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

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INTRODUCTION

Hyper tension 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 baseline blood pressure that would be measured at rest in a normal state. 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 cardiovascular 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 ≥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-c3).
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 capibility, 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 (LL)

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 I15, I17.104, 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’s 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 value is 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
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].

**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/m²)                                         | 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                                                   | 39,659 (71.4%)   | 38,276 (71.9%)              | 1383 (59.1%)              |         |
| 1                                                   | 12,522 (22.5%)   | 11,860 (22.3%)              | 662 (28.3%)               |         |
| ≥ 2                                                 | 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%)                 |         |
| Genitourinary                                       | 13,794 (24.8%)   | 13,221 (24.8%)              | 573 (24.5%)               |         |
| Musculoskeletal                                     | 5204 (9.4%)      | 5090 (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                                               | 2364 (4.6%)      | 2493 (4.7%)                 | 71 (3.0%)                 |         |
| Surgery time [min; median (IQR)]                    | 89 (52–152)      | 89 (52–153)                 | 102 (54–178)              | <0.001  |
| Anesthesia duration [min; median (IQR)]             | 152 (106–231)    | 151 (106–229)               | 168 (110–268)             | <0.001  |
| Anaesthesia type                                    |                  |                             |                           | <0.001  |
| General anesthesia ± epidural/nerve block           | 45,073 (83.1%)   | 43,785 (83.3%)              | 1288 (78.3%)              |         |
| Intraarterial 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 (0–60)         | 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]                        | 60–65            |                             |                           | 0.694   |
| <60                                                 | 12,660 (22.8%)   | 12,142 (22.8%)              | 504 (21.5%)               |         |
| 65–75                                               | 15,791 (28.4%)   | 15,113 (28.4%)              | 678 (29.0%)               |         |
| >75                                                 | 16,360 (29.5%)   | 15,866 (29.5%)              | 700 (29.9%)               |         |
| Baseline SBP (mmHg)                                 | 121.8 ± 10.5     | 121.8 ± 10.5                | 121.8 ± 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.
Of the 55,563 surgeries, 2,294 [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 \( \leq 49 \text{ mmHg} \) as reference), was 1.35 (1.11–1.59), \( P \) less than 0.001 (Table 3).

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 \( > 49 \text{ mmHg} \) or \( \leq 49 \text{ mmHg} \). The balanced characteristics of

**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) \( P = 0.646 \) | 0.98 (0.88–1.08) \( P = 0.720 \) |
| Age (<40 years)     |                                  |                                           |
| 40–50               | 1.64 (1.18–2.09) \( P < 0.001 \) | 1.64 (1.18–2.09) \( P < 0.001 \) |
| 50–60               | 2.72 (2.05–3.39) \( P < 0.001 \) | 2.70 (2.04–3.36) \( P < 0.001 \) |
| 60–70               | 5.24 (4.01–6.48) \( P < 0.001 \) | 5.17 (3.96–6.39) \( P < 0.001 \) |
| >70                 | 13.81 (10.63–17.00) \( P < 0.001 \) | 13.53 (10.40–16.65) \( P < 0.001 \) |
| Smoking             | 1.19 (1.02–1.36) \( P = 0.017 \) | 1.19 (1.02–1.36) \( P = 0.020 \) |
| BMI (18.5–24.9 kg/m\(^2\)) |                                    |                                           |
| <18.5               | 1.90 (1.56–2.25) \( P < 0.001 \) | 1.90 (1.56–2.25) \( P < 0.001 \) |
| 25.0–29.9           | 0.76 (0.67–0.84) \( P < 0.001 \) | 0.76 (0.67–0.84) \( P < 0.001 \) |
| >30.0               | 0.77 (0.65–0.89) \( P < 0.001 \) | 0.76 (0.65–0.88) \( P < 0.001 \) |
| Revised cardiac index (0) |                                  |                                           |
| 1                   | 2.51 (2.17–2.85) \( P < 0.001 \) | 2.50 (2.17–2.84) \( P < 0.001 \) |
| 2                   | 5.28 (4.39–6.16) \( P < 0.001 \) | 5.26 (4.38–6.15) \( P < 0.001 \) |
| ≥3                  | 14.22 (11.11–17.34) \( P < 0.001 \) | 14.03 (10.96–17.11) \( P < 0.001 \) |
| Dyslipidemia        | 0.92 (0.72–1.12) \( P = 0.457 \) | 0.92 (0.72–1.12) \( P = 0.450 \) |
| Antihypertensive    | 1.49 (1.27–1.72) \( P < 0.001 \) | 1.48 (1.26–1.71) \( P < 0.001 \) |
| Anesthesia type (GA) |                                    |                                           |
| GA + epidural/nerve block | 0.97 (0.82–1.11) \( P < 0.001 \) | 0.96 (0.82–1.11) \( P < 0.001 \) |
| Intraoperative blood transfusion | 0.43 (0.35–0.51) \( P < 0.001 \) | 0.42 (0.34–0.50) \( P < 0.001 \) |
| Cancer to benign surgery | 1.57 (1.40–1.74) \( P < 0.001 \) | 1.57 (1.40–1.73) \( P < 0.001 \) |
| Complexity of surgery |                                    |                                           |
| Low                 |                                  |                                           |
| Medium              | 1.56 (1.35–1.78) \( P = 1.36(78 \) | 1.57 (1.36–1.78) \( P = 1.36(78 \) |
| High                | 1.43 (1.21–1.66) \( P = 1.44(121 \) | 1.44 (1.21–1.67) \( P = 1.44(121 \) |
| Intraoperative blood transfusion | 3.37 (2.97–3.77) \( P < 0.001 \) | 3.36 (2.96–3.76) \( P < 0.001 \) |
| Intraoperative hypotension | 4.57 (3.34–5.80) \( P < 0.001 \) | 4.57 (3.33–5.80) \( P < 0.001 \) |
| Intraoperative mean heart rate, 60–65 bpm |                                    |                                           |
| <60                 | 1.00 (0.86–1.15) \( P < 0.001 \) | 1.00 (0.86–1.15) \( P < 0.001 \) |
| 65–75               | 1.14 (0.98–1.30) \( P < 0.001 \) | 1.14 (0.97–1.30) \( P < 0.001 \) |
| >75                 | 2.45 (2.10–2.79) \( P < 0.001 \) | 2.45 (2.11–2.80) \( P < 0.001 \) |
| Delta SBP (49 mmHg)  |                                  |                                           |
| >49                 |                                  |                                           |
| ≤49                 | 1.35 (1.11–1.59) \( P < 0.001 \) | 1.35 (1.11–1.59) \( P < 0.001 \) |

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.
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 ≤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 pressure. The recalculated logistic odds ratio for delta SBP cut-off point (delta SBP ≤49 mmHg as reference) was 1.28 (1.03–1.60), \( P = 0.028 \) (Table 3).

**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 weighing |         |      |         |      |            |      |
| ≤49                    | Reference | <0.001 | Reference | <0.001 | Reference | <0.001 |
| >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 weighing |         |      |         |      |            |      |
| ≤49                    | Reference | 0.021 | Reference | 0.024 | Reference | 0.028 |
| >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).
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 enlightened the direction for further research.

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| Subgroup                     | Delta SBP > 49 | Delta SBP ≤ 49 | Adjusted Odds Ratio (95% CI) | P value for Interaction |
|------------------------------|----------------|----------------|------------------------------|-------------------------|
| Overall effect               | 1.35 (1.11-1.60) |                |                              |                         |
| Gender                       |                |                |                              |                         |
| Female                       | 1.43 (1.12-1.83) | 1.27 (0.99-1.61) | 1.35 (1.11-1.59) | 0.16 |
| Male                         | 1.27 (0.99-1.61) | 1.12 (0.91-1.38) |                              |                         |
| Age (years)                  |                |                |                              |                         |
| <40                          | 2.23 (0.64-7.75) | 1.70 (0.60-4.79) | 1.40 (1.01-1.92) | 0.17 |
| 40-50                        | 2.78 (1.05-7.36) | 1.94 (0.70-5.31) | 1.80 (1.25-2.59) | 0.51 |
| 60-70                        | 1.09 (0.77-1.56) | 0.83 (0.51-1.35) | 1.30 (1.04-1.62) | 0.12 |
| BMI (kg/m²)                  |                |                |                              |                         |
| 18.5-25.0                    | 1.39 (1.03-1.88) | 0.85 (0.52-1.41) | 1.35 (1.11-1.59) | 0.66 |
| <18.5                        | 1.90 (1.00-3.59) | 1.20 (0.66-2.19) | 0.95 (0.70-1.28) | 0.52 |
| 25.0-29.9                    | 1.32 (1.02-1.71) | 0.92 (0.60-1.42) | 1.16 (0.88-1.53) | 0.66 |
| >29.9                        | 1.16 (0.74-1.81) | 0.66 (0.41-1.09) | 1.44 (1.11-1.88) | 0.12 |
| Smoking                      |                |                |                              |                         |
| no                           | 1.34 (1.12-1.62) | 1.09 (0.84-1.42) | 1.35 (1.11-1.59) | 0.66 |
| Yes                          | 1.34 (0.84-2.15) | 1.09 (0.52-2.23) |                             |                         |
| Revised cardiac risk index   |                |                |                              |                         |
| no                           | 1.24 (0.89-1.74) | 0.93 (0.65-1.33) | 1.35 (1.11-1.59) | 0.66 |
| 1                            | 1.28 (0.97-1.68) | 0.93 (0.65-1.33) | 0.95 (0.70-1.28) | 0.52 |
| 2                            | 1.35 (0.93-1.97) | 0.93 (0.65-1.33) | 0.95 (0.70-1.28) | 0.52 |
| 3 or higher                  | 1.45 (0.90-2.34) | 0.93 (0.65-1.33) | 0.95 (0.70-1.28) | 0.52 |
| Dyslipidemia                  |                |                |                              |                         |
| no                           | 1.34 (1.12-1.60) | 0.84 (0.51-1.40) | 1.35 (1.11-1.59) | 0.66 |
| Yes                          | 1.46 (0.73-2.91) | 0.84 (0.51-1.40) | 1.35 (1.11-1.59) | 0.66 |
| Anti-hypertensive drug        |                |                |                              |                         |
| no                           | 1.42 (1.18-1.72) | 1.27 (0.93-1.71) | 1.35 (1.11-1.59) | 0.66 |
| yes                          | 0.99 (0.65-1.52) | 0.93 (0.65-1.33) | 1.35 (1.11-1.59) | 0.66 |
| Cancer surgery               |                |                |                              |                         |
| no                           | 1.27 (0.93-1.71) | 0.93 (0.65-1.33) | 1.35 (1.11-1.59) | 0.66 |
| Yes                          | 1.41 (1.15-1.73) | 1.27 (0.93-1.71) | 1.35 (1.11-1.59) | 0.66 |
| Complexity of surgery        |                |                |                              |                         |
| low                          | 1.26 (0.85-1.87) | 0.85 (0.51-1.40) | 1.35 (1.11-1.59) | 0.66 |
| medium                       | 1.48 (1.13-1.95) | 0.93 (0.65-1.33) | 1.35 (1.11-1.59) | 0.66 |
| high                         | 1.26 (0.96-1.65) | 0.93 (0.65-1.33) | 1.35 (1.11-1.59) | 0.66 |
| Anesthesia type              |                |                |                              |                         |
| GA                           | 1.39 (1.15-1.69) | 0.93 (0.65-1.33) | 1.35 (1.11-1.59) | 0.66 |
| GA + epidural/nerveblock     | 1.11 (0.66-1.80) | 0.93 (0.65-1.33) | 1.35 (1.11-1.59) | 0.66 |
| Neuraxial or nerve block     | 1.38 (0.77-2.48) | 0.93 (0.65-1.33) | 1.35 (1.11-1.59) | 0.66 |
| Intraoperative hypotension   |                |                |                              |                         |
| no                           | 1.39 (1.17-1.65) | 1.39 (1.17-1.65) | 1.35 (1.11-1.59) | 0.66 |
| yes                          | 0.74 (0.28-2.00) | 0.74 (0.28-2.00) | 1.35 (1.11-1.59) | 0.66 |
| Blood infusion               |                |                |                              |                         |
| no                           | 1.30 (1.06-1.58) | 1.30 (1.06-1.58) | 1.35 (1.11-1.59) | 0.66 |
| yes                          | 1.52 (1.08-2.14) | 1.52 (1.08-2.14) | 1.35 (1.11-1.59) | 0.66 |
| Intraoperative HR (bpm)      |                |                |                              |                         |
| 60-65                        | 1.21 (0.81-1.83) | 1.21 (0.81-1.83) | 1.35 (1.11-1.59) | 0.66 |
| <60                          | 1.20 (0.85-1.70) | 1.20 (0.85-1.70) | 1.35 (1.11-1.59) | 0.66 |
| 65-75                        | 1.63 (1.20-2.22) | 1.63 (1.20-2.22) | 1.35 (1.11-1.59) | 0.66 |
| >75                          | 1.22 (0.87-1.72) | 1.22 (0.87-1.72) | 1.35 (1.11-1.59) | 0.66 |

**FIGURE 3** Subgroup analyses stratified by patient and operative variables. The adjusted covariates include: 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.
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. Aoronson 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 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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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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