

# 学位論文

The Association between Preoperative Blood  
Pressure Elevations and Postoperative Adverse  
Outcomes after Non-cardiac Surgery:A Single-center  
Retrospective Observational Study

香川大学大学院医学系研究科  
医学専攻

山鳥 佑輔

## The Association between Preoperative Blood Pressure Elevations and Postoperative Adverse Outcomes after Non-cardiac Surgery: A Single-center Retrospective Observational Study

Yusuke Yamadori<sup>a, b\*</sup>, Tomohiro Hirao<sup>b</sup>, Nlandu R. Ngatu<sup>b</sup>, Kanae Kanda<sup>b</sup>,  
Syed Mahfuz Al Hasan<sup>b</sup>, Akitsu Murakami<sup>a, b</sup>, Yukinori Mashima<sup>b, c</sup>, and Gotaro Shirakami<sup>a</sup>

<sup>a</sup>Departments of Anesthesiology, and <sup>b</sup>Public Health, Faculty of Medicine, Kagawa University,  
<sup>c</sup>Department of Medical Informatics, Kagawa University Hospital, Miki-cho, Kagawa 761-0793, Japan

Blood pressure (BP) often rises before surgery. This study investigated whether BP elevation immediately before surgery was associated with adverse outcomes. Medical records of 11,732 patients (average age: 61 years; male: 47.4%) who underwent non-cardiac elective inpatient surgery under general anesthesia at Kagawa University Hospital between January 2011 and June 2019 were reviewed. Differences between the first BP values measured on the day before surgery and the first BP values in the operating room were defined as  $\Delta$  systolic BP ( $\Delta$ SBP) and  $\Delta$  diastolic BP ( $\Delta$ DBP). The relationships between  $\Delta$ SBP/ $\Delta$ DBP and 30-day mortality, 30-day readmission, and over-the-standard length of hospital stay (OSLOS) were assessed. OSLOS was defined as a hospital stay longer than mean + 2 standard deviations and was calculated using the Japanese Diagnosis Procedure Combination data. In univariate analysis, the differences in  $\Delta$ SBP and  $\Delta$ DBP between the OSLOS and standard LOS groups were both 2 mmHg. In multivariate logistic regression analysis, only  $\Delta$ DBP was associated with OSLOS. The adjusted odds ratio (95% confidence interval) for the largest quartile was 1.31 (1.02-1.69) ( $p < 0.05$ ).  $\Delta$ DBP was associated with OSLOS; however, there may be little need to worry about large  $\Delta$ SBPs and  $\Delta$ DBPs in clinical practice.

**Key words:** preoperative blood pressure, pre-induction blood pressure, postoperative adverse outcomes, length of hospital stay, non-cardiac surgery

**B**lood pressure (BP) often becomes elevated immediately before surgery [1-5]. Previous studies have reported a relationship between preoperative high BP (uncontrolled hypertension before entering the operating room) and postoperative adverse outcomes [5-8]. A few studies have also been conducted on postoperative risk assessment in relation to pre-induction BPs, namely, those measured after entering the operating room [9,10]. In clinical practice, patients sometimes enter the operating room with a surprising elevation in BP

compared to baseline due to extreme anxiety [1-3]. However, the relationship between the magnitude of BP elevation during the preoperative period and postoperative adverse outcomes remains unclear.

Therefore, in the context of non-cardiac elective inpatient surgery, we investigated whether the differences between post-admission BPs measured in the surgical ward and pre-induction BPs measured in the operating room were associated with adverse outcomes and the clinical significance of these values.

Received October 10, 2021; accepted March 1, 2022.

\*Corresponding author. Phone: +81-87-891-2223; Fax: +81-87-891-2224  
E-mail: yamadori.yusuke@kagawa-u.ac.jp (Y. Yamadori)

Conflict of Interest Disclosures: No potential conflict of interest relevant to this article was reported.

## Materials and Methods

**Ethical considerations.** The present study was approved by the Kagawa University Hospital Ethics Committee (approval number 2019-189). The need for informed consent was waived because this was a retrospective observational study. However, the content of the study was announced on the hospital bulletin board and homepage to provide patients with the opportunity to censor their data. The study was conducted in accordance with the tenets of the Declaration of Helsinki.

**Study design and patients.** This was a single-center retrospective observational study conducted at Kagawa University Hospital, Japan. We reviewed the medical records of surgical patients aged 18 years or older who were admitted to our hospital between January 2011 and June 2019, and who underwent non-cardiac elective inpatient surgery under general anesthesia. When a patient underwent more than one surgery during the study period, only the first procedure was included. In addition, patients who were hospitalized for more than 10 days before their surgery were excluded because they may have been hospitalized preoperatively for purposes other than surgery (e.g., preoperative chemotherapy, diagnostic tests, or improvement of general condition).

General anesthesia was mostly induced with propofol, maintained with sevoflurane, desflurane, or propofol, and combined with regional anesthesia, such as an epidural or peripheral nerve block, at the discretion of the attending anesthesiologists. Oral medications were continued on the day of surgery following the American College of Cardiology/American Heart Association (ACC/AHA) guidelines [11, 12] or Japan Pharmaceutical

**BP measurement.** The first non-invasive BP measured on the day before surgery in the ward was defined as BP1 (systolic BP1 [SBP1]/diastolic BP1 [DBP1]). BP1 was measured using an automatic sphygmomanometer. The first non-invasive BP measured before the induction of general anesthesia was defined as BP2 (SBP2/DBP2). BP2 was measured using a biological information monitor (IntelliVue Monitors; Philips Medical Systems, Eindhoven, the Netherlands).  $\Delta$ BP, the elevation of BP before surgery, was defined as the difference between BP1 and BP2:  $\Delta$ SBP as SBP2 – SBP1; and  $\Delta$ DBP as DBP2 – DBP1. Patients with missing BP data on the day before surgery and those without non-invasive BP measurements within 10 min of enter-

ing the operating room were excluded from this study.

**Covariates.** Several variables were adopted as covariates for risk adjustment. BP1 was included in the covariates as a baseline for BP elevation. As found in previous reports [2],  $\Delta$ SBP and SBP1, and  $\Delta$ DBP and DBP1 were negatively correlated; however, the correlation coefficients were  $R = -0.15$  and  $R = -0.37$ , respectively, indicating no collinearity. Age and sex were included in the covariates as basic attributes, and the body mass index (BMI), American Society of Anesthesiologists physical status classification (ASA-PS), Revised Cardiac Risk Index (RCRI), and preoperative blood hemoglobin level (Hb) were included as known risk factors [13-16]. Preoperative oral medications were included in the covariates to adjust for the risk of comorbidities; the duration of surgery and intraoperative blood loss were used to adjust for the risk of surgical invasiveness, and the surgical sites were used to adjust for the case-mix of the hospital.

Information on these variables was extracted from electronic medical records. The BMI was calculated using the following formula:  $BMI = \text{weight (kg)}/\text{height}^2 (\text{m}^2)$ . The RCRI is an index of the postoperative cardiovascular risk of non-cardiac surgery based on six factors: “high-risk surgery,” “history of ischemic heart disease,” “history of congestive heart failure,” “history of cerebrovascular disease,” “preoperative treatment with insulin,” and “preoperative serum creatinine level (sCr) > 2.0 mg/dL” [15]. The RCRI was scored on a 4-point scale according to the presence of 0, 1, 2, or  $\geq 3$  of these factors. The Hb and sCr levels before surgery were extracted from the last preoperative blood test results. Patients without blood test data within 90 days before surgery were excluded from this study. The preoperative oral medications evaluated were the following when prescribed within 1 year before surgery: angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin II receptor blockers (ARBs), calcium channel blockers,  $\beta$ -blockers, other antiarrhythmic drugs, aspirin, other antiplatelet drugs, anticoagulants, diuretics, antidiabetics, and/or statins. Surgical sites were classified into one of five categories, namely, head/neck, thoracic, abdominal, limb/spine and “other”. Patients with incomplete covariate information were excluded from this study.

**Outcome variables.** The following three outcomes were measured: mortality on postoperative day 30 (30d-mortality), unplanned readmission within

30 days of hospital discharge (30d-readmission), and over-the-standard length of hospital stay (OSLOS). These data were also extracted from electronic medical records. OSLOS was defined as a hospital stay longer than mean + 2 standard deviation (SD) days and was calculated using the Diagnosis Procedure Combination (DPC) data published by the Japanese Ministry of Health, Labor, and Welfare. DPC data are widely used in Japanese acute care hospitals for payments [17]. Assessing LOS (length of stay) using DPC data made it possible to assess patients with different diseases and injuries using a single endpoint.

**Statistical analyses.** We dichotomized the entire cohort into Non-survived vs. Survived, Readmission vs. No readmission, and OSLOS vs. Standard LOS in the outcome categories of 30d-mortality, 30d-readmission, and OSLOS, respectively. Student's *t*-test was performed to compare the  $\Delta$ SBP and  $\Delta$ DBP between the two groups. When the relationship between outcomes and either of these values was significant, univariate and multivariate logistic regression analyses were performed to assess whether  $\Delta$ SBP or  $\Delta$ DBP was independently associated with adverse outcomes. In the logistic regression analysis,  $\Delta$ SBP and  $\Delta$ DBP were

divided into quartiles, and the odds ratio for each quartile was calculated by comparing it to the quartile with the least change in the preoperative BP.

As a secondary assessment and to completely exclude the effect of cardiovascular drugs on  $\Delta$ SBP/ $\Delta$ DBP values on the day of surgery, we also evaluated the relationship between these values and adverse outcomes in patients who did not take cardiovascular drugs. Multivariate logistic regression analyses were performed and adjusted for SBP1/DBP1 values and covariates.

Statistical significance was set at  $p < 0.05$ . All analyses were performed using JMP<sup>®</sup> Pro 16.1.0 (SAS Institute Inc., Cary, NC, USA). Because the present study was exploratory, the number of samples was not established *a priori*.

## Results

### Selection process and patient characteristics.

Figure 1 shows a flowchart of the selection process for the study patients. Between January 2011 and June 2019, 26,388 adult surgeries were performed under general anesthesia at Kagawa University Hospital. Although 13,531 patients met the inclusion criteria,

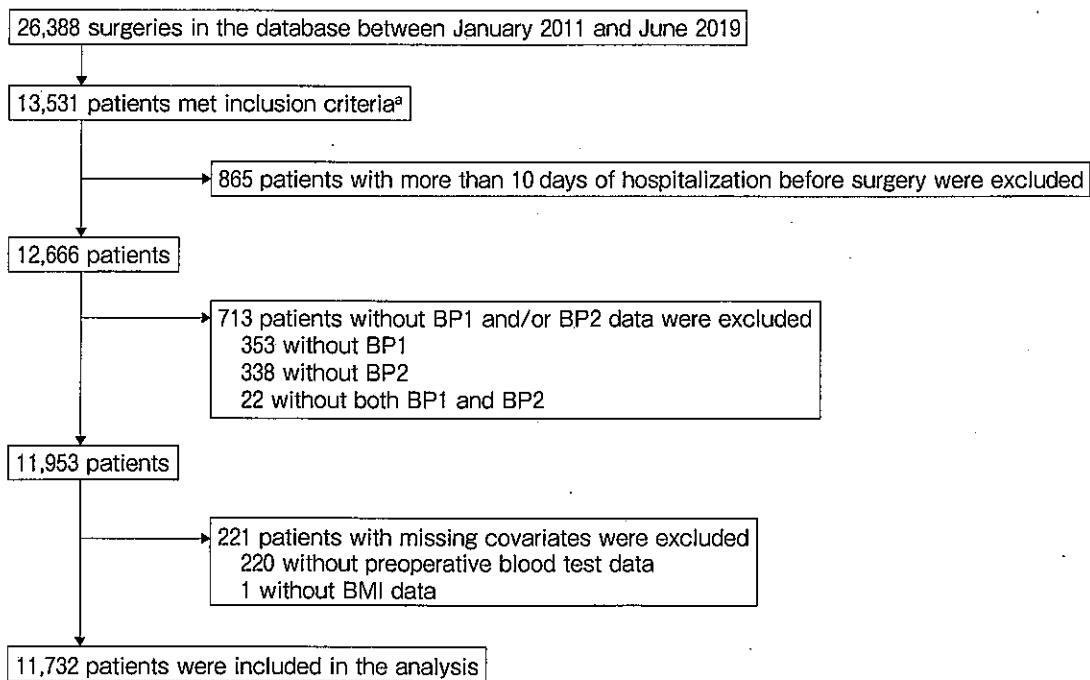


Fig. 1 Study flow diagram. <sup>a</sup>Inclusion criteria: adult non-cardiac inpatient elective surgery constituting the patient's first (or only) procedure during the study period. BP1, the first blood pressure measured on the day before surgery; BP2, the first blood pressure measured in the operating room; BMI, body mass index.

1,799 were excluded (865 with more than 10 days of hospitalization before surgery; 713 without SBP1/DBP1 and/or SBP2/DBP2 data; 220 without preoperative blood test data; 1 without BMI data). The remaining 11,732 patients were included in this study.

Table 1 shows the patient characteristics and preoperative BP values. Pre-induction BP (SBP2/DBP2) values were significantly higher than post-admission BP (SBP1/DBP1) values ( $p < 0.05$ ). The  $\Delta$ SBP and  $\Delta$ DBP were  $33 \pm 22$  (mean  $\pm$  SD) and  $8 \pm 14$  mmHg, respectively.

**BPs and adverse outcomes.** The proportions of 30d-mortality, 30d-readmission, and OSLOS were 0.1%, 0.1%, and 4.4%, respectively. No significant differences were observed in either  $\Delta$ SBP or  $\Delta$ DBP between the non-surviving group and the surviving group for the category of 30d-mortality; similar results were obtained for the categories of 30d-readmission (Table 2).  $\Delta$ SBP and  $\Delta$ DBP were significantly higher in the OSLOS group than in the Standard LOS group ( $p < 0.01$ ). The differences in  $\Delta$ SBP and  $\Delta$ DBP between the OSLOS and the standard LOS groups were both 2 mmHg. DBP1 was associated only with OSLOS ( $p < 0.01$ ); SBP1, SBP2, and DBP2 were not associated with postoperative adverse outcomes.

**Univariate and multivariate logistic regression analyses of OSLOS.**  $\Delta$ SBP and  $\Delta$ DBP values showed normal distribution in both the OSLOS and the standard LOS groups (Fig. 2). The entire cohort was divided into quartiles according to the distribution of  $\Delta$ SBP and  $\Delta$ DBP. The quantile points of  $\Delta$ SBP were 17, 31, and 46, and the quantile points of  $\Delta$ DBP were -1, 8, and 16. Univariate logistic regression analysis showed that OSLOS was associated with the largest quartiles of  $\Delta$ SBP ( $p < 0.05$ ) and  $\Delta$ DBP ( $p < 0.01$ ) and with each of the following other variables: DBP1, ASA-PS, preoperative Hb, diuretic medication, the duration of surgery, intraoperative blood loss, and head/neck, abdominal, and limb/spine surgery sites ( $p < 0.01$ , respectively) (Table 3). In the multivariate analysis, we constructed two models: Model 1 for  $\Delta$ SBP and Model 2 for  $\Delta$ DBP. After adjusting for risk factors, the largest quartile of  $\Delta$ DBP was associated with OSLOS ( $p < 0.05$ ); however, that of  $\Delta$ SBP was not. The adjusted odds ratio (95% confidence interval [CI]) compared to the reference quartile was 1.31 (1.02-1.69). Regarding the risk factors, age, ASA-PS, preoperative Hb, diuretic medication, the duration of surgery, and head/neck and limb/spine surgery sites were associated with OSLOS in both

Table 1 Perioperative patient characteristics and blood pressure

	All patients (n = 11,732)
Age (y)	61 $\pm$ 16
Male	5,565 (47.4)
Body mass index (kg/m <sup>2</sup> )	23.7 $\pm$ 4.1
ASA-PS	
1	1,754 (15.0)
2	8,153 (69.5)
3	1,757 (15.0)
4	68 (0.6)
Revised Cardiac Risk Index	
0	9,226 (78.6)
1	2,044 (17.4)
2	360 (3.1)
$\geq$ 3	102 (0.9)
Preoperative hemoglobin (g/dL)	13.3 $\pm$ 1.8
Preoperative oral medications	
ACEIs/ARBs	1,613 (13.7)
Calcium channel blockers	1,866 (15.9)
$\beta$ -Blockers	541 (4.6)
Other antiarrhythmic drugs	138 (1.2)
Aspirin	295 (2.5)
Other antiplatelet drugs	391 (3.3)
Anticoagulants	320 (2.7)
Diuretics	530 (4.5)
Antidiabetics	821 (7.0)
Statins	1,105 (9.4)
Duration of surgery (min)	154 [85; 248]
Intraoperative blood loss (mL)	36 [0; 200]
Surgical site	
Head/neck	2,135 (18.2)
Thoracic	1,582 (13.5)
Abdominal	3,760 (32.0)
Limb/spine	3,040 (25.9)
Other	1,215 (10.3)
BP1	
SBP1 (mmHg)	122 $\pm$ 18
DBP1 (mmHg)	73 $\pm$ 12
BP2	
SBP2 (mmHg)	155 $\pm$ 26*
DBP2 (mmHg)	81 $\pm$ 15*
$\Delta$ BP	
$\Delta$ SBP (mmHg)	33 $\pm$ 22
$\Delta$ DBP (mmHg)	8 $\pm$ 14

Values are shown as the mean  $\pm$  standard deviation, number (%), or median [interquartile range], \* $p < 0.05$ , vs. BP1.

ASA-PS, American Society of Anesthesiologists physical status classification; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; SBP, systolic blood pressure; DBP, diastolic blood pressure; BP1 (SBP1/DBP1), the first blood pressure measured on the day before surgery; BP2 (SBP2/DBP2), the first blood pressure measured in the operating room;  $\Delta$  BP ( $\Delta$  SBP/ $\Delta$  DBP), the difference between BP1 and BP2.

Table 2 Blood pressure elevations and adverse outcomes

Blood pressures	30d-mortality			30d-readmission			OSLOS		
	Non-survived (n=13)	Survived (n=11,719)	P-value	Readmission (n=11)	No readmission (n=11,721)	P-value	OSLOS (n=516)	Standard LOS (n=11,216)	P-value
<b>BP1</b>									
SBP1 (mmHg)	128 ± 21	122 ± 18	0.273	119 ± 15	122 ± 18	0.512	121 ± 18	122 ± 18	0.124
DBP1 (mmHg)	72 ± 12	73 ± 12	0.837	70 ± 11	73 ± 12	0.411	71 ± 13	73 ± 12	0.001
<b>BP2</b>									
SBP2 (mmHg)	155 ± 33	155 ± 26	0.986	140 ± 16	155 ± 26	0.060	157 ± 28	155 ± 26	0.182
DBP2 (mmHg)	76 ± 10	81 ± 15	0.232	74 ± 12	81 ± 15	0.144	81 ± 15	81 ± 15	0.549
<b>Δ BP</b>									
Δ SBP (mmHg)	28 ± 22	33 ± 22	0.399	21 ± 18	33 ± 22	0.090	35 ± 23	33 ± 22	0.005
Δ DBP (mmHg)	4 ± 10	8 ± 14	0.274	5 ± 12	8 ± 14	0.413	10 ± 14	8 ± 14	<0.001

Values are shown as the mean ± standard deviation.

OSLOS, over-the-standard length of stay; LOS, length of stay; SBP, systolic blood pressure; DBP, diastolic blood pressure; BP1 (SBP1/DBP1), the first blood pressure measured on the day before surgery; BP2 (SBP2/DBP2), the first blood pressure measured in the operating room; Δ BP (Δ SBP/Δ DBP), the difference between BP1 and BP2.

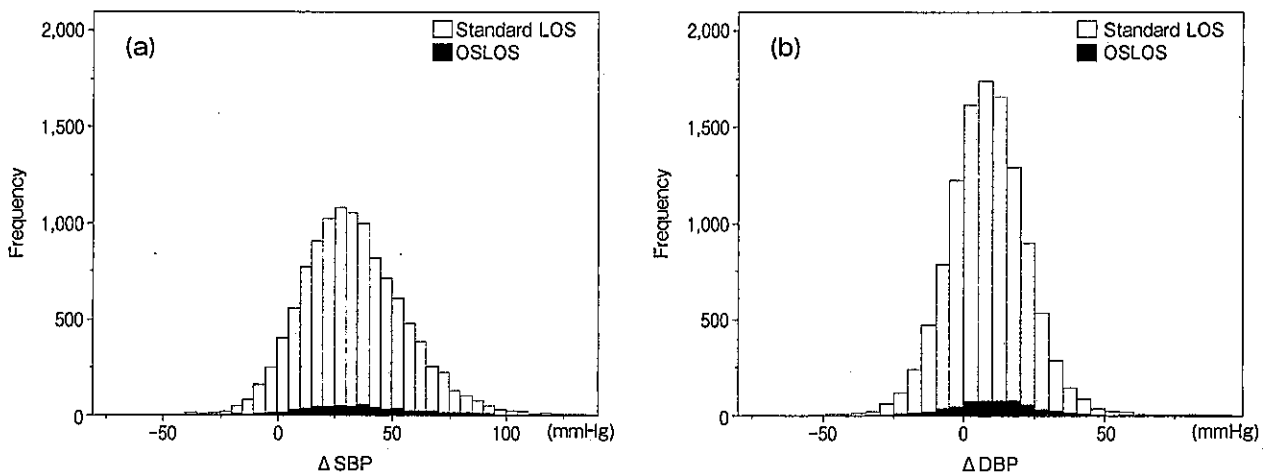


Fig. 2 Distribution of Δ BP in the OSLOS and standard LOS groups. Distributions of Δ SBP (a) and Δ DBP (b) in the OSLOS and standard LOS groups. SBP, systolic blood pressure; DBP, diastolic blood pressure; Δ BP (Δ SBP/Δ DBP), the difference between the first blood pressure measured on the day before surgery and the first blood pressure measured in the operating room; OSLOS, over-the-standard length of stay; LOS, length of stay.

models ( $p < 0.01$ ).

**Multivariate logistic regression analyses of OSLOS for patients not taking cardiovascular drugs.**

The proportion of OSLOS ( $n = 412$ ) among patients not taking cardiovascular drugs ( $n = 9,172$ ) was 4.5%. Multivariate analyses were performed with two models: Model 3 for ΔSBP and Model 4 for ΔDBP (Table 4). The adjusted odds ratios (95% CI) for the largest quartile of ΔSBP and ΔDBP, compared to the reference quartile, were 1.39 (1.01–1.92;  $p < 0.05$ ) and 1.35 (1.02–1.78;  $p < 0.05$ ), respectively.

**Discussion**

The study results indicate that ΔDBP, but not ΔSBP, was associated with OSLOS independent of DBP1. To the best of our knowledge, this is the first study to demonstrate a relationship between ΔSBP/ΔDBP (elevation in SBP/DBP immediately before surgery compared to baseline) and adverse outcomes after adult non-cardiac inpatient surgery. The differences in ΔSBP and ΔDBP between the OSLOS and the Standard LOS groups were small but statistically significant. In the

Table 3 Univariate and multivariate logistic regression analyses of OSLOS

Variables	Univariate analysis		Model 1 Multivariate analysis for $\Delta$ SBP		Model 2 Multivariate analysis for $\Delta$ DBP	
	Crude OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
$\Delta$ SBP quartiles (mmHg)						
≤ 16	(n=2,760)	Reference	Reference			
17 to 30	(n=2,966)	1.14 (0.88–1.48)	1.09 (0.83–1.44)	0.521		
31 to 45	(n=2,942)	1.18 (0.91–1.53)	1.20 (0.91–1.58)	0.208		
46 ≤	(n=3,064)	1.32 (1.02–1.70)	1.27 (0.96–1.69)	0.097		
$\Delta$ DBP quartiles (mmHg)						
≤ -2	(n=2,740)	0.94 (0.72–1.24)			1.00 (0.77–1.37)	0.990
-1 to 7	(n=3,027)	Reference			Reference	
8 to 15	(n=2,775)	1.09 (0.84–1.41)			0.97 (0.75–1.28)	0.853
16 ≤	(n=3,190)	1.47 (1.16–1.87)			1.31 (1.02–1.69)	0.018
BP1						
SBP1, per 10 mmHg		0.96 (0.91–1.01)	1.00 (0.95–1.06)	0.969		
DBP1, per 10 mmHg		0.89 (0.83–0.96)			0.97 (0.90–1.06)	0.555
Age, per 10 years		0.98 (0.93–1.03)	0.85 (0.80–0.91)	<0.001	0.87 (0.82–0.92)	<0.001
Male		0.95 (0.79–1.13)	1.02 (0.82–1.26)	0.873	1.00 (0.81–1.23)	0.991
Body mass index, per 1 kg/m <sup>2</sup>		1.01 (0.98–1.03)	0.99 (0.96–1.01)	0.260	0.99 (0.97–1.01)	0.374
ASA-PS, per category		1.27 (1.09–1.48)	1.28 (1.07–1.53)	0.008	1.28 (1.07–1.54)	0.008
Revised Cardiac Risk Index, per category		1.06 (0.91–1.24)	0.91 (0.77–1.09)	0.312	0.91 (0.77–1.08)	0.294
Preoperative hemoglobin, per 1 g/dL		0.91 (0.87–0.96)	0.92 (0.86–0.97)	0.004	0.92 (0.86–0.97)	0.005
Preoperative oral medications						
ACEIs/ARBs		0.92 (0.70–1.19)	0.83 (0.59–1.18)	0.303	0.83 (0.59–1.17)	0.284
Calcium channel blockers		0.89 (0.70–1.15)	0.94 (0.68–1.29)	0.688	0.95 (0.69–1.31)	0.761
$\beta$ -Blockers		0.92 (0.59–1.42)	0.80 (0.49–1.33)	0.391	0.80 (0.48–1.32)	0.381
Other antiarrhythmic drugs		1.16 (0.54–2.50)	1.26 (0.55–2.87)	0.580	1.23 (0.54–2.79)	0.624
Aspirin		0.92 (0.51–1.65)	0.98 (0.50–1.90)	0.948	0.97 (0.50–1.89)	0.938
Other antiplatelet drugs		0.86 (0.51–1.46)	0.83 (0.46–1.49)	0.524	0.82 (0.45–1.46)	0.495
Anticoagulants		1.55 (0.99–2.43)	1.05 (0.65–1.71)	0.834	1.05 (0.65–1.71)	0.834
Diuretics		1.68 (1.19–2.38)	1.99 (1.32–2.98)	<0.001	1.96 (1.30–2.94)	0.001
Antidiabetics		1.00 (0.70–1.41)	0.95 (0.65–1.39)	0.810	0.97 (0.67–1.42)	0.888
Statins		1.03 (0.77–1.39)	1.14 (0.80–1.61)	0.468	1.13 (0.80–1.61)	0.487
Duration of surgery, per 30 min		1.07 (1.06–1.09)	1.11 (1.10–1.13)	<0.001	1.11 (1.09–1.13)	<0.001
Intraoperative blood loss, per 100 mL		1.01 (1.01–1.02)	1.00 (0.99–1.01)	0.894	1.00 (0.99–1.01)	0.901
Surgical site						
Head/neck		0.30 (0.21–0.42)	0.52 (0.32–0.85)	0.009	0.53 (0.32–0.86)	0.010
Thoracic		0.82 (0.62–1.08)	1.30 (0.84–2.01)	0.234	1.32 (0.86–2.04)	0.210
Abdominal		0.64 (0.52–0.78)	0.89 (0.61–1.31)	0.559	0.90 (0.61–1.32)	0.585
Limb/spine		3.24 (2.71–3.87)	4.78 (3.30–6.93)	<0.001	4.78 (3.30–6.93)	<0.001

OSLOS, over-the-standard length of stay; SBP, systolic blood pressure; DBP, diastolic blood pressure; BP1 (SBP1/DBP1), the first blood pressure measured on the day before surgery;  $\Delta$  BP ( $\Delta$  SBP/ $\Delta$  DBP), the difference between BP1 and the first blood pressure measured in the operating room; OR, odds ratio; CI, confidence interval; ASA-PS, American Society of Anesthesiologists physical status classification; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker.

logistic regression analysis, the odds ratios of the largest quartiles of  $\Delta$ SBP and  $\Delta$ DBP were close to 1, and no threshold for increased risk could be identified. Therefore, there may be little need to worry about spikes in pre-induction BPs in clinical practice.

The causal relationship between  $\Delta$ DBP and OSLOS remains unclear. However, several factors may be involved in preoperative BP increases. First, the patient's preoperative control of hypertension may affect  $\Delta$ SBP and  $\Delta$ DBP. In this study, the status of preopera-

Table 4 Multivariate logistic regression analyses of OSLOS for patients not taking cardiovascular drugs

Variables	Model 3 Multivariate analysis for $\Delta$ SBP		Model 4 Multivariate analysis for $\Delta$ DBP	
	Adjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
$\Delta$ SBP quartiles (mmHg)				
≤ 16 (n=2,326)	Reference			
17 to 30 (n=2,434)	1.14 (0.84–1.54)	0.393		
31 to 45 (n=2,220)	1.36 (1.00–1.86)	0.049		
46 ≤ (n=2,192)	1.39 (1.01–1.92)	0.042		
$\Delta$ DBP quartiles (mmHg)				
≤ -2 (n=2,140)			1.05 (0.77–1.44)	0.766
-1 to 7 (n=2,379)			Reference	
8 to 15 (n=2,161)			1.01 (0.74–1.36)	0.972
16 ≤ (n=2,492)			1.35 (1.02–1.78)	0.037
BP1				
SBP1, per 10 mmHg	1.03 (0.97–1.10)	0.354		
DBP1, per 10 mmHg			0.98 (0.89–1.07)	0.634

OSLOS, over-the-standard length of stay; SBP, systolic blood pressure; DBP, diastolic blood pressure; BP1 (SBP1/DBP1), the first blood pressure measured on the day before surgery;  $\Delta$  BP ( $\Delta$  SBP/ $\Delta$  DBP), the difference between BP1 and the first blood pressure measured in the operating room; OR, odds ratio; CI, confidence interval.

tive cardiovascular disease management was unclear, and the influence of antihypertensive and antiarrhythmic medications administered on the day of surgery was not evaluated. In the secondary assessment (Table 4), large  $\Delta$ SBP and  $\Delta$ DBP values were associated with OSLOS among patients not taking cardiovascular drugs. This result suggests that the relationship between  $\Delta$ DBP and OSLOS cannot be explained only by the effect of cardiovascular drugs taken on the day of surgery. Second, the relationship between  $\Delta$ DBP and OSLOS may be influenced by the patient's preoperative anxiety. Several studies have reported an association between perioperative anxiety and prolonged LOS [18,19]. Because patients are often nervous preoperatively, their BPs may become elevated due to increased sympathetic activities. Preoperative anxiety may elevate preinduction BPs and prolong LOS. Whitecoat hypertension, a common type of anxiety-related hypertension, is considered to be associated with arteriosclerosis [20,21], which may cause cardiovascular impairments and organ damage [22–24]. Cardiovascular impairments may be associated with elevated  $\Delta$ SBP/ $\Delta$ DBP and OSLOS.

In addition to  $\Delta$ DBP, several risk factors were associated with OSLOS: ASA-PS, preoperative Hb, diuretic medication, and the duration of surgery. These are factors known to influence postoperative outcomes, and they presented trends similar to those reported in

previous studies. Some surgical sites, namely, head/neck and limb/spine, were also associated with OSLOS. These are factors for adjusting for the case-mix of the hospital, and therefore make it difficult to generalize the results obtained.

In this study, DBP1 was significantly lower in the OSLOS group than in the Standard LOS group (Table 2). The lower DBP1 in the OSLOS group might have affected the relationship between  $\Delta$ DBP and OSLOS. Conversely, 30d-mortality and 30d-readmission were not associated with SBP1/DBP1, SBP2/DBP2, or  $\Delta$ SBP/ $\Delta$ DBP in the univariate analysis. One of the reasons for this lack of association could be the low proportion of these outcomes among the study population. Because of the limited number of incidents, multivariate analysis to evaluate the relationship between  $\Delta$ SBP/ $\Delta$ DBP and 30d-mortality and 30d-readmission could not be performed. Further studies are required to elucidate the relationship between preoperative BP elevation and postoperative adverse outcomes.

The definition of preoperative BP (baseline BP) remains a concern. Previous studies have demonstrated that perioperative BP management should be based on daily or usual BP measured at home [5,25]; however, data regarding pre-hospital BP are often lacking because many patients do not routinely measure their BP at home. Therefore, surrogate baseline BP, such as



post-admission BP or pre-induction BP, is the only available data for perioperative management in most patients. In this study, the BP measured the day before surgery (SBP1/DBP1) was used as the baseline because many of the patients scheduled for elective inpatient surgery under general anesthesia at our hospital were admitted the day before surgery. A sensitivity analysis—limited to patients admitted the day before surgery ( $n=3,814$ )—also showed a higher risk in the largest quartile of  $\Delta$ DBP with an adjusted odds ratio of 2.34 (1.18–4.63;  $p<0.05$ ).

Several studies have reported a relationship between preoperative BPs and postoperative adverse outcomes [5–10]; however, currently, there is insufficient evidence to recommend a specific threshold beyond which the postoperative risk increases [5]. This may be partially attributed to variations in the data acquisition times of preoperative BP for risk assessments. Although many studies have investigated preoperative BP, since their timing of preoperative BP measurement often differs, the data cannot be readily compared across studies. Nonetheless, it is notable that a difference of 10 mmHg or more has been reported between pre-hospital BP and pre-induction BP values [1,2]. Our study suggests that the magnitude of BP elevation during the preoperative period may not be clinically important by itself. However, clinicians need to make an individualized risk assessment when BP is elevated before surgery.

This study has several strengths. The sample size was large (more than 10,000 cases), and all data used in this study were electronic. Since Kagawa University Hospital is a national institution that meets the medical standards in Japan, the quality of the included data was high. In addition, this study used DPC data from Japan. Since OSLOS in this study was defined as a hospital stay longer than mean + 2 SD days calculated using DPC data, it reflected a deviation from the standard length of hospital stay for a given procedure in Japan.

This study also had several limitations. This was a retrospective, single-center, observational study. The dose and medication used on the day of surgery were not investigated; therefore, the effects of the drug on BP during the perioperative period were not evaluated. Of the 13,531 patients who met the selection criteria, 934 were excluded due to missing data. The possibility of selection bias cannot be ruled out. Another limitation is the potential measurement bias. Because the BP measurement position differed between the ward (sit-

ting position in most cases) and the operating room (supine position), changes in the BP due to body position [26] cannot be ruled out. Finally, there is a possibility of unknown confounding factors.

In conclusion,  $\Delta$ DBP was associated with OSLOS in adult non-cardiac inpatient surgery, but the odds ratio was close to 1. Moreover, neither  $\Delta$ SBP nor  $\Delta$ DBP was associated with serious outcomes, namely 30d-mortality or 30d-readmission. In clinical settings, there may be little need to worry about differences between BP values after hospital admission and those before the induction of general anesthesia.

**Acknowledgments.** We thank Ms. Madoka Nakano, Department of Medical Informatics, for the extraction of electronic data.

## References

1. Koutsaki M, Thomopoulos C, Achimastos A, Kallistratos M, Batistaki C, Chatziagelaki E, Soulioti E, Poulimenos L, Koutsaki S, Mela A, Mancina G and Manolis AJ: Perioperative SBP changes during orthopedic surgery in the elderly: clinical implications. *J Hypertens* (2019) 37: 1705–1713.
2. van Klei WA, van Waes JA, Pasma W, Kappen TH, van Wolfswinkel L, Peelen LM and Kalkman CJ: Relationship Between Preoperative Evaluation Blood Pressure and Preinduction Blood Pressure: A Cohort Study in Patients Undergoing General Anesthesia. *Anesth Analg* (2017) 124: 431–437.
3. Drummond JC, Blake JL, Patel PM, Clopton P and Schulteis G: An observational study of the influence of “white-coat hypertension” on day-of-surgery blood pressure determinations. *J Neurosurg Anesthesiol* (2013) 25: 154–161.
4. Schonberger RB, Burg MM, Holt N, Lukens CL, Dai F and Brandt C: The relationship between preoperative and primary care blood pressure among veterans presenting from home for surgery; is there evidence for anesthesiologist-initiated blood pressure referral? *Anesth Analg* (2012) 114: 205–214.
5. Sanders RD, Hughes F, Shaw A, Thompson A, Bader A, Hoefft A, Williams DA, Grocott MPW, Mythen MG, Miller TE and Edwards MR: Perioperative Quality Initiative consensus statement on preoperative blood pressure, risk and outcomes for elective surgery. *Br J Anaesth* (2019) 122: 552–562.
6. Venkatesan S, Myles PR, Manning HJ, Mozid AM, Andersson C, Jorgensen ME, Hardman JG, Moonesinghe SR, Foex P, Mythen M, Grocott MPW and Sanders RD: Cohort study of preoperative blood pressure and risk of 30-day mortality after elective non-cardiac surgery. *Br J Anaesth* (2017) 119: 65–77.
7. Howell SJ, Sear JW and Foex P: Hypertension, hypertensive heart disease and perioperative cardiac risk. *Br J Anaesth* (2004) 92: 570–583.
8. Howell SJ, Hemming AE, Allman KG, Glover L, Sear JW and Foex P: Predictors of postoperative myocardial ischaemia. The role of intercurrent arterial hypertension and other cardiovascular risk factors. *Anaesthesia* (1997) 52: 107–111.
9. Abdelmalak BB, Abd-Elsayed AA, Dalton JE, Abdelmalak JB, Lawrence JP, Doyle DJ, Schreiber MJ and Sear JW: The associ-

- ation between preinduction arterial blood pressure and postoperative cardiovascular, renal, and neurologic morbidity, and in-hospital mortality in elective noncardiac surgery: an observational study. *J Hypertens* (2018) 36: 2251–2259.
10. Wax DB, Porter SB, Lin HM, Hossain S and Reich DL: Association of preanesthesia hypertension with adverse outcomes. *J Cardiothorac Vasc Anesth* (2010) 24: 927–930.
  11. Fleisher LA, Fleischmann KE, Auerbach AD, Barnason SA, Beckman JA, Bozkurt B, Davila-Roman VG, Gerhard-Herman MD, Holly TA, Kane GC, Marine JE, Nelson MT, Spencer CC, Thompson A, Ting HH, Uretsky BF and Wijeyesundera DN: 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* (2014) 130: e278–333.
  12. Fleisher LA, Beckman JA, Brown KA, Calkins H, Chaikof E, Fleischmann KE, Freeman WK, Froehlich JB, Kasper EK, Kersten JR, Riegel B, Robb JF, Smith SC, Jr., Jacobs AK, Adams CD, Anderson JL, Antman EM, Buller CE, Creager MA, Ettinger SM, Faxon DP, Fuster V, Halperin JL, Hiratzka LF, Hunt SA, Lytle BW, Nishimura R, Ornato JP, Page RL, Riegel B, Tarkington LG and Yancy CW: ACC/AHA 2007 Guidelines on Perioperative Cardiovascular Evaluation and Care for Noncardiac Surgery: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). *Circulation* (2007) 116: 1971–1996.
  13. Ortiz VE and Kwo J: Obesity: physiologic changes and implications for preoperative management. *BMC Anesthesiol* (2015) 15: 97.
  14. Hopkins TJ, Raghunathan K, Barbeito A, Cooter M, Stafford-Smith M, Schroeder R, Grichnik K, Gilbert R and Aronson S: Associations between ASA Physical Status and postoperative mortality at 48 h: a contemporary dataset analysis compared to a historical cohort. *Perioper Med (Lond)* (2016) 5: 29.
  15. Lee TH, Marcantonio ER, Mangione CM, Thomas EJ, Polanczyk CA, Cook EF, Sugarbaker DJ, Donaldson MC, Poss R, Ho KK, Ludwig LE, Pedan A and Goldman L: Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation* (1999) 100: 1043–1049.
  16. Fowler AJ, Ahmad T, Phull MK, Allard S, Gillies MA and Pearse RM: Meta-analysis of the association between preoperative anaemia and mortality after surgery. *Br J Surg* (2015) 102: 1314–1324.
  17. Ishii M: DRG/PPS and DPC/PDPS as Prospective Payment Systems. *Japan Med Assoc J* (2012) 55: 279–291.
  18. Schaal NK, Hepp P, Heil M, Wolf OT, Hagenbeck C, Fleisch M and Fehm T: Perioperative anxiety and length of hospital stay after caesarean section-A cohort study. *Eur J Obstet Gynecol Reprod Biol* (2020) 248: 252–256.
  19. AbuRuz ME, Al-Dweik G and Al-Akash HY: Checking the moderating effect of perceived control on the relationship between anxiety and postoperative hospital length of stay among coronary artery bypass graft patients. *Int J Gen Med* (2019) 12: 79–85.
  20. Cai P, Peng Y, Wang Y and Wang X: Effect of white-coat hypertension on arterial stiffness: A meta-analysis. *Medicine (Baltimore)* (2018) 97: e12888.
  21. Barochiner J, Aparicio LS, Alfie J, Morales MS, Cuffaro PE, Rada MA, Marin MJ, Galarza CR and Waisman GD: Arterial Stiffness in Treated Hypertensive Patients With White-Coat Hypertension. *J Clin Hypertens (Greenwich)* (2017) 19: 6–10.
  22. Choi JS, Oh SJ, Sung YW, Moon HJ and Lee JS: Pulse wave velocity is a new predictor of acute kidney injury development after off-pump coronary artery bypass grafting. *PLoS One* (2020) 15: e0232377.
  23. Vasan RS, Short MI, Niiranen TJ, Xanthakis V, DeCarli C, Cheng S, Seshadri S and Mitchell GF: Interrelations Between Arterial Stiffness, Target Organ Damage, and Cardiovascular Disease Outcomes. *J Am Heart Assoc* (2019) 8: e012141.
  24. Wu S, Chen D, Zeng X, Wen J, Zhou C, Xiao K, Hu P and Chen W: Arterial stiffness is associated with target organ damage in subjects with pre-hypertension. *Arch Med Sci* (2018) 14: 1374–1380.
  25. 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 and Jaber S: 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: 1346–1357.
  26. Eser I, Khorshid L, Gunes UY and Demir Y: The effect of different body positions on blood pressure. *J Clin Nurs* (2007) 16: 137–140.