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Automated Ambulatory Blood Pressure Measurements and Intraoperative Hypotension in Patients Having Noncardiac Surgery with General Anesthesia

A Prospective Observational Study

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Intraoperative hypotension is associated with significant postoperative complications
- Intraoperative hypotension has been defined relative to preinduction blood pressure
- Blood pressure varies during the day, and the relationship between preinduction blood pressure and usual blood pressure over 24 h is incompletely described
- Similarly the relationship between low blood pressure intraoperatively and 24-h usual blood pressure is unknown

What This Article Tells Us That Is New

- There is a <u>poor correlation</u> between <u>preinduction</u> blood pressure and the <u>usual</u> blood pressure over 24 h
- In two thirds of patients, the lowest postinduction and intraoperative pressures were lower than the lowest nighttime blood pressure

ABSTRACT

Background: Normal blood pressure varies among individuals and over the circadian cycle. Preinduction blood pressure may not be representative of a patient's normal blood pressure profile and cannot give an indication of a patient's usual range of blood pressures. This study therefore aimed to determine the relationship between ambulatory mean arterial pressure and preinduction, postinduction, and intraoperative mean arterial pressures.

Methods: Ambulatory (automated oscillometric measurements at 30-min intervals) and preinduction, postinduction, and intraoperative mean arterial pressures (1-min intervals) were prospectively measured and compared in 370 American Society of Anesthesiology physical status classification I or II patients aged 40 to 65 yr having elective noncardiac surgery with general anesthesia.

Results: There was only a weak correlation between the first preinduction and mean daytime mean arterial pressure (r = 0.429, P < 0.001). The difference between the first preinduction and mean daytime mean arterial pressure varied considerably among individuals. In about two thirds of the patients, the lowest postinduction and intraoperative mean arterial pressures were lower than the lowest nighttime mean arterial pressure. The difference between the lowest nighttime mean arterial pressure and a mean arterial pressure of 65 mmHg varied considerably among individuals. The lowest nighttime mean arterial pressure was higher than 65 mmHg in 263 patients (71%).

Conclusions: Preinduction mean arterial pressure cannot be used as a surrogate for the normal daytime mean arterial pressure. The lowest postinduction and intraoperative mean arterial pressures are lower than the lowest nighttime mean arterial pressure in most patients.

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Intraoperative hypotension is common during noncardiac surgery with general anesthesia¹ and is associated with postoperative kidney and myocardial injury²⁻⁵ and death.⁶⁻⁸ Despite its apparent importance, there is no uniform definition for intraoperative hypotension.¹ It is even unclear whether intraoperative hypotension should be defined based on absolute thresholds⁵ or a decrease from baseline pressure.⁸⁻¹⁰

To further complicate matters, there is also no clear definition of baseline blood pressure, which can refer to values assessed immediately before the induction of general anesthesia or to values assessed at various times and under various conditions before surgery.¹ Consequently, the definition of physiologically relevant perioperative hypotension remains elusive, as are appropriate intraoperative blood

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pressure targets. However, a mean arterial pressure (MAP) less than 65 mmHg is associated with harm in the noncardiac surgical population⁵ and is therefore increasingly used as a population harm threshold in clinical practice.¹¹

Normal blood pressure vazies considerably among individuals and over the 24-h circadian cycle within individuals.^{12,13} We therefore considered the theory that hypotension might be best defined individually, based on personal normal blood pressure profiles.^{10,14} Both physiologic sleep and pharmacologically induced general anesthesia represent states of reduced metabolic and sympathetic nervous system activity. Although the lowest safe blood pressure during surgery with general anesthesia remains unclear, it is plausible that patients may safely tolerate their lowest normal blood pressure that usually occurs at night during sleep. We therefore explored the theory that the MAP observed during physiologic sleep might serve as a surrogate for the definition of an individual harm threshold with regard to adequate organ perfusion during general anesthesia.

Personalized definitions of "baseline blood pressure" and "intraoperative hypotension" may require determining individual normal values well before surgery.¹⁴ In this context, ambulatory blood pressure measurements might reflect the individual blood pressure physiology better than single clinic blood pressure measurements.¹⁵ Based on these considerations, we sought to answer four questions:

- What is the relationship between MAP measured shortly before the induction of general anesthesia and mean daytime MAP? In other words, can the preinduction MAP be used as a surrogate for the individual normal daytime MAP?
- 2) How do postinduction and intraoperative MAP relate to ambulatory MAP? Especially, how often is intraoperative MAP below the lowest preoperative nighttime MAP?
- 3) Is there a consistent relationship between MAP measured shortly before the induction of general anesthesia and the lowest nighttime MAP that might be used to define an individual intraoperative target MAP, assuming that the lowest nighttime MAP value constitutes a safe minimum target?
- 4) What is the relationship between the individual lowest nighttime MAP (assuming this is an individual safe threshold) and 65 mmHg, which represents a population harm threshold?

We addressed these questions prospectively in an observational study in which we recorded ambulatory MAP preoperatively along with perioperative MAP during noncardiac surgery with general anesthesia.

Materials and Methods

Study Design and Setting

Our prospective observational study was approved by the ethics committee (Ethikkommission der Ärztekammer Hamburg, Hamburg, Germany; ethics committee number PV4778); all participating patients provided written informed consent. It was conducted in the Department of Anesthesiology, Center of Anesthesiology and Intensive Care Medicine, University Medical Center Hamburg– Eppendorf (Hamburg, Germany) between January 2015 and May 2016.

Inclusion and Exclusion Criteria

Patients were eligible for study inclusion when they were scheduled for elective noncardiac surgery with general anesthesia in our university hospital and presented as outpatients to our preoperative anesthesia evaluation clinic before admission to the hospital for surgery. Additional inclusion criteria were: age between 40 and 65 yr and American Society of Anesthesiology (ASA) physical status classification I or II. Patients were excluded when automated ambulatory blood pressure monitoring at the nondominant arm was impossible for technical, anatomical, or medical reasons. Patients were also excluded because of pregnancy; secondary chronic arterial hypertension; diabetes mellitus of any type; history of congestive heart failure, chronic kidney disease, or cardiac arrhythmia; abdominal, neurologic, or thoracic surgery; and intraoperative positioning other than supine.

Automated Ambulatory Blood Pressure Monitoring

Participating patients had oscillometric noninvasive automated ambulatory blood pressure monitoring with a BOSO TM2430 device (Bosch + Sohn, Germany) that is validated according to the Association for Advancement of Medical Instrumentation standards.¹⁶ Patients were fitted with a standard or large adult cuff according to the recommendations of the manufacturer using the nondominant arm. We obtained oscillometric blood pressure measurements at 30-min intervals for 1 day and the following night. Automated ambulatory blood pressure monitoring was initiated either in the anesthesia evaluation clinic or at home after training in the clinic. Patients were instructed to follow their daily routine and take prescribed medications as usual.

We defined daytime as 9:00 AM to 9:00 PM and nighttime as 12:00 AM to 06:00 AM.^{17,18} We thus excluded retiring and rising periods because pressures during these periods vary considerably among individuals.^{17,18}

Artifactual readings were reduced by discarding pressure recordings that included: diastolic arterial pressure less than 40 or more than 140 mmHg, diastolic arterial pressure exceeding the preceding or subsequent systolic arterial pressure; pulse pressure less than 20 or more than 100 mmHg; heart rate less than 40 or more than 125 bpm; and systolic arterial pressure less than 50 or more than 240 mmHg.¹⁷⁻¹⁹ Additionally, we excluded measurements that the BOSO TM2430 device considered erroneous, such as absent or nonanalyzable oscillations, zero point adjustment not possible, cuff leak present, and measurement cancelled by user.

Perioperative Blood Pressure Monitoring

We monitored blood pressure with Infinity Delta patient monitors (Dräger Medical, Germany) while patients were in the operating room. Blood pressure was monitored either oscillometrically from an upper-arm cuff at 3-min intervals or continuously from an arterial catheter. We extracted blood pressure values at 1-min intervals for the initial 2h of surgery.

Definition of Perioperative Periods

We differentiated among various perioperative periods (fig. 1).²⁰ The preinduction period lasted from the arrival of the patient in the induction area until the beginning of the induction of general anesthesia. We defined an early postinduction period (first 20 min after the induction of general anesthesia) and a late postinduction period (from the end of the early postinduction period until the start of surgery).²⁰ To characterize the intraoperative period, we defined an early intraoperative period (first 30 min after beginning surgery) and a late intraoperative period from then until the end of surgery (blood pressure recordings were ceased 2h after the start of surgery).²⁰ The postoperative period was defined as the time between the end of surgery and the admission of the patient to the postanesthesia care unit.

Data Acquisition and Statistical Analysis

We extracted medical, biometric, and demographic data, along with procedural information from electronic medical and anesthesia records. We used IBM SPSS Statistics, version 25 (IBM Corp., USA) for statistical analyses. Descriptive results are presented as medians (with 25th and 75th percentiles) for continuous data and as absolute frequencies and percentages for categorical data. Ambulatory and perioperative MAP values are presented as box plots. The frequency distributions of MAP differences between

the first preinduction MAP and the mean daytime MAP, between the first preinduction MAP and the lowest nighttime MAP, and between the lowest nighttime MAP and a MAP of 65 mmHg are shown in histograms. Relations between the first preinduction MAP and the mean daytime MAP and between the first preinduction MAP and the lowest nighttime MAP were examined by scatterplots with trends estimated *via* locally weighted smoothing²¹ and described by Spearman correlation coefficients with associated P values. To compare the preinduction MAP with (1) the mean daytime MAP and (2) the lowest nighttime MAP, we performed Bland-Altman analysis²² and calculated the mean of the differences with SD and 95% limits of agreement ($\pm 2 \times SD$). The relationships between means and differences shown in the Bland-Altman plots were examined by linear regression analyses. We calculated differences between MAP measurements at different time points, tabulated the differences as medians with 25th and 75th percentiles, and tested for significance employing Wilcoxon signed-rank tests for related samples. All statistical tests were two-sided, and P values less than 0.05 were considered statistically significant. Considering a drop-out rate of about 10% and assuming that the incidence of intraoperative hypotension would be around 25% in eligible patients, we estimated that a total number of 450 patients would be sufficient to adequately describe the relation of ambulatory and perioperative MAP.

Results

Patients and Patient Characteristics

We enrolled 450 patients but excluded 80 before the final analysis (fig. 2). We therefore included a total of 370 patients in our analysis. The patients' demographic, biometric, and medical data are shown in table 1.



Fig. 1. Definition of perioperative periods. Schematic illustration showing the preinduction period, early postinduction period, late postinduction period, early intraoperative period, late intraoperative period, and postoperative period. Max = maximum.



Fig. 2. Patient enrollment. Flow diagram illustrating patient enrollment and reasons for exclusion.

Ambulatory MAP

Automated ambulatory blood pressure monitoring was performed a median of 5 (3 to 8) days before the day of surgery. The median number of available ambulatory MAP values was 22 (18 to 24) during the day and 13 (12 to 13) at night. Altogether, 1,771 of 12,314 ambulatory blood pressure measurements (14%) were classified as artifactual readings and excluded (daytime: 1,550 of 7,842 [20%], nighttime: 221 of 4,472 [5%]). The first MAP measured during automated ambulatory blood pressure monitoring and the mean and lowest ambulatory MAP measured during the predefined daytime and nighttime periods are shown in table 2 and figure 3.

The median lowest nighttime MAP was 70 (64 to 78) mmHg with a minimum of 50 mmHg and a maximum of 123 mmHg. The mean nighttime MAP was lower than the mean daytime MAP in 351 patients (95%). The lowest nighttime MAP was lower than the lowest daytime MAP in 253 patients (68%). The differences between the mean daytime and night-time MAP and the lowest daytime and nighttime MAP values are shown in Supplementary Digital Content 1 (http://links.lww.com/ALN/B921), Supplementary Digital Content 2 (http://links.lww.com/ALN/B922), and Supplementary Digital Content 3 (http://links.lww.com/ALN/B923).

Perioperative MAP

The MAP measured during the preinduction period, the early and late postinduction periods, the early and late intraoperative periods, and the postoperative period are shown in table 2 and figure 3.

Research question 1: What is the relationship between MAP measured shortly before the induction of general anesthesia and mean daytime MAP?

Table 1. Patient Characteristics

Patient Characteristics	
Age, yr	52 (47-57)
Sex, female, male, transgender; n (%)	172 (47), 196 (53), 2 (1)
Height, cm	172 (165–180)
Actual body weight, kg	76 (66–89)
American Society of Anesthesiology physical	84 (23), 286 (77)
status classification I, II; n (%)	
Type of surgery	
Ear nose and throat, n (%)	135 (37)
Oral and maxillofacial, n (%)	63 (17)
Gynecology, n (%)	59 (16)
Urology, n (%)	50 (14)
Trauma, n (%)	29 (8)
General, n (%)	29 (8)
Others, n (%)	5 (1)
Clinical characteristics	
Rapid-sequence induction, n (%)	12 (3)
Chronic arterial hypertension, n (%)	87 (24)
Coronary artery disease, n (%)	7 (2)
Cerebrovascular disease, n (%)	4 (1)
Peripheral artery occlusive disease, n (%)	5 (1)
Oral premedication with midazolam 3.75 or	314 (85)
7.5 mg, n (%)	
Antihypertensive medication	
Angiotensin-converting enzyme inhibitors, n (%);	36 (10);
continued, n (% of patients with medication)	5 (14)
Angiotensin II type 1 receptor blocker, n (%);	30 (8);
continued, n (% of patients with medication)	7 (23)
β blockers, n (%); continued, n (% of patients	43 (12);
with medication)	42 (98)
Calcium antagonists, n (%); continued, n (% of	23 (6);
patients with medication)	14 (61)
Diuretics, n (%); continued, n (% of patients with	13 (4);
medication)	2 (15)
Potassium-sparing diuretics, n (%); continued, n	2 (1);
(% of patients with medication)	1 (50)
Aldosterone antagonists, n (%); continued, n (% o	f 2 (1);
patients with medication)	1 (50)
α 1 blockers, n (%); continued, n (% of patients	1 (0);
with medication)	1 (100)
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The differences between the first preinduction and the mean daytime MAP are illustrated in figure 4A. The differences varied considerably among individuals. In 167 patients (45%), the first preinduction MAP was higher than the mean daytime MAP. In 67 patients (18%), the first preinduction MAP was more than 10 mmHg higher than the mean daytime MAP. In 80 patients (22%), the first preinduction MAP was higher than 110 mmHg. In 37 of these 80 patients (46%), the mean daytime MAP was higher than 110 mmHg. There was a statistically significant but weak correlation between the first preinduction MAP and the mean daytime MAP (r = 0.429, P < 0.001; fig. 4B). The mean of the differences between the first preinduction MAP and the mean daytime MAP was 0 mmHg with a SD of 13 mmHg and 95% limits of agreement of -26 to 26 mmHg (fig. 4C).

Research question 2: How do postinduction and intraoperative MAP relate to ambulatory MAP?

Table 2. Ambulatory and Perioperative Mean Arterial Pressure

	Mean Arterial Pressure, mmHg		
	Median (25th–75th Percentile)	Minimum	Maximum
Ambulatory mean arterial pressure			
First measurement	109 (98–123)	56	176
Daytime, mean value	100 (94–108)	<u>79</u>	<u>143</u>
Daytime, lowest value	77 (69–85)	50	118
Nighttime, mean value	84 (78–92)	64	138
Nighttime, <mark>lowest</mark> value	<mark>70</mark> (64–78)	50	123
Perioperative mean arterial pressure			
Preinduction, first measurement	100 (91–109)	55	154
Preinduction, lowest value	97 (88–105)	53	149
Early postinduction, lowest value	64 (58–71)	34	138
Late postinduction, lowest value	61 (56–68)	35	121
Early intraoperative, lowest value	64 (58–72)	39	101
Late intraoperative, lowest value	70 (63–77)	46	114
Postoperative, lowest value	<mark>75</mark> (66–86)	29	137

In most patients, the lowest MAP values during the postinduction and intraoperative periods were lower than the lowest daytime MAP (fig. 3; Supplementary Digital Content 4, http://links.lww.com/ALN/B924). In about two thirds of the patients, the lowest MAP values in the postinduction periods and the early intraoperative period were below the lowest nighttime MAP.

Research question 3: Is there a consistent relationship between MAP measured shortly before the induction of general anesthesia and the lowest nighttime MAP?

The differences between the first preinduction MAP and the lowest nighttime MAP are shown in figure 5A. There was a statistically significant but weak correlation between the first preinduction MAP and the lowest nighttime MAP (r = 0.390, P < 0.001; fig. 5B). The mean of the differences between the first preinduction MAP and the lowest nighttime MAP was 30 mmHg with a SD of 14 mmHg and 95% limits of agreement of 2 to 58 mmHg (fig. 5C). In 44 (55%) of the 80 patients with a first preinduction MAP higher than 110 mmHg, the mean nighttime MAP was higher than 90 mmHg.

Research question 4: What is the relationship between the individual lowest nighttime MAP (assuming this is an individual safe threshold) and 65 mmHg, which represents a population harm threshold)

The difference between the lowest nighttime MAP and a MAP of 65 mmHg is shown in figure 6. The differences varied considerably among individuals. In 263 patients (71%), the lowest nighttime MAP was above 65 mmHg.

Discussion

We evaluated differences between ambulatory and perioperative MAP in patients who had elective noncardiac surgery with general anesthesia. One aim of the study was

to determine whether the preinduction MAP can serve as a surrogate for the patient's individual normal daytime MAP. Previous studies suggested that preinduction MAP is about 10 mmHg higher than normal daytime MAP.^{23,24} We observed only a weak correlation (and wide limits of agreement) between the first preinduction MAP and the mean daytime MAP. Marked variability between preinduction MAP and mean daytime MAP among individuals indicates that MAP assessed just before the induction of general anesthesia cannot serve as a surrogate for the individual normal daytime MAP. Only about half the patients who had a preinduction MAP exceeding 110 mmHg also had a mean daytime MAP exceeding 110 mmHg or a mean nighttime MAP exceeding 90 mmHg. High preinduction MAP values thus often represent situational hypertension induced by preoperative stress or anxiety. Our finding is consistent with a retrospective analysis that compared systolic preinduction blood pressure values with baseline ambulatory blood pressure (defined as the average of at least three ambulatory blood pressure measurements obtained during separate outpatient clinic visits in the 7 months before surgery) in elective noncardiac surgery patients.25 That study showed that in most patients, preinduction blood pressures usually exceed baseline ambulatory blood pressures. Our results extend previous findings by showing that there is considerable variability such that preinduction pressures provide little guidance about a patient's usual blood pressure.

We also aimed to evaluate how postinduction MAP and intraoperative MAP relate to ambulatory MAP. MAP during surgery with general anesthesia was markedly lower than the mean daytime MAP, mean nighttime MAP, and lowest preinduction MAP in most patients. Moreover, the lowest MAP values during the postinduction and intraoperative periods were lower than the lowest daytime MAP in

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most patients. In fact, in about two thirds of our patients, the lowest MAP values in the <u>postinduction</u> periods and the early <u>intraoperative</u> period were even <u>lower</u> than the <u>lowest</u> <u>nighttime</u> MAP value.

We aimed to define hypotension individually based on personal normal blood pressure profiles^{10,14} and determine whether there is a consistent relationship between preinduction MAP and the lowest nighttime MAP that might be used to define individual perioperative target MAP, assuming that the lowest nighttime MAP value constitutes an individual safe minimum target. We observed marked interindividual variability, weak correlation, and poor agreement between the preinduction MAP and the lowest nighttime MAP. Therefore, perioperative target MAP for individual patients cannot be defined based on preinduction MAP values. The definition of physiologically relevant perioperative hypotension remains elusive, but a MAP of 65 mmHg is increasingly used as a pragmatic population harm threshold.⁵ Therefore, we finally investigated the relationship between the individual lowest nighttime MAP and 65 mmHg. Importantly, the population harm threshold is defined by the pressure at which harm accumulates in the most sensitive members of the population. Most members will safely tolerate lower pressures, although it may be hard or impossible to *a priori* distinguish sensitive from tolerant members. To further complicate matters, the population is a statistical construct; there surely are at least some patients who truly require higher pressures.

In more than two thirds of our patients, the lowest nighttime MAP was above 65 mmHg. Some patients with a lowest nighttime MAP above 65 mmHg may need

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Fig. 4. First preinduction mean arterial pressure (MAP) *versus* mean daytime MAP. (*A*) Histogram showing the frequency (n; y axis; n total = 361) of the differences between the first preinduction MAP and the mean daytime MAP. The median difference (25th and 75th percentile) was -1 (-8 and +8) mmHg (P < 0.001). The *dotted vertical line* represents the median difference. (*B*) Correlation between the first preinduction MAP and the mean daytime MAP (r = 0.429, P < 0.001). (*C*) Bland–Altman plot comparing the first preinduction MAP and the mean daytime MAP (r = 0.429, P < 0.001). (*C*) Bland–Altman plot comparing the two MAP values, and the *dotted horizontal lines* show the upper and lower 95% limits of agreement ($2 \cdot$ SD). The relationship between mean values and differences is shown by linear regression analyses (*green continuous line*).



Fig. 5. First preinduction mean arterial pressure (MAP) *versus* lowest nighttime MAP. (*A*) Histogram showing the frequency (n; y axis; n total = 361) of the differences between the first preinduction MAP and the lowest nighttime MAP. The median difference (25th and 75th percentile) was +30 (+22 to +39) mmHg (P < 0.001). The *dotted vertical line* represents the median difference. (*B*) Correlation between the first preinduction MAP and the lowest nighttime MAP (r = 0.390, P < 0.001). (*C*) Bland–Altman plot comparing the first preinduction MAP and the lowest nighttime MAP (r = 0.390, P < 0.001). (*C*) Bland–Altman plot some structure between the two MAP and the lowest nighttime MAP. The *continuous horizontal line* shows the mean of the differences between the two MAP values, the *dotted horizontal lines* show the upper and lower 95% limits of agreement (2 · SD). The relationship between mean values and differences is shown by linear regression analyses (*green continuous line*).

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Fig. 6. Difference between lowest nighttime mean arterial pressure (MAP) and a MAP of 65 mmHg. Histogram showing the frequency (n; y axis; n total = 370) of the difference between the lowest nighttime MAP and a MAP of 65 mmHg. The median difference (25th to 75th percentile range) was +5 (-1 to +13) mmHg. The *dotted vertical line* represents the median difference.

higher intraoperative pressures, meaning that their individual harm threshold is higher than the population harm threshold of 65 mmHg, but of course some may simply have maintained pressure well above their individual thresholds, thus providing little usable information. At this point, we cannot distinguish one response from the other. A further limitation of our approach is that physiologic sleep and general anesthesia have similarities but are hardly identical. Furthermore, hypotension during anesthesia may be associated with low cardiac output, active bleeding, hypoxemia, and other pathophysiologic abnormalities that are rare during natural sleep. Further research is needed to confirm the assumption that physiologic sleep and general anesthesia represent comparable metabolic and physiologic states.

There are only limited data on the relationship between blood pressure profiles of individual patients (including the circadian variation in blood pressure^{12,13}) and blood pressure values obtained during surgery under general anesthesia. In a small prospective observational study published in 1984, Berger *et al.*²⁶ continuously monitored blood pressure with an arterial catheter from the evening before to the morning after surgery in 34 women having gynecologic cancer surgery. The authors hypothesized that physiologic nadirs in blood pressure observed during sleep at nighttime are well tolerated and could thus be used to define physiologically important hypotension.²⁶ In patients younger than 65 yr, they found no clinically important difference between the mean lowest MAP values during anesthesia and the mean lowest nighttime MAP values.²⁶ However, in patients older than 65 yr, intraoperative blood pressures were frequently lower than nighttime blood pressure (mean MAP value during sleep 77 mmHg vs. mean MAP value during anesthesia 67 mmHg; P < 0.05).²⁶ Our study differs both in patient selection and measurement method. Invasive measurements of blood pressure during sleep in the hospital may not reflect the patient's nighttime blood pressure during sleep at home. The use of nighttime sedation, premedication, and epidural anesthesia may also have compromised perioperative blood pressure readings. Soo et al.23 also conducted a prospective study in 18 patients (median age, 65 yr) having elective day surgery and compared blood pressure values assessed by ambulatory blood pressure monitoring with blood pressure values measured before and during general anesthesia. The lowest intraoperative MAP was often lower than the lowest nighttime MAP value in this study as well.

The recently published INPRESS study⁹ provided evidence that individualized intraoperative blood pressure management using a treatment strategy targeting a systolic blood pressure compared with standard management reduces the risk of postoperative organ dysfunction in high-risk elective noncardiac surgery patients. However, in the INPRESS study, the preoperative resting blood pressure was determined using a single noninvasive measurement obtained during either the preoperative anesthesiology consultation or by a nurse on the surgical ward the day before surgery.

Such single clinic blood pressures can vary markedly from ambulatory or home blood pressure readings because of "white coat hypertension" or "masked hypertension."²⁷ Automated ambulatory blood pressure monitoring is currently the best way to assess blood pressure profiles and was feasible and generally well tolerated in our study cohort. However, ambulatory blood pressure monitoring using oscillometric upper-arm cuff measurements is time-consuming and organizationally challenging. Future research might help to identify subgroups of high-risk patients in whom personalized blood pressure management based on ambulatory blood pressure readings might be especially beneficial, such as patients with chronic arterial hypertension or altered baseline renal function. Additionally, novel technologies will surely facilitate ambulatory and home blood pressure monitoring, which will help define individual blood pressure patterns.28-30

We restricted our analysis to middle-aged ASA physical status classification I and II patients having elective lowto intermediate-risk noncardiac surgery. Our results may therefore generalize poorly to the elderly, patients with serious cardiovascular disease, patients with ASA physical status classification of III or higher, and those having emergency or high-risk surgery. Very few patients with a history of coronary artery disease, cerebrovascular disease, or peripheral artery occlusive disease were included in our study,

although these patients would be considered ASA physical status classification III.

Preinduction use of midazolam may have also affected preinduction MAP, although probably not to a substantive degree. Our study was observational; thus, standard clinical management of hypotension (including administration of fluids and vasoactive agents) may have affected the lowest measurement.

Because automated ambulatory blood pressure monitoring was performed intermittently, the recorded lowest daytime and nighttime MAP values may not necessarily be the actual lowest MAP values. As in clinical practice, we used different devices for ambulatory and perioperative blood pressure monitoring. We measured ambulatory and perioperative blood pressure to describe the variation in blood pressure within individual patients over time. However, it needs to be considered that in addition to changes in true blood pressure, measurement error also contributes to the variation in the observed blood pressure values. To minimize the influence of measurement error on the variation in blood pressure and to ensure that the observed variation in blood pressure largely represents changes in true blood pressure over time, we used validated and widely clinically used systems to measure ambulatory and perioperative blood pressures.

In this observational study, we did not standardize anesthesiologic management, and therefore cannot systematically analyze confounding factors that might have influenced intraoperative blood pressure (such as depth of anesthesia, fluid therapy, and use of regional anesthesia). Additionally, we did not seek to describe patient outcomes (*i.e.*, mortality or complications).

Future research may aim at investigating other hemodynamic variables such as heart rate and stroke volume because the product of these two variables, cardiac output, is the primary determinant of organ tissue perfusion and oxygen delivery. Extending our approach to higher-risk patients is a priority. Eventually, the results of the present study may serve as the basis for interventional studies targeting personalized blood pressure targets.

Conclusions

Preinduction MAP cannot be used as a surrogate for the individual normal daytime MAP. In most patients, the lowest postinduction and intraoperative MAPs are markedly lower than the lowest daytime MAP and, in about two thirds of the patients, even lower than the lowest nighttime MAP. The preinduction MAP cannot be used to define individual intraoperative target MAP, assuming that the lowest nighttime MAP constitutes a safe minimum target. In more than two thirds of our patients, the lowest nighttime MAP exceeded 65 mmHg, suggesting that some of these patients may need intraoperative pressures exceeding the population harm threshold of 65 mmHg.

Research Support

Support was provided solely from institutional and/or departmental sources.

Competing Interests

The authors declare no competing interests.

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References

- Bijker JB, van Klei WA, Kappen TH, van Wolfswinkel L, Moons KG, Kalkman CJ: Incidence of intraoperative hypotension as a function of the chosen definition: Literature definitions applied to a retrospective cohort using automated data collection. ANESTHESIOLOGY 2007; 107:213–20
- Walsh M, Devereaux PJ, Garg AX, Kurz A, Turan A, Rodseth RN, Cywinski J, Thabane L, Sessler DI: Relationship between intraoperative mean arterial pressure and clinical outcomes after noncardiac surgery: Toward an empirical definition of hypotension. ANESTHESIOLOGY 2013; 119:507–15
- 3. Sun LY, Wijeysundera DN, Tait GA, Beattie WS: Association of intraoperative hypotension with acute kidney injury after elective noncardiac surgery. ANESTHESIOLOGY 2015; 123:515–23
- van Waes JA, van Klei WA, Wijeysundera DN, van Wolfswinkel L, Lindsay TF, Beattie WS: Association between intraoperative hypotension and myocardial injury after vascular surgery. ANESTHESIOLOGY 2016; 124:35–44
- Salmasi V, Maheshwari K, Yang D, Mascha EJ, Singh A, Sessler DI, Kurz A: Relationship between intraoperative hypotension, defined by either reduction from baseline or absolute thresholds, and acute kidney and myocardial injury after noncardiac surgery: A retrospective cohort analysis. ANESTHESIOLOGY 2017; 126:47–65
- 6. Mascha EJ, Yang D, Weiss S, Sessler DI: Intraoperative mean arterial pressure variability and 30-day mortality in patients having noncardiac surgery. ANESTHESIOLOGY 2015; 123:79–91

- Monk TG, Bronsert MR, Henderson WG, Mangione MP, Sum-Ping ST, Bentt DR, Nguyen JD, Richman JS, Meguid RA, Hammermeister KE: Association between Intraoperative hypotension and hypertension and 30-day postoperative mortality in noncardiac surgery. ANESTHESIOLOGY 2015; 123:307–19
- Stapelfeldt WH, Yuan H, Dryden JK, Strehl KE, Cywinski JB, Ehrenfeld JM, Bromley P: The SLUScore: A novel method for detecting hazardous hypotension in adult patients undergoing noncardiac surgical procedures. Anesth Analg 2017; 124:1135–52
- 9. Futier E, Lefrant JY, Guinot PG, Godet T, Lorne E, Cuvillon P, Bertran S, Leone M, Pastene B, Piriou V, Molliex S,Albanese J,Julia JM, Tavernier B, Imhoff E, Bazin JE, Constantin JM, Pereira B, Jaber S; INPRESS Study Group: Effect of individualized vs. standard blood pressure management strategies on postoperative organ dysfunction among high-risk patients undergoing major surgery: A randomized clinical trial. JAMA 2017; 318:1346–57
- 10. Saugel B, Reuter DA, Reese PC: Intraoperative mean arterial pressure targets: Can databases give us a universally valid "magic number" or does physiology still apply for the individual patient? ANESTHESIOLOGY 2017; 127:725–6
- 11. Sessler DI, Khanna AK: Perioperative myocardial injury and the contribution of hypotension. Intensive Care Med 2018; 44:811–22
- 12. Snyder F, Hobson JA, Goldfrank F: Blood pressure changes during human sleep. Science 1963; 142:1313–4
- 13. Millar-Craig MW, Bishop CN, Raftery EB: Circadian variation of blood-pressure. Lancet 1978; 1:795–7
- 14. Saugel B, Vincent JL, Wagner JY: Personalized hemodynamic management. Curr Opin Crit Care 2017;23:334–41
- Banegas JR, Ruilope LM, de la Sierra A, Vinyoles E, Gorostidi M, de la Cruz JJ, Ruiz-Hurtado G, Segura J, Rodríguez-Artalejo F, Williams B: Relationship between clinic and ambulatory blood-pressure measurements and mortality. N Engl J Med 2018; 378:1509–20
- 16. Palatini P, Frigo G, Bertolo O, Roman E, Da Cortà R, Winnicki M:Validation of the A&D TM-2430 device for ambulatory blood pressure monitoring and evaluation of performance according to subjects' characteristics. Blood Press Monit 1998; 3:255–60
- 17. O'Brien E, Parati G, Stergiou G, Asmar R, Beilin L, Bilo G, Clement D, de la Sierra A, de Leeuw P, Dolan E, Fagard R, Graves J, Head GA, Imai Y, Kario K, Lurbe E, Mallion JM, Mancia G, Mengden T, Myers M, Ogedegbe G, Ohkubo T, Omboni S, Palatini P, Redon J, Ruilope LM, Shennan A, Staessen JA, vanMontfrans G, Verdecchia P, Waeber B, Wang J, Zanchetti A, Zhang Y; European Society of Hypertension Working Group on Blood Pressure Monitoring: European Society of Hypertension position paper on ambulatory blood pressure monitoring. J Hypertens 2013; 31:1731–68
- Parati G, Stergiou G, O'Brien E, Asmar R, Beilin L, Bilo G, Clement D, de la Sierra A, de Leeuw P, Dolan

E, Fagard R, Graves J, Head GA, Imai Y, Kario K, Lurbe E, Mallion JM, Mancia G, Mengden T, Myers M, Ogedegbe G, Ohkubo T, Omboni S, Palatini P, Redon J, Ruilope LM, Shennan A, Staessen JA, vanMontfrans G, Verdecchia P, Waeber B, Wang J, Zanchetti A, Zhang Y; European Society of Hypertension Working Group on Blood Pressure Monitoring and Cardiovascular Variability: European Society of Hypertension practice guidelines for ambulatory blood pressure monitoring. J Hypertens 2014; 32:1359–66

- Winnicki M, Canali C, Mormino P, Palatini P: Ambulatory blood pressure monitoring editing criteria: Is standardization needed? Hypertension and Ambulatory Recording Venetia Study (HARVEST) Group, Italy. Am J Hypertens 1997; 10:419–27
- Südfeld S, Brechnitz S, Wagner JY, Reese PC, Pinnschmidt HO, Reuter DA, Saugel B: Post-induction hypotension and early intraoperative hypotension associated with general anaesthesia. Br J Anaesth 2017; 119:57–64
- 21. Cleveland WS: Robust locally weighted regression and smoothing scatterplots. J Am Stat Assoc 1979; 74: 829–36
- 22. Bland JM, Altman DG: Measuring agreement in method comparison studies. Stat Methods Med Res 1999; 8:135–60
- 23. Soo JC, Lacey S, Kluger R, Silbert BS: Defining intra-operative hypotension: A pilot comparison of blood pressure during sleep and general anaesthesia. Anaesthesia 2011; 66:354–60
- van Klei WA, van Waes JA, Pasma W, Kappen TH, van Wolfswinkel L, Peelen LM, Kalkman CJ: Relationship between preoperative evaluation blood pressure and preinduction blood pressure: A cohort study in patients undergoing general anesthesia. Anesth Analg 2017; 124:431–7
- 25. Drummond JC, Blake JL, Patel PM, Clopton P, Schulteis G: An observational study of the influence of "white-coat hypertension" on day-of-surgery blood pressure determinations. J Neurosurg Anesthesiol 2013; 25:154–61
- Berger JJ, Donchin M, Morgan LS, van der Aa J, Gravenstein JS: Perioperative changes in blood pressure and heart rate. Anesth Analg 1984; 63:647–52
- Kallioinen N, Hill A, Horswill MS, Ward HE, Watson MO: Sources of inaccuracy in the measurement of adult patients' resting blood pressure in clinical settings: A systematic review. J Hypertens 2017; 35:421–41
- 28. Michard F: Smartphones and e-tablets in perioperative medicine. Korean J Anesthesiol 2017; 70:493–9
- 29. Michard F: A sneak peek into digital innovations and wearable sensors for cardiac monitoring. J Clin Monit Comput 2017; 31:253–9
- Michard F, Pinsky MR, Vincent JL: Intensive care medicine in 2050: NEWS for hemodynamic monitoring. Intensive Care Med 2017; 43:440–2