Original Article

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Relation between elevated first SBP from baseline (delta SBP) and postoperative outcome

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Background: Hypertension is associated with increased postoperative risk. However, no consensus was accepted whether elevated blood pressure in the operating room with normal blood pressure at rest related to additional cardiovascular risk.

Methods: This was a single-center retrospective cohort study based on patients who underwent elective noncardiac surgery from 1 January 2012, to 31 December 2018. We evaluated the relationship between the delta SBP (the difference between first operating room blood pressure and baseline blood pressure) and the development of postoperative major adverse cardiac events (MACEs) in patients with normal baseline blood pressure. Multivariate logistic regression before and after propensity score weighting was performed to adjust for perioperative variables, and the minimum *P* value approach was used to identify the possible threshold of delta SBP that independently indicated the risk of MACE.

Results: Of the 55 563 surgeries, in 4.1%, postoperative MACE occurred. The threshold for the delta SBP was 49 mmHg. The adjusted odds ratio for MACE before and after propensity score weighting for the delta SBP threshold was 1.35 (95% CI, 1.11–1.59); *P* less than 0.001 and 1.28 (1.03–1.60); $P = 0.028$, respectively.

Conclusion: Delta SBP contributed to the elevated risk over and beyond the SBP at rest in patients who underwent elective noncardiac surgery. A rise of SBP of more than 49 mmHg from baseline in the operating room was significantly associated with an increased risk of postoperative MACE.

Keywords: first operating room systolic pressure, hypertension, major adverse cardiac events, noncardiac surgery

Abbreviations: ACE, angiotensin-converting enzyme; CVD, cardiovascular disease; GAM, General Additive Model; ICD, *International Classification of Disease*; MACE, major adverse cardiac events; MJHSC, Modified John Hopkins hospital criteria

INTRODUCTION

Hypertension is a common disease in adults and is associated with increased postoperative risk. The blood pressure of patients in the operating room is often higher than the pressure at rest. Some patients' blood pressure in the operating theater is so high that operations have to be postponed or even canceled, while their baseline blood pressure remains much lower or relatively normal [1,2]. There is no consensus on what level of SBP change from baseline to first SBP (delta SBP) poses a risk to patients during surgery [3–11].

The hypothesis is that there is a possible threshold of delta SBP over which the risk of postoperative cardiac complications increases significantly. This retrospective study aimed to investigate the relationship between delta SBP (the difference between first operating room blood pressure and baseline blood pressure) and the development of a postoperative major adverse cardiac event (MACE) during elective noncardiac surgeries and to identify an optimal threshold that predicts the differential risks of MACE.

METHODS

Study design, setting, population, and data collection

This single-center retrospective cohort study was conducted at Peking University First Hospital, a teaching hospital in China with 1500 beds. This study was approved by the Peking University First Hospital Ethics Committee. Due to the retrospective feature and none patient follow-up and no patients' identification information was involved, the requirement for written informed consent was waived by the Ethics Committee of the Peking University First Hospital.

This study used data obtained from the perioperative database of Peking University First Hospital, which contains the perioperative information of inpatients from 2012 onward. This study analyzed data from adults (age $\geq$18 years old) who underwent elective noncardiac surgery between 1 January 2012, and 31 December 2018. Noncardiac surgery was identified based on the *International Classification of Diseases and Procedures, Ninth Clinical Revision volume 3* (*ICD-9-v3*).

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Patients with baseline SBP higher than 140 mmHg or DBP higher than 90 mmHg were removed from the acquisition of data. The procedures included otolaryngology, general surgery, urology, gynecology, orthopedics, neurosurgery, vascular and thoracic surgery while excluding cardiac surgery, obstetrics, and emergency surgery. Only the first procedure record was used by patients who have been operated more than two times a year. If the time interval between the two operations were less than 3 months, the second operation would not be registered. Surgery under local infiltration anesthesia was also omitted from this analysis.

Variables in the study

The variables collected in this study include patients' essential characteristics (BMI, gender, age, smoking, and alcohol habits); variables of preoperative disorder (hypertension, coronary artery disease, myocardial infarction, revised cardiac risk index, rCRI); intraoperative variables [intraoperative hypotension, blood infusion, anesthesia type, the modified John Hopkins Hospital criteria (MJHSC), mean intraoperative heart rate] [12,13].

Patients' diagnosis of preoperative hypertension, coronary artery disease, myocardial infarction was all confirmed by ICD code (Table S1, http://links.lww.com/HJH/B644).

intraoperative hypotension

According to existing literature [9–11], we defined intraoperative hypotension as intraoperative SBP below 70 mmHg or DBP below 30 mmHg or mean blood pressure below 49 mmHg for more than or equal to 5 min, or when the mean blood pressure decreased by more than 30% from the baseline for more than or equal to 5 min (definitions of variables are listed in Supplementary Table S1, http://links.lww.com/HJH/B644).

The rCRI is a well-developed and validated risk index for predicting postoperative MACE in all types of patients undergoing general surgery, including those with diabetes mellitus, active congestive heart failure, preoperative renal insufficiency [14,15]. The MJHSC was used for categorizing the surgical complexity [12,13].

First SBP, baseline SBP, and delta SBP

The 'first SBP' in the operating room was defined as the first blood pressure value in the intraoperative blood pressure record. All first SBP were obtained using a noninvasive cuff on the upper arm in the supine position.

Baseline blood pressure was defined as the mean of three to five blood pressure records from a patient in a quiet mood obtained at the presurgical testing clinic or surgical department ward. For patients with mobile capability, blood pressure was obtained in a sitting position on the right or left upper arm with the cuff on the same level of patients' heart. For patients lying in bed, blood pressure was obtained at the bedside in the supine position with the cuff on the same level as the patients' heart. When new patients were admitted into the hospital, automatic blood pressure was necessary to increase efficiency and save time. Furthermore, there were several types of monitors listed in the supplementary file (Supplementary Table S10, http://links.lww.com/HJH/B644). All nurses were trained before clinical practice.

Delta SBP was the difference between first operating room blood pressure and baseline blood pressure.

Study endpoints

The endpoint included acute myocardial infarction, heart failure, nonfatal cardiac arrest) within 7 days in the hospital. For one patient with multiple events, only the first MACE was counted.

Definitions of outcomes

The definitions of our perioperative database outcomes were based on the following protocols: acute myocardial infarction, heart failure, nonfatal cardiac arrest within 7 days in the hospital. All MACE events were reconfirmed by a cardiologist (L.L.)

Acute myocardial infarction: patients were discharged with a diagnosis with an ICD code I21, I22. Once again, the case files were reviewed for the diagnosis.

Heart failure: patients discharged with a diagnosis with an ICD code I50, I97.104, T81.810, I11.001, I13.201, I97.106, N18.820, O29.102, O74.202, O75.402, O89.102, O99.408, O99.423 was suspected as heart failure. The case files were reviewed for the diagnosis.

Non-fatal cardiac arrest: patients were discharged with a diagnosis with an ICD code I46. The records of resuscitation or death were also reviewed [16–23].

Statistical analysis

Patients were divided into two groups according to the delta SBP cut-off point. Continuous variables with a normal distribution were compared using the Student t test, and those with nonnormal distribution were compared with the Mann–Whitney U test. The Kolmogorov–Smirnov test was used to determine whether the data were normally distributed or not. Categorical variables were compared using the chi-square test or continuity-corrected chi-square test. Rank variables were compared using the Kruskal–Wallis H test. Statistical significance was defined by a two-tailed P less than 0.05.

Nonlinear relationship detection between delta SBP and major adverse cardiac event

We examined the unadjusted relationship between the delta SBP and the risk of MACE using a cubic spline function in General Additive Models (GAM). We used the inflection point to find the possible threshold that divide the delta SBP into two categories that were clinically meaningful [24–28]. If we observed an area of inflation, the optimal threshold for the delta SBP was determined using the minimum P value approach. This approach evaluated every possible threshold of the delta SBP at intervals of 1 mmHg in the multivariate logistic regression models. The delta SBP that demonstrated the smallest statistically significant P value was selected as the optimal threshold to divide the delta SBP into two groups.

Multivariate logistic regression to detect any association between the delta SBP and major adverse cardiac event

This study created crude, age, and sex-adjusted, and fully adjusted multivariate logistic models. The variables in the full model contain the following: age, gender, smoking, revised cardiac index, antihypertensive, dyslipidemia,

anesthesia type, cancer surgery, surgical complexity, intraoperative blood transfusion, intraoperative hypotension, intraoperative mean heart rate. In addition, the need for an intraoperative blood transfusion and intraoperative hypotension were included in the model to adjust for the type and invasiveness of the surgery. The revised cardiac risk index (rCRI) were used to adjust for the preoperative risk of MACE. The rCRI is a well-developed and validated risk index for predicting postoperative MACE in patients undergoing general surgery and includes diabetes mellitus, active congestive heart failure, surgery with high risk, and preoperative renal insufficiency [14,15]. The MJHSC was used for categorizing the surgical complexity [12,13]. Level 1 patients had minor procedures, level 2 underwent moderately to significantly invasive procedures, and level 3 had highly invasive procedures. According to these criteria, medium and high level represents major surgery.

Multicollinearity among these variables was assessed by the variance inflation factor, with a reference value of 3. Discrimination of the multivariate model was assessed based on the c-statistic. The goodness of fit was tested using the Hosmer–Lemeshow test. We assessed whether the addition of the delta SBP to the model could improve the predictive ability for MACE by calculating the category-free net reclassification improvement (NRI) and the integrated discrimination improvement (IDI).

A heterogeneity analysis was used to determine any differences in the treatments' effects among different subgroups by covariates in the model mentioned above.

We also used sensitivity analysis to assess the robustness of our findings. Sensitivity models were constructed as a logistic regression identical to the primary model above, except: with MACE only up to 30 days after surgery; adjusting for the duration of the surgery; using the first three records of the SBP, instead of the first record, as the first SBP; and excluding patients with intraoperative hypotension, and re-analyzing full dataset including baseline hypertensive patients and calculating odds ratio using re-identified threshold.

Analysis of the propensity score weighting

Due to the systematic differences between patients with higher and lower delta SBP (age, BMI, smoking and drinking habits, co-existing disorders, and surgery duration), the present study balanced the two groups using the propensity score-weighting method. A propensity score weighting is a method to diminish the effects of measured confounding factors and obtain a less biased result in observational studies.

In the present study, the propensity score weights were calculated using gradient boosted regression models, in which patients with higher and lower delta SBP were the dependent variables [12,13]. The following factors [age, gender, BMI, smoking and drinking habits, co-existing disorders (including coronary arterial disease, hypertension, heart insufficiency, arrhythmia, peripheral arterial disease, stroke, diabetes mellitus, chronic renal disease, COPD, dyslipidemia, and

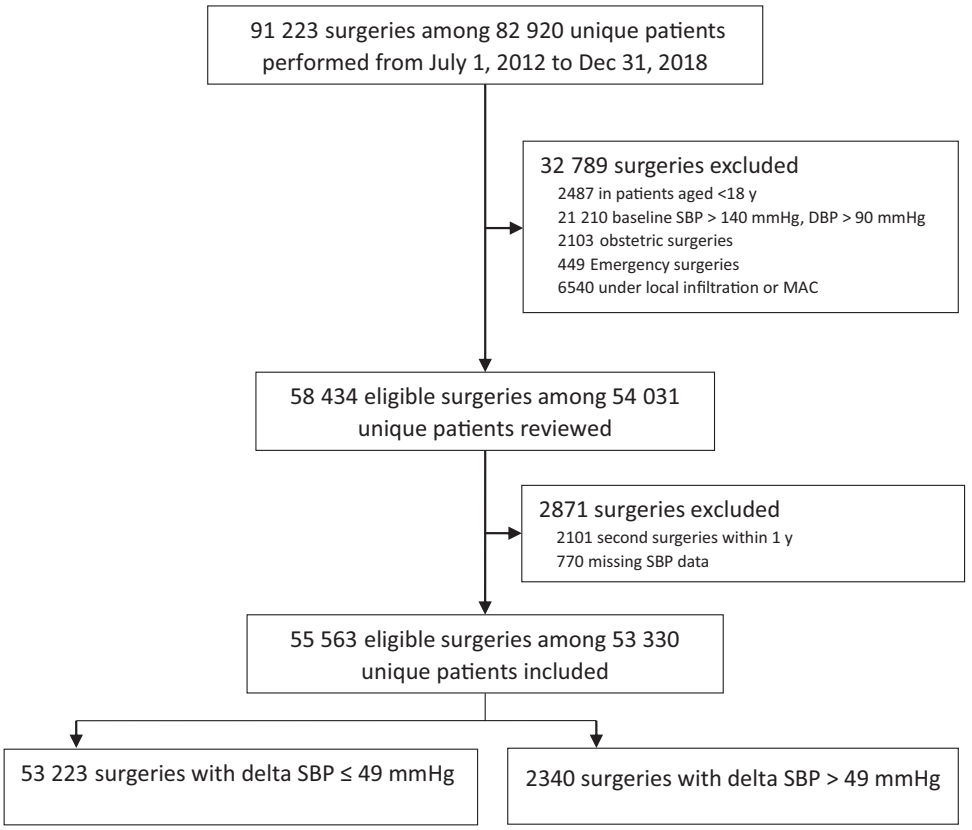

FIGURE 1 Flow diagram of the study population. Delta SBP, the difference between first operating room blood pressure (first SBP) and baseline blood pressure (bSBP); MACE, major adverse cardiac events.

anemia), preoperative hemoglobin and creatinine level, preoperative antihypertensive and statin use, cancer surgery, surgical complexity, surgical site, surgical duration, anesthesiology experience] were included as independent variables. Compared with inverse probability weight (IPW), the propensity score weights calculated using the gradient boosted regression models need no collinearity consideration and usually obtain improved balanced performance [12,13]. Compared with the original two groups, we could create two new groups with different patients using the propensity score weights. Each patient's value may not be an integer as the initial value for each patient was multiplied by a specific propensity score value. The logistic analysis with the propensity score weighting could lead to less biased results [15].

Statistical packages

All data management and statistical analysis were performed using the R programming language (v.3.5.2; R Foundation, Vienna, Austria).

RESULT

For the period, March 2012 to December 2018, 91 233 elective noncardiac surgeries were screened, and ultimately a total of 55 563 surgery were analyzed (Fig. 1).

The median age was 68 years old, 44.7% men, the mean BMI was $24.4 \pm 3.7\,kg/m^2$, mostly ASA class II and III. The most common surgery was the digestive tract (42.9%) and genital/urinary surgery (24.8%), with a median operation duration of 89 (52–154 interquartile range, IQR) minutes, and the median delta SBP was 14 (from 20 to 60) mmHg (Table 1).

TABLE 1. Patient characteristics and operative variables stratified by delta SBP

Characteristic	All ($n = 55\,595$)	Delta SBP ≤ 49 ($n = 53\,243$)	Delta SBP > 49 ($n = 2352$)	*P* value
Age [years; median (IQR)]	68 (60–75)	67 (59–74)	74 (67–80)	<0.001
Female sex [*n* (%)]	24 849 (44.7%)	23 778 (44.7%)	1071 (45.8%)	0.308
BMI (kg/m^2)	24.4 ± 3.7	24.4 ± 3.6	24.2 ± 3.7	0.022
Co-existing disease				
Hypertension	13 398 (24.1%)	12 372 (23.2%)	1026 (43.8%)	<0.001
Coronary artery disease	6186 (11.1%)	5739 (10.8%)	447 (19.1%)	<0.001
Heart failure	462 (0.8%)	421 (0.8%)	41 (1.8%)	<0.001
Arrhythmia	1259 (2.3%)	1170 (2.2%)	89 (3.8%)	<0.001
Peripheral arterial disease	636 (1.1%)	583 (1.1%)	53 (2.3%)	<0.001
Stroke	3114 (5.6%)	2851 (5.4%)	263 (11.2%)	<0.001
Diabetes mellitus	40 047 (72.1%)	38 495 (72.3%)	1552 (66.3%)	<0.001
Renal insufficiency	823 (1.5%)	751 (1.4%)	72 (3.1%)	<0.001
rCRI				<0.001
0	39 659 (71.4%)	38276 (71.9%)	1383 (59.1%)	
1	12 522 (22.5%)	11 860 (22.3%)	662 (28.3%)	
2	2606 (4.7%)	2404 (4.5%)	202 (8.6%)	
≥3	776 (1.4%)	683 (1.3%)	93 (4.0%)	
Surgery type				<0.001
Eye/ear/throat	2108 (3.8%)	2076 (3.9%)	32 (1.4%)	
Integumentary	1623 (2.9%)	1565 (2.9%)	58 (2.5%)	
Genital/urinary	13 794 (24.8%)	13221 (24.8%)	573 (24.5%)	
Musculoskeletal	5204 (9.4%)	5005 (9.4%)	199 (8.5%)	
Nervous	2266 (4.1%)	2137 (4.0%)	129 (5.5%)	
Vascular	1111 (2.0%)	1063 (2.0%)	48 (2.1%)	
Digestive	23 828 (42.9%)	22 724 (42.7%)	1104 (47.2%)	
Respiratory	3065 (5.5%)	2939 (5.5%)	126 (5.4%)	
Other	2564 (4.6%)	2493 (4.7%)	71 (3.0%)	
Surgery time [min; median (IQR)]	89 (52–154)	89 (52–153)	102 (54–178)	<0.001
Anesthesia duration [min; median (IQR)]	152 (106–231)	151 (106–229)	168 (110–268)	<0.001
Anesthesia type				<0.001
General anesthesia ± epidural/nerve block	45 073 (83.1%)	43 785 (83.3%)	1288 (78.3%)	
Intrathecal/nerve block	9151 (16.9%)	8795 (16.7%)	356 (21.7%)	
Intraoperative fluid administration [ml/kg; median (IQR)]				
Infusion volume	23 (15–36)	23 (16–36)	21 (14–34)	<0.001
Crystal	20 (14–30)	20 (14–30)	19 (13–29)	<0.001
Colloid	0 (0–7)	0 (0–7)	0 (0–7)	<0.001
Estimated blood loss [ml; median (IQR)]	0 (0–80)	0 (0–60)	0 (0–100)	<0.001
Intraoperative blood infusion	4820 (8.7%)	4567 (8.6%)	253 (10.8%)	<0.001
Urine [ml; median (IQR)]	0 (0–300)	0 (0–300)	0 (0–400)	<0.001
Intraoperative hypotension	447 (0.8%)	421 (0.8%)	26 (1.1%)	0.115
Intraoperative mean HR (bpm)				0.694
60–65	12 646 (22.8%)	12142 (22.8%)	504 (21.5%)	
<60	15 791 (28.4%)	15113 (28.4%)	678 (29.0%)	
65–75	16 386 (29.5%)	15 686 (29.5%)	700 (29.9%)	
>75	10740 (19.3%)	10 282 (19.3%)	458 (19.6%)	
Baseline SBP (mmHg)	121.8 ± 10.5	121.8 ± 10.5	121.9 ± 10.9	0.601
Baseline DBP (mmHg)	74.3 ± 7.7	74.3 ± 7.6	74.0 ± 8.0	0.049

Delta SBP, the difference between first operating room blood pressure (1stSBP) and baseline blood pressure (bSBP). IQR, interquartile; rCRI, revised cardiac risk index.

TABLE 2. Models to predict postoperative major adverse cardiac event; adjusted odds ratio; confidence interval

	Patient/operative variables only		Patient/operative variables and Delta SBP	
	aOR (95% CI)	*P* value	aOR (95% CI)	*P* value
Gender (female)	0.98 (0.87–1.08)	0.646	0.98 (0.88–1.08)	0.720
Age (<40 years)	Reference	<0.001	Reference	<0.001
40–50	1.64 (1.18–2.09)		1.64 (1.18–2.09)	
50–60	2.72 (2.05–3.39)		2.70 (2.04–3.36)	
60–70	5.24 (4.01–6.48)		5.17 (3.96–6.39)	
>70	13.81 (10.63–17.00)		13.53 (10.40–16.65)	
Smoking	1.19 (1.02–1.36)	0.017	1.19 (1.02–1.36)	0.020
BMI (18.5–24.9 kg/m^2)	Reference		Reference	
<18.5	1.90 (1.56–2.25)	<0.001	1.90 (1.56–2.25)	<0.001
25.0–29.9	0.76 (0.67–0.84)		0.76 (0.67–0.84)	
>30.0	0.77 (0.65–0.89)		0.76 (0.65–0.88)	
Revised cardiac index (0)	Reference	<0.001	Reference	<0.001
1	2.51 (2.17–2.85)		2.50 (2.17–2.84)	
2	5.28 (4.39–6.16)		5.26 (4.38–6.15)	
≥3	14.22 (11.11–17.34)		14.03 (10.96–17.11)	
Dyslipidemia	0.92 (0.72–1.12)	0.457	0.92 (0.72–1.12)	0.450
antihypertensive	1.49 (1.27–1.72)	<0.001	1.48 (1.26–1.71)	<0.001
Anesthesia type (GA)	reference	<0.001	reference	<0.001
GA + epidural/nerve block	0.97 (0.82–1.11)		0.96 (0.82–1.11)	
Intrathecal/nerve block	0.43 (0.35–0.51)		0.42 (0.34–0.50)	
Cancer to benign surgery	1.57 (1.40–1.74)	<0.001	1.57 (1.40–1.73)	<0.001
Complexity of surgery		<0.001		<0.001
Low	Reference		Reference	
Medium	1.56 (1.35–1.78)		1.57 (1.36–1.78)	
High	1.43 (1.21–1.66)		1.44 (1.21–1.67)	
Intraoperative blood transfusion	3.37 (2.97–3.77)	<0.001	3.36 (2.96–3.76)	<0.001
Intraoperative hypotension	4.57 (3.34–5.80)	<0.001	4.57 (3.33–5.80)	<0.001
Intraoperative mean heart rate, 60–65 bpm	Reference	<0.001	Reference	<0.001
<60	1.00 (0.86–1.15)		1.00 (0.86–1.15)	
65–75	1.14 (0.98–1.30)		1.14 (0.97–1.30)	
>75	2.45 (2.10–2.79)		2.45 (2.11–2.80)	
Delta SBP (≤ 49 mmHg)	Reference	–	Reference	<0.001
>49	–		1.35 (1.11–1.59)	

Complexity of surgery, according to modified Johns Hopkins Surgical Criteria. aOR, adjusted odds ratio; CI, confidence interval; delta SBP, the difference between first operating room blood pressure (first SBP) and baseline blood pressure (bSBP); GA, general anesthesia.

Of the 55 563 surgeries, 2294 [4.1%; 95% confidence interval 4.0%-4.3%] developed MACE; Patients with higher delta SBP had a longer hospitalization (4 vs. 3 days; $P < 0.001$). The logistic regression showed that in addition to old age, extreme BMI, smoking, cancer or major surgery, intraoperative hypotension, and blood transfusion were all risk factors (Table 2).

Nonlinear relationship detection between delta SBP and major adverse cardiac event

The cubic spline using the GAM models describing the delta SBP to MACE was a 'J' shaped curve, with an inflection point at approximately 30 mmHg, after which the probability of MACE rose straight up (Fig. 2). The minimal *P* value approach showed that 49 mmHg of delta SBP was the cut-off point.

Logistic regression for detecting any association between delta SBP and major adverse cardiac event

The results of the multivariate logistic regression results showed an association between delta SBP and postoperative MACE. The odds ratio for delta SBP cut-off point (delta SBP < 49 mmHg as reference), was 1.35 (1.11–1.59), *P* less than 0.001 (Table 3).

In the multivariate logistic regression, each variable included in the models demonstrated a variance inflation factor of no more than 3, suggesting no multicollinearity. Multivariate models with or without delta SBP showed good discrimination (c-statistics was 0.895 and 0.899).

Heterogeneity and sensitivity analysis

An analysis of patients' subgroups based on their characteristics showed interaction in intraoperative hypotension. Patients with higher delta SBP are inclined to meet the criteria of intraoperative hypotension (Fig. 3). The relationship between delta SBP and MACE was qualitatively preserved across the sensitivity analyses (Supplementary Tables S4–S7, http://links.lww.com/HJH/B644). Re-analyzed full dataset including baseline hypertensive patients (more than 70 000 surgeries) showed similar odds ratio with re-identified threshold (still 49 mmHg) (Supplementary Table S8, http://links.lww.com/HJH/B644).

Results of the analysis after the propensity score weighting

After the propensity score weighting, we divided the dataset into two groups, that is, patients with delta SBP 49 mmHg or less or more than 49 mmHg. The balanced characteristics of

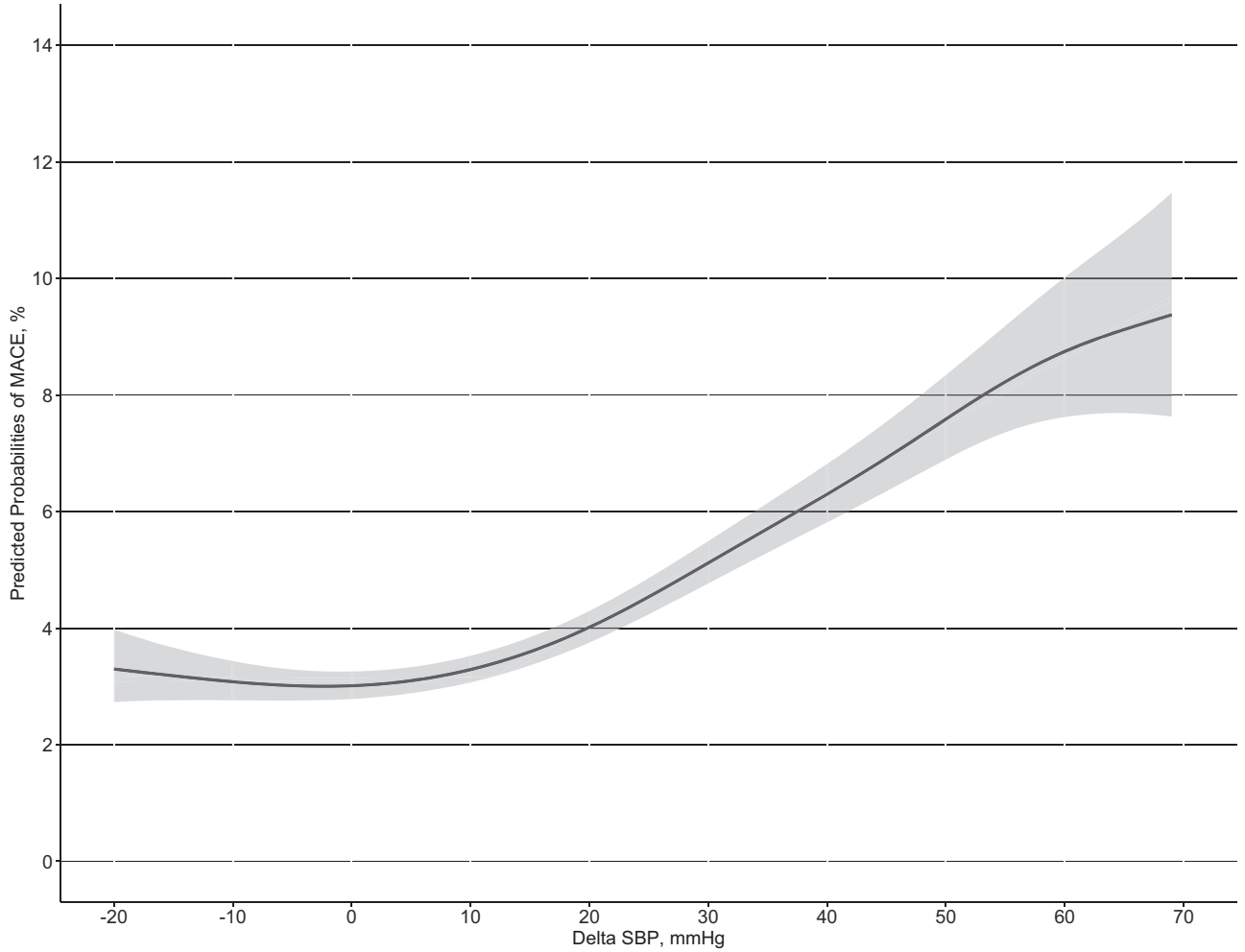

FIGURE 2 Cubic spline function curves of the unadjusted relationship between delta SBP and the probability of major adverse cardiac events. Shaded areas represent 95% confidence intervals. Delta SBP, the difference between first operating room blood pressure (first SBP) and baseline blood pressure (bSBP); MACE, major adverse cardiac events.

the two cohorts were showed in Table S9, http://links.lww.com/HJH/B644. The recalculated logistic odds ratio was for delta SBP cut-off point (delta SBP $\leq$49 mmHg as reference) was 1.28 (1.03–1.60), $P = 0.028$ (Table 3).

DISCUSSION

The present study showed that postoperative MACE occurred in 4.1% of adult patients with normal blood

TABLE 3. Odds ratio of Delta SBP as continuous variable, as categorical variable by interquartile range or cut-point in crude and adjusted models

	Model 1		Model 2		Full model	
	aOR (95% CI)	*P* value	aOR (95% CI)	*P* value	aOR (95% CI)	*P* value
Continuous Delta SBP	1.02 (1.02–1.02)	<0.001	1.00 (1.00–1.00)	0.083	1.00 (1.00–1.01)	0.028
Delta SBP quintile (mmHg)						
9–18	Reference		Reference		Reference	
<0	0.89 (0.76–1.02)	0.108	1.17 (0.99–1.35)	0.04	1.15 (0.96–1.34)	0.1
0–9	0.87 (0.74–1.01)	0.08	1.05 (0.89–1.22)	0.52	1.05 (0.87–1.22)	0.6
18–30	1.35 (1.17–1.53)	<0.001	1.12 (0.96–1.27)	0.12	1.16 (0.98–1.34)	0.06
>30	1.97 (1.72–2.23)	<0.001	1.21 (1.05–1.36)	0.01	1.25 (1.07–1.43)	<0.001
Delta SBP cut-point before PS weighting	Reference	<0.001	Reference	<0.001	Reference	<0.001
≤49						
>49	2.40 (2.05–2.76)		1.29 (1.09–1.49)		1.35 (1.11–1.59)	
Delta SBP cut-point after PS weighting	Reference	0.021	Reference	0.024	Reference	0.028
≤49						
>49	1.24 (1.03–1.48)		1.23 (1.03–1.47)		1.28 (1.03–1.60)	

Model 1: crude model. Model 2: crude model + age, gender. Full model: model 2 + smoking, revised cardiac index, antihypertensive, dyslipidemia, anesthesia type, cancer surgery, surgical complexity, intraoperative blood transfusion, intraoperative hypotension, intraoperative mean heart rate. aOR, adjusted odds ratio; CI, confidence interval; delta SBP, the difference between first operating room blood pressure (1stSBP) and baseline blood pressure (bSBP).

Subgroup	No. of Events / Total: Delta SBP > 49	No. of Events / Total: Delta SBP ≤ 49	Adjusted Odds Ratio (95% CI)	*P* value for Interaction
Overall effect			**1.35 (1.11-1.59)**	
Gender				
Female	883/29445	105/1269	1.43 (1.12-1.83)	0.16
Male	1201/23778	105/1071	1.27 (0.99-1.61)	
Age (years)				
<40	82/14245	4/166	2.23 (0.64-7.75)	0.17
40-50	109/10194	6/262	2.78 (1.05-7.36)	
50-60	271/11476	21/503	1.82 (1.10-3.01)	
60-70	560/9892	41/647	1.09 (0.77-1.56)	
>70	1062/7416	138/762	1.32 (1.06-1.64)	
BMI (kg/m^2)				
18.5-25.0	215/2689	21/84	1.39 (1.03-1.88)	
<18.5	767/18473	71/637	1.90 (1.00-3.59)	0.48
25.0-29.9	824/23319	89/1176	1.32 (1.02-1.71)	
>29.9	278/8742	29/443	1.16 (0.74-1.81)	
Smoking				
no	1722/47172	184/2088	1.34 (1.12-1.62)	0.66
Yes	362/6051	26/252	1.34 (0.84-2.15)	
Revised cardiac risk index				
0	543/38276	47/1383	1.24 (0.89-1.74)	0.93
1	855/11860	71/662	1.28 (0.97-1.68)	
2	430/2404	48/202	1.35 (0.93-1.97)	
3 or higher	256/683	44/93	1.45 (0.90-2.34)	
Dyslipidemia				
no	1970/51596	196/2225	1.34 (1.12-1.60)	0.84
Yes	114/1627	14/115	1.46 (0.73-2.91)	
Anti-hypertensive drug				
no	1774/50939	169/2138	1.42 (1.18-1.72)	0.12
yes	310/2284	41/202	0.99 (0.65-1.52)	
Cancer surgery				
no	638/27626	53/1139	1.27 (0.93-1.75)	0.79
Yes	1446/25597	157/1201	1.41 (1.15-1.73)	
Complexity of surgery				
low	328/18899	37/937	1.26 (0.85-1.87)	0.52
medium	798/25599	81/941	1.48 (1.13-1.95)	
high	958/8725	92/462	1.26 (0.96-1.65)	
Anesthesia type				
GA	1654/40930	168/1648	1.39 (1.15-1.69)	0.81
GA + epidural/nerveblock	301/3414	27/189	1.11 (0.68-1.80)	
Neuraxial or nerve block	129/8879	15/503	1.38 (0.77-2.48)	
Intraoperative hypotension				
no	1924/52802	202/2314	1.39 (1.17-1.65)	0.01
Yes	160/421	8/26	0.74 (0.28-2.00)	
Blood infusion				
no	1466/48656	146/2087	1.30 (1.06-1.58)	0.88
Yes	618/4567	64/253	1.52 (1.08-2.14)	
Intraoperative HR (bpm)				
60-65	443/15113	51/678	1.21 (0.81-1.83)	
<60	359/12142	37/504	1.20 (0.85-1.70)	0.51
65-75	540/15686	67/700	1.63 (1.20-2.22)	
>75	742/10282	55/458	1.22 (0.87-1.72)	

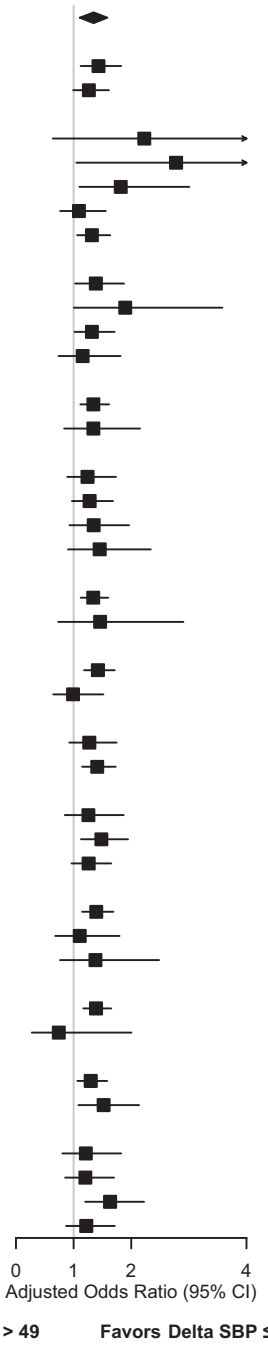

FIGURE 3 Subgroup analyses stratified by patient and operative variables. The adjusted coviarates incude: age, gender, revised cardiac index, antihypertensive, dyslipidemia, anesthesia type, cancer surgery, surgical complexity, intraoperative blood transfusion, intraoperative hypotension, intraoperative mean heart rate. Delta SBP, the difference between first operating room blood pressure (first SBP) and baseline blood pressure (bSBP); GA, general anesthesia; HR, heart rate.

pressure at rest who were undergoing elective noncardiac surgery. Multivariable adjustment before or after propensity score weighting showed that higher delta SBP was strongly associated with increased MACE occurrence following noncardiac surgery.

For elective surgical patients, unsatisfactory management of blood pressure, preoperative stress, decreased quality of sleep, and disease symptoms may result in high blood pressure in the operating room. Some patients' blood pressure met the criteria for hypertensive crisis; some of the surgeries were postponed or even canceled. Radical management of first operating room blood pressure may result in severe hypotension intraoperatively. However, there is no consensus on cardiac risk of what level of first SBP elevation from baseline SBP, especially those with normal SBP and DBP at rest. This study made its efforts and enlighted the direction for further research. The newest US and ESC/ESH Clinical Practice Guidelines

recommended a delay of surgery for patients with SBP greater than 180 mmHg or DBP greater than 110 mmHg except for emergency situations [29]. Among patients undergoing carotid endarterectomy, Towne and Bernhard [30] observed an increased risk of postoperative hypertension and neurological defects. Aronson *et al.* [11] observed an increased risk of cardiovascular disease (CVD) morbidity after coronary artery bypass graft surgery in patients with isolated systolic hypertension. Although Crowther *et al.* [10] reported there was no association between preoperative hypertension and perioperative hemodynamic changes known to be associated with major morbidity and mortality. The sample sizes in most of the research mentioned above were small, leading to uncertainty in the relationship between systolic hypertension and surgical risk [4–8,20].

To the best of our knowledge, this is the first study focusing on operating room hypertension with normal blood pressure at rest for noncardiac surgeries based on an analysis of real-world clinical data.

Our research has some advantages. We found that after stratifying our analyses by perioperative variables, our results remained reliable. This suggests that the relationship between delta SBP and MACE does not change significantly depending on patient characteristics, the time frame of MACE, or antihypertensive medication. We also proved the robustness of our conclusion by multiple sensitivity analyses and propensity score weighting analysis.

Although we tried our best to implement the best research methods and improve the quality of the database, various shortcomings and errors were still inevitable. These include: the results of this study only draw associations and cannot imply causality. Thus, we cannot suggest that the management of preoperative blood pressure to achieve a delta SBP below 49 will reduce the risk of MACE. Further randomized trials are needed. The single-center retrospective design might limit the generalizability of the present study, and external validation is warranted. Postoperative lab tests and examinations were not performed on every patient but were based on clinical observations when symptoms and signs were suspected, which may result in an underestimation of the rate of the primary outcome.

In conclusion, delta SBP contributed to the elevated risk over and beyond the SBP at rest in patients who underwent elective noncardiac surgery. A rise of SBP to more than 49 mmHg from baseline in the operating room was significantly associated with an increased risk of postoperative MACE.

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Registration of Clinical Trials: This study was approved by the Peking University First Hospital Ethics Committee [2015 (965)]. Due to the retrospective feature and none patient follow-up, the requirement for written informed consent was waived by the IRB. **IRB Contact Information:** Peking University First Hospital Ethics Committee. Tel: 010-82805563.

The corresponding author confirms on behalf of all authors that there have been no involvements that might raise the question of bias in the work reported or in the conclusions, implications. Support was provided solely from institutional and departmental sources. The authors declare no competing interests.

Authors' contributions: Y.Z. conceived and designed the study, performed data collection and analysis, drafted and critically revised the manuscript. L.L helped to design the study and revised the manuscript. H.-Y.Y. helped in collecting laboratory test results in the database and gave some advice.

Conflicts of interest

There are no conflicts of interest.

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