiC and Edwards Lifesciences (to POQI-3). Cheetah, Deltex, Getinge, LiDCo, Pharmacosmos and MSD grants (to EBPOM CiC).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2019.01.019.

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Handling editor: H.C. Hemmings Jr