Original Article

Treatment threshold for intra-operative hypotension in clinical practice—a prospective cohort study in older patients in the UK

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Summary

Intra-operative hypotension frequently complicates anaesthesia in older patients and is implicated in peri-operative organ hypoperfusion and injury. The prevalence and corresponding treatment thresholds of hypotension are incompletely described in the UK. This study aimed to identify prevalence of intra-operative hypotension and its treatment thresholds in UK practice. Patients aged ≥ 65 years were studied prospectively from 196 UK hospitals within a 48-hour timeframe. The primary outcome was the incidence of hypotension (mean arterial pressure <65 mmHg; systolic blood pressure reduction >20%; systolic blood pressure <100 mmHg). Secondary outcomes included the treatment blood pressure threshold for vasopressors; incidence of acute kidney injury; myocardial injury; stroke; and in-hospital mortality. Additionally, anaesthetists providing care for included patients were asked to complete a survey assessing their intended treatment thresholds for hypotension. Data were collected from 4750 patients. Hypotension affected 61.0% of patients when defined as mean arterial pressure <65 mmHg, 91.3% of patients had >20% reduction in systolic blood pressure from baseline and 77.5% systolic blood pressure <100 mmHg. The mean (SD) blood pressure triggering vasopressor therapy was mean arterial pressure 64.2 (11.6) mmHg and the mean (SD) stated intended treatment threshold from the survey was mean arterial pressure 60.6 (9.7) mmHg. A composite adverse outcome of myocardial injury, kidney injury, stroke or death affected 345 patients (7.3%). In this representative sample of UK peri-operative practice, the majority of older patients experienced intra-operative hypotension and treatment was delivered below suggested thresholds. This highlights both potential for intra-operative organ injury and substantial opportunity for improving treatment of intra-operative hypotension.

Introduction

Intra-operative hypotension frequently complicates anaesthesia and has been extensively associated with myocardial injury, acute kidney injury (AKI), stroke and death [1–8]. Older patients are particularly vulnerable to peri-operative haemodynamic disturbances and organ dysfunction [9] due to a combination of comorbid disease and frailty. Although the measurement of blood pressure is only one component and a simplification of haemodynamic status, intra-operative hypotension is increasingly implicated in the pathogenesis of peri-operative end-organ dysfunction via concomitant effects of hypoperfusion and ischaemia [10]. Extensive evidence from large retrospective observational studies has led to clinical recommendations to avoid peri-operative hypotension, particularly in older patients [10–12]. Although large randomised trials confirming that avoidance of intra-operative hypotension reduces organ dysfunction are awaited, emerging evidence supports a treatment effect for tighter blood pressure control [13]. However, it is notable that such studies have stimulated debate concerning how closely control group treatment thresholds reflect normal practice [12].

What is the lower threshold of blood pressure that anaesthetists will tolerate before intervening in routine clinical practice given this evidence of harm? It is possibly lower than is recommended based on recent research findings. An understanding of the degree of intra-operative hypotension that stimulates intervention to increase blood pressure is needed to define normal practice in the UK, and is essential for future quality improvement or interventional studies. The peri-operative quality initiative consensus statement on intra-operative hypotension recommends avoiding a mean arterial pressure (MAP) <65 mmHg and systolic blood pressure (SBP) <100 mmHg [12]. In their meta-analysis of observational studies, Wesselink et al. identified that a threshold MAP <60–65 mmHg was associated with increasing organ dysfunction [10]. Best practice guidelines for the peri-operative care of the elderly from the Association of Anaesthetists recommend that intra-operative hypotension should be avoided in patients aged ≥65 y and define intra-operative hypotension as a 20% decrease in SBP [11]. However, multiple factors mean that defining optimal treatment for individual patients is not straightforward, including variability in the definition of hypotension [14]; patient vulnerability to hypoperfusion and ischaemia; and the physiological complexity of haemodynamic regulation. Multiple large observational studies highlight a high incidence of intra-operative hypotension, ranging from 41 to 93% depending on the definition used [14, 15]. Although these studies include large patient numbers, many involve data from a limited number of academic centres where practice may not be generalisable to the entire population of anaesthetists [10]. How anaesthetists manage intra-operative hypotension in routine clinical practice has not been defined in a cross-section of UK practice settings. Importantly, it is also unknown to what extent the high level of reported intra-operative hypotension reflects unintended hypotension, or whether anaesthetists are applying a low treatment threshold.

We hypothesised that the majority of older patients in the UK experience intra-operative hypotension below consensus defined thresholds (MAP <65 mmHg, <20% decrease in SBP or SBP <100 mmHg) and this is associated with an intra-operative hypotension treatment threshold that is similarly low. In this study, we aim to describe the incidence of intra-operative hypotension in older patients and define both the intended blood pressure treatment threshold, and the clinically applied treatment threshold for intra-operative hypotension in UK anaesthetic practice.

Methods

The study was designed and conducted by the Research and Audit Federation of Trainees, a UK-based national anaesthetic trainee-led research collaborative. The study received ethical approval from the West London and Gene Therapy Advisory Committee Research Ethics Committee. The Confidentiality Advisory Group of the Health Research Authority approved the collection and transfer of anonymised patient data without consent in England and Wales. The Public Benefit and Privacy Panel provided similar approvals for data acquisition in Scotland.

Patients aged ≥65 y in the UK (England, Scotland and Wales) were enrolled into a prospective observational cohort study during a 48-h weekday period at each site, within an overall 4-week recruitment window from November to December 2016. Enrolled patients were followed-up for 30 days after surgery. Anaesthetists (of any grade or physicians' assistant) providing care for enrolled patients were asked to complete a survey assessing their intended treatment thresholds for intra-operative hypotension. Intra-operative data including blood pressure were evaluated from the paper or electronic anaesthetic record. Intra-operative hypotension data were recorded in the case report form using the definitions specified below. Thirty-day follow-up data were collected from medical records. Data were collated on a Research Electronic Data Capture (REDCap) database (version 6.11.4).

Patients were eligible if they were aged ≥65 y and received general or regional anaesthesia either alone or in combination for elective or emergency surgery. Patients having conscious sedation alone, cardiopulmonary bypass, electroconvulsive therapy, coronary angioplasty procedures or where blood pressure was not recorded during the procedure were excluded. Any anaesthetists who provided intra-operative care to eligible patients were invited to complete the intra-operative hypotension treatment survey.

The primary outcome of the cohort study was the incidence of intra-operative hypotension documented using these conventionally applied definitions: MAP <65 mmHg; SBP reduction >20% from the pre-operative baseline; and SBP <100 mmHg [2, 12, 16]. The nadir intra-operative blood pressure was defined as the lowest SBP recorded on the anaesthetic chart and its associated diastolic blood pressure value. The duration of this event was the period of time that the preceding and following SBP recordings remained within 5 mmHg of the single lowest SBP value; 5-min epochs were used. Two separate baseline blood pressures were recorded: the pre-operative blood pressure was defined as the most recent blood pressure from a pre-operative assessment, clinical letter or ward recording, and the pre-induction blood pressure was defined as the blood pressure value recorded immediately before induction of anaesthesia. Cumulative duration of intra-operative hypotension was defined as the total number of minutes where the SBPs recorded were at least 20% lower than the baseline blood pressure. For cumulative duration, baseline was calculated from the pre-induction blood pressure value. Vasopressor therapy was recorded and blood pressure temporally related to any vasopressor bolus or start of a new vasopressor (if an infusion was used) noted. Relative (percentage change) and absolute (mmHg) blood pressure targets were evaluated against clinical outcomes (AKI, myocardial injury, stroke, death) but the study was not specifically powered for these analyses. Comorbidities were recorded from the anaesthetic chart. Cerebrovascular disease was recorded if transient ischaemic attack or a stroke was documented; chronic kidney disease was recorded if chronic kidney disease stage 1–4 was documented; heart failure was recorded if the anaesthetic chart noted left, right or biventricular failure; ischaemic heart disease was recorded if a past history of angina, myocardial infarction, coronary stents or coronary artery bypass grafting was documented. Urgency of surgery was defined using the NCEPOD Revised Classification of Intervention 2004 [17]. Operative severity was defined using a combination of sources [18–20] (see online Supporting Information, Appendix S2). Baseline creatinine was the pre-operative value taken closest to the date of surgery. The postoperative value was the highest creatinine concentration in the first 7 days after surgery. Creatinine was considered to have risen if the postoperative value exceeded the pre-operative value by >10%, including patients with AKI. We defined AKI using the Kidney Disease Improving Global Outcomes (KDIGO) definition [21], whereby an increase in creatinine concentration ≥1.5 times the baseline value or ≥26.5 µmol.l^{-1} constituted AKI. Myocardial injury was defined as a postoperative troponin enzyme concentration within 7 days of surgery that was above the upper reference limit of the assay manufacturer [22], in keeping with previous work from other groups [1, 2]. Stroke was defined from brain imaging within 7 days of surgery. Mortality was defined as inpatient death within 30 days of surgery. All blood tests and imaging were at the discretion of the clinical teams and were not mandated by the study.

The survey of anaesthetic practice assessed intended intra-operative hypotension treatment thresholds for each practitioner (see online Supporting Information, Appendix S3). This was adapted from a survey by Burns et al. [23] and evaluated the use of relative and absolute blood pressure values which would trigger treatment. The blood pressure treatment threshold was evaluated by both observing the blood pressure that was temporally related to vasopressor administration (clinically applied threshold) and a clinician survey of treatment thresholds (intended treatment threshold). Each anaesthetist completed the survey once, irrespective of the number of their patients included.

Statistical analyses were calculated using R version 3.6.1 (R Core Team) [24] according to the predefined analysis plan. All tests were two-tailed with $p < 0.05$ indicating statistical significance. Based on the previous literature [1], univariable associations between intra-operative hypotension (as defined above) and pre-specified outcomes were performed: mortality; troponin rise; AKI; and a rise in creatinine [1]. Multivariable logistic regression was conducted to adjust for the following baseline confounders: ASA physical status; age; sex; surgical urgency; operative severity; and a pre-existing diagnosis of hypertension.

Results

Data were collected from 4750 patients and surveys completed by 3366 anaesthetists at 196 sites in the UK. Thirty-two patient datasets were excluded from analysis; 26 were incomplete and 6 patients received neither general nor regional anaesthesia. Data were collected from 93.9% of

potentially eligible patients and surveys completed by 89.2% of eligible anaesthetists.

Patient characteristics, operative and anaesthetic details are described in Table 1. The majority of patients (54.2%) were aged 65–74 y, received general anaesthesia (82.7%) and were chronically treated with antihypertensive medications (59%). Total intravenous anaesthesia was used in 19.6% and regional anaesthesia in 36.6% of cases. Further details on the anaesthetic techniques are described in the online Supporting Information, Table S1.

Non-invasive blood pressure recording was used in 4057 (85.9%) patients and invasive monitoring via an arterial catheter in 667 (14.1%). Intra-operative blood pressure data were obtained from hand-written anaesthetic charts (3963, 83.9%) or electronic records (761, 16.1%). The lowest recorded (nadir) SBP (mean difference −9.5 mmHg, 95%CI −8.1 to −10.9 mmHg, p < 0.001) and MAP (mean difference −4.3 mmHg, 95%CI −3.2 to −5.5 mmHg, p < 0.001) were significantly lower in data obtained from electronic records compared with hand-written records.

Figure 1 illustrates variation in the frequency of hypotension as a function of the definition used. The incidence of intra-operative hypotension at key thresholds included: MAP <65 mmHg (61.0%); SBP <100 mmHg (77.5%); >20% reduction in MAP (90.5%); and >20% reduction in SBP (91.3%). The lowest recorded blood pressure most frequently occurred during the first 30 min of anaesthesia (64.6%). The duration of this nadir blood pressure is described in further detail in Table 2. In the majority of patients, the episode lasted <10 min, whether compared against pre-induction (56.0%) or pre-operative blood pressure (64.9%). Mean pre-induction SBP and MAP were higher than that measured pre-operatively, with a SBP difference of 6.3 mmHg (95%CI 5.6–7.1 mmHg, p < 0.001, mean (SD) pre-operative SBP 141.9 mmHg (20.7 mmHg), mean pre-induction SBP 148.3 mmHg (23.9 mmHg)) and MAP difference 0.7 mmHg (95%CI 0.2–1.3 mmHg, p = 0.005, mean pre-operative MAP 98.3 mmHg (SD 13.2 mmHg), mean pre-induction MAP 99.0 mmHg (17.6 mmHg)). The times spent below the 20% and 40% blood pressure thresholds are illustrated in Table 3. The majority (2728, 57.9%) of patients spent >30 min >20% below a pre-induction baseline blood pressure (Table 3). A total of 2130 (45.2%) patients experienced a SBP ≥40% below their pre-induction baseline; this lasted >30 min in 620 (13.2%) of patients.

When managing intra-operative hypotension, most anaesthetists administered vasopressors as boluses (4274,

90.7%). Mean (SD) blood pressure values documented on anaesthetic records as triggering vasopressor boluses were SBP 92.0 (17.2) mmHg and MAP 64.2 (11.6) mmHg. Infusions were used in 439 (9.3%) cases; metaraminol was the most commonly used drug (278, 63.3%) followed by phenylephrine (87, 19.8%) and noradrenaline (58, 13.2%). A small proportion of patients (40, 0.9%) received a vasopressor infusion pre-operatively. Vasopressor infusions were continued in the post-anaesthetic care unit in 88 (20.0%) cases where they were used intra-operatively.

Three hundred and forty-five patients (7.3%) had a composite adverse outcome of renal injury, myocardial injury, stroke or death. Creatinine measurements were performed pre-operatively in 4477 (95.0%) patients and in the first 7 days postoperatively in 2513 (53.3%) patients. Median (IQR [range]) pre-operative creatinine was 78 (66-96 (29–1130) μmol.l^{-1} and postoperatively 82 (66–108 [31–1129]) μmol.l^{-1}. Postoperative creatinine was >10% higher than the pre-operative value in 1412 (56.2%) patients who had both pre- and postoperative values. Acute kidney injury (KDIGO criteria) occurred in 211 (8.4%) patients overall (KDIGO stage 1, 110 patients (4.4%); stage 2, 41 (1.6%); and stage 3, 60 (2.4%)). Cardiac enzymes were assayed in 112 (2.4%) patients in the first 7 days after surgery; 70 of these (62.5%) had a value above the reference range. Forty-seven (0.99%) patients were investigated for stroke using brain imaging in the first 7 days postoperatively; one had an ischaemic stroke. Sixty-three (1.3%) patients died in hospital within 30 days of surgery, a median of 11 (IQR 4.0–19.5 [0–30.0]) days postoperatively. Using univariable analysis (see Table 4), there was no association between an isolated MAP <65 mmHg and any of these outcomes. There was an association between cumulative time spent with SBP >20% below pre-induction value with death (OR 0.68, 95%CI 0.46–0.94, p = 0.04) and a creatinine rise (OR 1.16, 95%CI 1.09–1.23, p < 0.001). On multivariable analysis, there was an association between cumulative duration of systolic hypotension >20% below baseline and creatinine rise (OR 1.09, 95%CI 1.02–1.16, p = 0.01) within the first 7 postoperative days. The associations between blood pressure thresholds and creatinine rise, renal injury according to KDIGO criteria and elevated troponin within 7 days of surgery and in-hospital mortality within 30 days of surgery are described in the online Supporting Information, Table S2-S5.

The survey was completed by 3366 anaesthetists, comprising consultants (1991, 59.2%); registrars (493, 14.6%); associate specialists (388, 11.5%); core trainees (443, 13.2%); and a small number of physicians' assistants (30, 0.9%). Anaesthetists stated they used systolic (2399,

Table 1 Baseline patient characteristics, surgical and anaesthetic details with proportion developing intra-operative hypotension defined as a lowest intra-operative mean arterial pressure (MAP) <65 mmHg. Values are number (proportion).

	Total population	Proportion who developed intra-operative hypotension
Sex		
Female	2359 (50.0%)	1485 (63.0%)
Male	2359 (50.0%)	1349 (57.2%)
Age; y		
65–74	2558 (54.2%)	1540 (60.2%)
75–84	1661 (35.2%)	981 (59.1%)
85–94	470 (10.0%)	293 (62.3%)
≥95	29 (0.6%)	20 (69.0%)
Comorbidities		
Hypertension	2439 (51.7%)	1416 (58.1%)
Ischaemic heart disease	771 (16.3%)	454 (58.9%)
Diabetes mellitus	751 (15.9%)	448 (59.7%)
Cerebrovascular disease	431 (9.1%)	252 (58.5%)
Chronic kidney disease	387 (8.2%)	227 (58.7%)
Heart failure	194 (4.1%)	118 (60.8%)
Peripheral vascular disease	180 (3.8%)	104 (57.8%)
Nil	1493 (31.6%)	943 (63.2%)
Antihypertensives		
ACE-inhibitor/ angiotensin-2 receptor antagonist	1586 (33.6%)	941 (59.3%)
Beta-blocker	895 (19.0%)	555 (62.0%)
Calcium channel blocker	1084 (23.0%)	601 (55.4%)
Diuretic	788 (16.7%)	460 (58.4%)
Other	233 (4.9%)	133 (57.1%)
Vasodilator infusion, e.g. GTN	24 (0.5%)	11 (45.8%)
Nil / not recorded	1935 (41.0%)	1187 (61.3%)
Number in use		
1	1460 (30.9%)	873 (59.8%)
2	898 (19.0%)	539 (60.0%)
3+	427 (9.1%)	237 (55.5%)
ASA physical status		
1	256 (5.4%)	164 (64.1%)
2	2192 (46.5%)	1333 (60.8%)
3	1556 (33.0%)	915 (58.8%)
4	217 (4.6%)	129 (59.4%)
5	4 (0.1%)	2 (50.0%)
Not recorded	493 (10.4%)	291 (59.0%)
Surgical speciality		
Orthopaedics	1239 (26.3%)	701 (56.6%)
General surgery (upper and lower GI, HPB, breast, bariatrics etc.)	1078 (22.8%)	694 (64.4%)
Urology	787 (16.7%)	433 (55.0%)
ENT/ Head and Neck	308 (6.5%)	188 (61.0%)
Trauma	263 (5.6%)	180 (68.4%)

Table 1 (*continued*)

	Total population	Proportion who developed intra-operative hypotension
Gynaecology	230 (4.9%)	144 (62.6%)
Vascular	184 (3.9%)	104 (56.5%)
Ophthalmology	151 (3.2%)	67 (44.4%)
Other	103 (2.2%)	69 (67.0%)
Thoracic	97 (2.1%)	76 (78.4%)
Neurosurgery	91 (1.9%)	51 (56.0%)
Plastic surgery	88 (1.9%)	55 (62.5%)
Spinal	54 (1.1%)	36 (66.7%)
Cardiac (not using cardiopulmonary bypass)	45 (1.0%)	36 (80.0%)
Surgical urgency		
Elective	3358 (71.3%)	1952 (58.0%)
Expedited	468 (9.9%)	301 (64.3%)
Urgent	798 (16.9%)	522 (65.5%)
Immediate	89 (1.9%)	59 (66.3%)
Operative severity		
Minor	954 (20.2%)	494 (51.8%)
Intermediate	1731 (36.7%)	1014 (58.6%)
Major	1301 (27.6%)	836 (64.3%)
Major plus	732 (15.5%)	490 (66.9%)
Procedure where surgeon might request hypotension[a]	171 (3.6%)	117 (68.4%)
General anaesthesia	3906 (82.7%)	2531 (64.8%)
Inhalational	3149 (79.5%)	2082 (66.1%)
Total intravenous anaesthesia	778 (19.6%)	455 (58.5%)
Regional anaesthesia	1729 (36.6%)	932 (53.9%)
Neuraxial block	1127 (23.9%)	530 (47.0%)
Peripheral nerve block	603 (12.8%)	336 (55.7%)

GTN, glyceryl trinitrate; GI, gastrointestinal; HPB, hepatopancreaticobiliary; ENT, ear, nose and throat.
See online supporting information Table S6 for more definitions of intra-operative hypotension.
[a]Procedures listed were: maxillofacial surgery, middle ear surgery, endoscopic sinus surgery, spinal surgery, major orthopaedic surgery and prostatectomy.

71.3%), mean (2662, 79.1%) and diastolic blood pressure (558, 16.6%) to titrate vasopressor therapy. Figure 2 illustrates absolute and relative thresholds for SBP and MAP comparing the clinically applied treatment threshold (documented blood pressure trigger threshold associated with vasopressor administration in the anaesthetic record), and the intended treatment threshold (blood pressure treatment threshold stated in the survey). The clinically applied threshold (vasopressor administration) and intended threshold (survey) had a similar distribution for absolute SBP and MAP (Fig. 2). Median absolute SBP threshold for both the clinically applied treatment threshold and intended treatment threshold from the survey occurred at a SBP of 90–95 mmHg. Median (IQR [range]) absolute

MAP intended treatment threshold was stated as 60 (55–65 [30–90]) mmHg in the survey and the clinically applied threshold was 63 (57–70 [27–142]) mmHg. Anaesthetists most frequently stated that they intended to treat a 20% decrease in SBP or MAP; the most frequent SBP and MAP percentage decreases triggering treatment were 40% reductions (see Fig. 2).

Discussion

We have demonstrated that intra-operative hypotension is documented in the majority of patients aged ≥65 y undergoing surgery in the UK using any of the applied definitions. Prolonged intra-operative hypotension was also prevalent in the majority of patients. Although this could
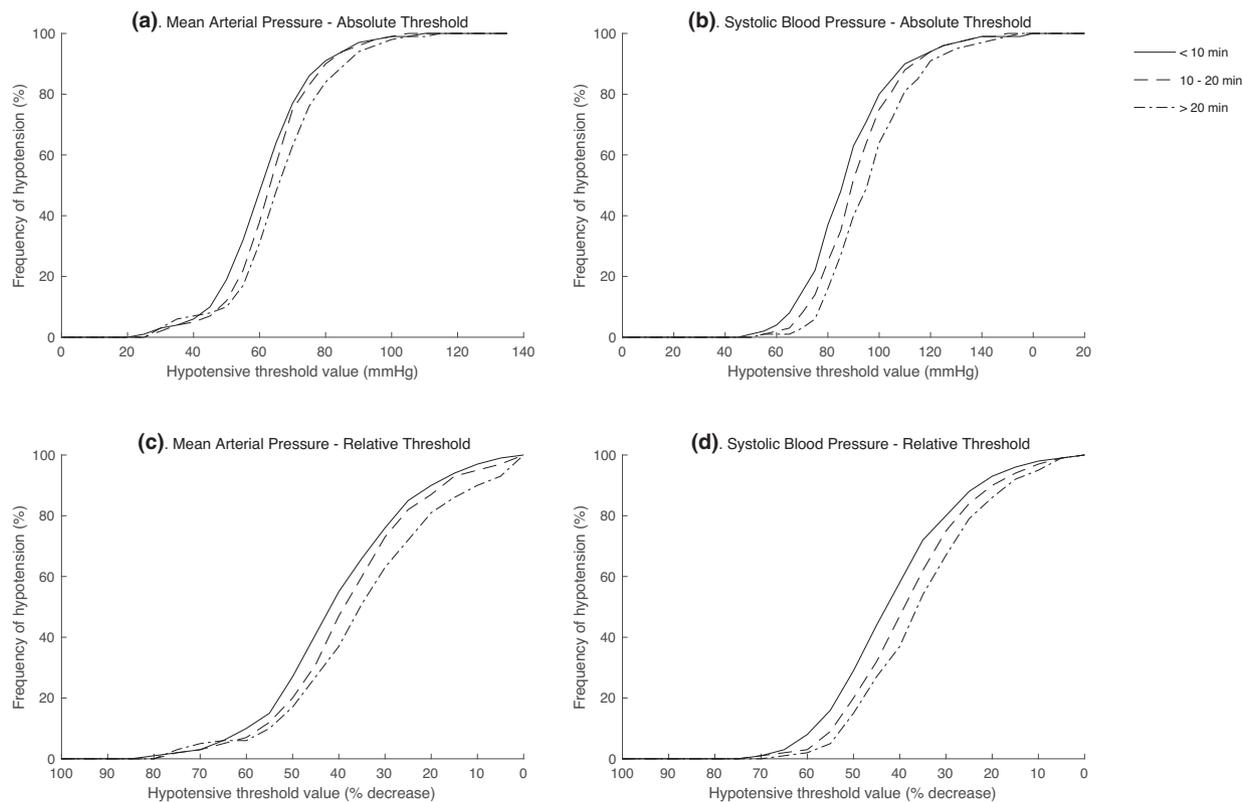
Figure 1 Proportion of patients who are hypotensive at given different thresholds to define hypotension. Y-axis denotes the proportion of patients hypotensive given the defining threshold on the x-axis for (a) absolute mean arterial pressure; (b) absolute systolic blood pressure; (c) relative change in mean arterial pressure from pre-operative blood pressure; and (d) relative change in systolic blood pressure from pre-operative blood pressure. This is defined for decreases lasting <10 min (—), 10–20 min (— —) and >20 min (_. _.).

Table 2 Duration of nadir blood pressure (BP) defined by relative decrease in systolic blood pressure. This is described as the percentage of patients experiencing a decrease lasting the different time categories. For the isolated nadir, the majority of patients experienced <10 min hypotension. Frequencies are similar whether pre-induction BP (top row) or pre-operative BP (bottom row) is used.

		Duration of nadir intra-operative BP (min)			
		<10	**10–20**	**20–30**	**>30**
vs. pre-induction BP	<20%	6.1	2.5	0.4	0.7
	20–40%	21.6	10.5	2.1	1.5
	>40%	28.3	9.0	1.5	0.8
vs. pre-operative BP	<20%	8.3	4.1	0.9	0.8
	20–40%	28.0	13.0	2.4	1.9
	>40%	28.6	8.9	1.4	0.7

reflect patient frailty and lack of haemodynamic reserve, the survey (intended treatment threshold) and vasopressor administration data (applied threshold) suggest the majority of anaesthetists are applying an absolute target that is below the treatment thresholds suggested in the literature (median intended treatment threshold SBP <90 mmHg, MAP <65 mmHg) [12]. The relative decrease definitions are less congruent, while anaesthetists stated in the survey that they intended to treat a >20% decrease, the median applied treatment threshold was >40% decrease, and may highlight that clinicians are acting on absolute targets rather than calculating relative thresholds. This

Table 3 Proportion of patients with cumulative duration of intra-operative hypotension below different thresholds of reduction from the pre-induction baseline systolic blood pressure (SBP).

Reduction in SBP	Cumulative time spent below pre-induction SBP (min)		
	0–30	30–60	>60
20–40%	39.0%	20.9%	23.8%
>40%	32.0%	8.2%	5.0%

exposure to intra-operative hypotension is associated with organ dysfunction, as has been highlighted in numerous previous investigations [1–7]. The cumulative exposure to SBP >20% below baseline was associated with increased postoperative creatinine concentrations, highlighting the potential impact of the intra-operative hypotension observed in our study on renal function. Because troponin is not routinely evaluated postoperatively and only a small number of tests were reported, this study lacks the power to detect any associations with postoperative troponin concentration that have been demonstrated in other studies.

Although the majority of anaesthetic records evaluated were handwritten, these data are still likely to highlight the blood pressure threshold anaesthetists intend to target and this is a key focus to consider during the design of future quality improvement projects and trials. The incidence of intra-operative hypotension identified is greater than previous evaluations. Bijker et al. demonstrated incidence

of intra-operative hypotension (from electronic records) of SBP <100 mmHg (71%); MAP <65 mmHg (49%), relative decrease >20% in SBP (88%) in a non-cardiac surgery population [14], whilst White et al. identified a 90% incidence of >20% relative SBP decrease and 77% incidence of SBP <100 mmHg in a UK hip fracture population [16]. The incidence of intra-operative hypotension in this study could be underestimating the true value as it is based largely on handwritten records and the data from electronic records showed significantly lower intra-operative nadir SBP and MAP values. The widely described association between intra-operative hypotension with AKI, myocardial injury and death may mean that we are potentially exposing older patients to excessive avoidable complications.

Our results also have implications for the generalisability of intra-operative hypotension research to the UK population and design of intra-operative hypotension studies. In the INPRESS trial of intra-operative hypotension management, Futier et al. randomised participants to an intervention group, where SBP was maintained within 10% of resting baseline SBP using a peripheral noradrenaline infusion, or a control group that received ephedrine boluses if a threshold SBP of <80 mmHg or relative decrease >40% SBP occurred [13]. While the control group has been questioned as non-representative of normal treatment [12], our results suggest the large relative decrease (40%) is consistent with normal UK practice. Likewise, the ongoing POISE-3 trial targets a MAP >60 mmHg in its control group; 50% of our studied

Table 4 The relationship between different blood pressure variables and outcomes.

Outcome	Lowest isolated MAP <65 mmHg				
	Univariable		Adjusted		
	Odds ratio (95%CI)	p value	Odds ratio (95%CI)	p value	
Creatinine rise > 10%	1.04 (0.91–1.18)	0.54	0.99 (0.86–1.14)	0.89	
AKI (KDIGO stages 1–3)	1.05 (0.77–1.46)	0.73	1.06 (0.76–1.49)	0.75	
Elevated troponin	1.12 (0.69–1.85)	0.63	1.02 (0.6–1.79)	0.93	
Death	1.58 (0.93–2.78)	0.09	1.67 (0.93–3.12)	0.10	
	Cumulative duration >20% below pre-induction SBP				
Creatinine rise > 10%	1.16 (1.09–1.23)	<0.001	1.09 (1.02–1.16)	0.01	
AKI (KDIGO stages 1–3)	1.11 (0.98–1.25)	0.07	1.1 (0.94–1.24)	0.19	
Elevated troponin	1.11 (0.89–1.29)	0.27	1.15 (0.9–1.39)	0.19	
Death	0.68 (0.46–0.94)	0.04	0.73 (0.48–1.04)	0.11	

MAP, mean arterial pressure; SBP, systolic blood pressure; AKI, acute kidney injury; KDIGO, Kidney Disease: Improving Global Outcomes.
Creatinine rise included all patients with a postoperative creatinine value that was ≥ 10% of the pre-operative value and included those patients meeting the criteria for AKI.
Elevated troponin was defined as a postoperative troponin enzyme concentration within 7 days of surgery above the upper reference limit of the assay manufacturer.
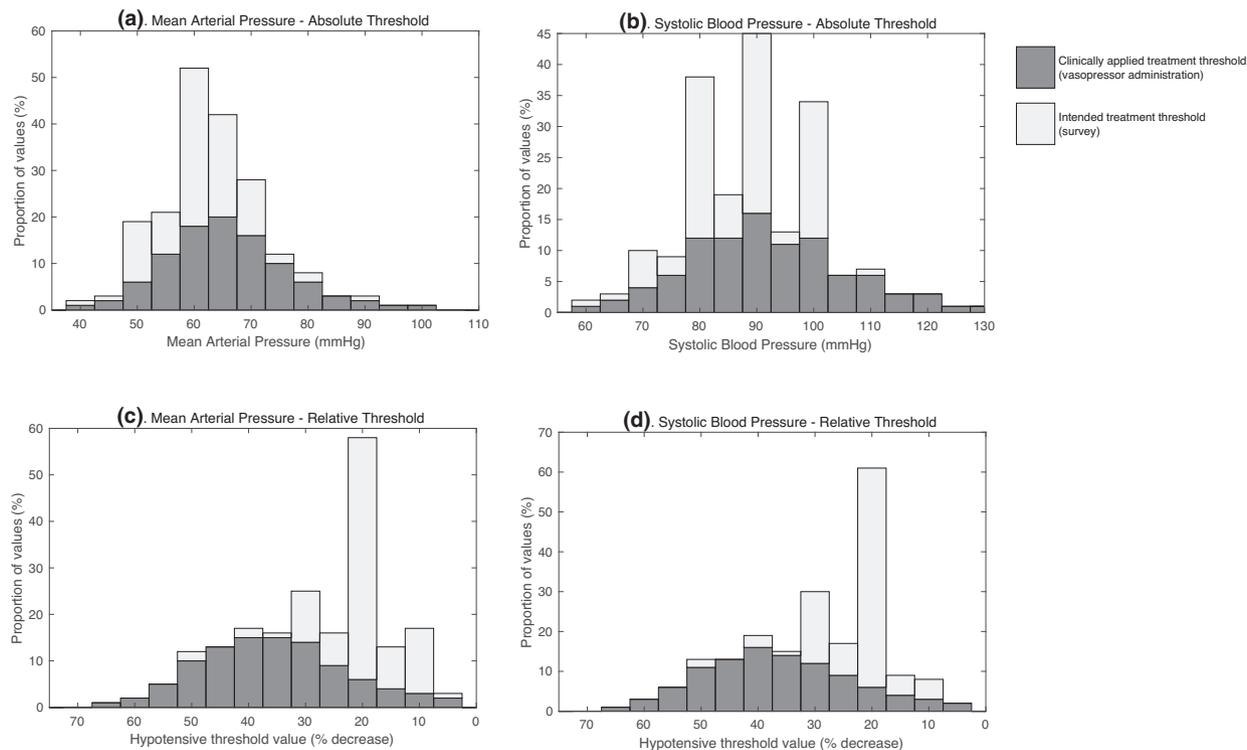
Figure 2 Thresholds at which anaesthetists give vasopressor treatments and their intended treatment thresholds. Y-axis denotes the proportion of patient episodes/respondents given the defining threshold on the x-axis for (a) absolute mean arterial pressure; (b) absolute systolic blood pressure; (c) relative change in mean arterial pressure from pre-operative blood pressure; and (d) relative change in systolic blood pressure from pre-operative blood pressure.

anaesthetists treat below this threshold. Some consensus is needed between the level of intra-operative hypotension that mandates therapy from a quality improvement standpoint and the minimally allowed intra-operative blood pressure level as a control group in research studies. The high rate of intra-operative hypotension (and intended treatment target) below MAP 60 mmHg and >40% decrease in MAP mean there is a large proportion of patients who could potentially benefit from tighter control (if it were beneficial), and the generalisability of intra-operative hypotension studies may be affected by a control group which does not reflect the high levels of intra-operative hypotension observed in normal clinical care in the UK.

This study provides a reliable estimate of the current documented incidence and management of intra-operative hypotension in England, Scotland and Wales. It took place in 196 centres across these countries and in a wide variety of surgical specialities involving a large number of anaesthetists. Many other studies have retrospectively studied a single organisation's dataset or taken place within trials in academic centres.

There are limitations to our study which warrant discussion. First, it relied on handwritten anaesthetic records with 5-min intervals whose reliability has been questioned [22]. However, such intervals are standard for UK practice and the written blood pressure is likely to be consistent with anaesthetists' intended treatment thresholds, which was the key parameter of interest in this study. Second, we reported treatment thresholds based on vasopressor administration only as this is readily identifiable from most anaesthetic records but may not reflect that fluid infusion rate or adjustments to anaesthetic dose may have been the first reaction to intra-operative hypotension. Third, we used pre-induction blood pressure as a value for comparison to evaluate the duration of relative blood pressure changes. The blood pressure immediately pre-induction is widely considered to be elevated due to patient anxiety before surgery. However, our study, and others [25, 26], found only a small difference between mean pre-operative and pre-induction MAP. The broader issue is the high degree of blood pressure variation in individuals throughout any 24-h period, such that using any single point blood pressure as baseline is only an estimate of the mean blood pressure for an individual over this period [26]. Fourth, we assessed patients for cardiovascular comorbidities, but did not adjust for frailty, which is related

to the outcome of interest. This was for pragmatic reasons due to the non-consenting nature of the study. Finally, the study was not designed to evaluate the association between intra-operative hypotension and AKI, myocardial injury or stroke, and as such not all patients received testing for these outcomes. This may confound the results as patients perceived as comorbid by the clinical teams are more likely to be investigated for these conditions.

These findings are of importance for anaesthetists caring for older patients. Intra-operative hypotension occurs frequently and is a potentially modifiable risk-factor for peri-operative harm. Why UK anaesthetists do not treat intra-operative hypotension in line with recommendations warrants further research. Although intra-operative hypotension may result in an unanticipated fashion from patient factors, the treatment thresholds identified in this study (both intended and applied) are also below consensus defined as intra-operative hypotension thresholds. The wide range of lowest blood pressure values also has implications for future guidelines, where different thresholds and management strategies (e.g. use of prophylactic vasopressor infusions) might be recommended for different cohorts of patients. Increased pharmacological intervention has the potential to reduce the incidence of intra-operative hypotension, but a balance must be struck between acting on associations derived from observational studies and awaiting results from emerging clinical trials which may inform on specific haemodynamic therapies [13] and monitoring [27] to improve outcome. Additionally, anaesthetists must be mindful of the potential risks associated with increased use of vasoactive medicines, particularly in patients with ischaemic heart disease, such as profound hypertension and its sequelae, drug errors and extravasation injuries. Other areas of research that could inform future randomised trials include qualitative and quantitative work on whether anaesthetists adopt different blood pressure management strategies in different patients; which interventions are used to manage intra-operative hypotension; the factors that influence these choices; and whether anaesthetists react differently to prolonged or refractory intra-operative hypotension.

Intra-operative hypotension is an extremely common occurrence in patients aged ≥65 y undergoing surgery in the UK. Our sample is reflective of a broad range of UK practice, and the high rates of intra-operative hypotension mean there is potential for substantial secondary organ injury. While increasing vigilance and recalibration of clinical intra-operative hypotension treatment thresholds could be recommended, well-designed clinical trials are required to define specific therapies that optimally address

the pathophysiology of intra-operative hypotension to improve outcome following surgery.

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Supporting Information

Additional supporting information may be found online via the journal website.

Table S1: Further details on mode of anaesthesia and regional anaesthetic techniques.

Table S2: Intra-operative hypotension associations with post-operative creatinine rise within 7 days of surgery.

Table S3: Intra-operative hypotension associations with renal injury defined by KDIGO criteria within 7 days of surgery.

Table S4: Intra-operative hypotension associations with troponin values above the reference range for the hospital within 7 days of surgery.

Table S5: Intra-operative hypotension associations with in-hospital mortality within 30 days of surgery.

Table S6: Baseline patient characteristics, surgical and anaesthetic details with proportion developing intra-operative hypotension by various definitions.

Appendix S1: Trainee Research Network Leads and Collaborators.

Appendix S2: Operative severity.

Appendix S3: Anaesthetist survey.