Supplementary Material Table of Contents

measured *n* number of BP values ($x_1, x_2, .. x_n$) with mean value ($\overline{x}$).

Supplemental Method 3. Details of the statistical analysis.

Supplemental Table 1. Variation parameters according to intraoperative and surgery-related characteristics.

Characteristic and subgroup	Standard deviation (mmHg)	Coefficient of variation (%)	Average real variability (mmHg/measurement)	Variation independent of mean (units)
Surgery departments				
SPARK-discovery				
General surgery (*N* = 20,282)	13.2 [10.9-15.9]	15.7 [13.2-18.6]	7.4 [6.0-9.1]	0.09 [0.08-0.11]
Neurosurgery (*N* = 4234)	12.1 [9.7-15.0]	15.0 [12.1-18.5]	5.8 [4.5-7.5]	0.09 [0.07-0.11]
Obstetrics and gynecology (*N* =7171)	11.0 [9.0-13.4]	13.3 [11.1-15.9]	6.1 [4.9-7.6]	0.08 [0.07-0.09]
Orthopedics (*N* = 10,331)	11.9 [8.8-15.3]	14.3 [10.6-18.2]	5.8 [4.2-8.0]	0.08 [0.06-0.11]
Urologic surgery (*N* = 3502)	12.5 [9.7-15.4]	14.9 [11.6-18.2]	6.7 [4.7-9.0]	0.09 [0.07-0.11]
SPARK-validation				
General surgery (*N* = 9865)	11.7 [9.8-13.9]	14.2 [12.0-16.7]	8.0 [6.4-9.9]	0.25 [0.21-0.29]
Neurosurgery (*N* = 2410)	9.5 [7.7-12.0]	12.0 [9.8-15.2]	5.7 [4.4-7.4]	0.21 [0.17-0.26]
Obstetrics and gynecology (*N* = 589)	11.3 [9.3-13.6]	14.2 [11.8-16.8]	8.0 [6.4-9.8]	0.25 [0.21-0.29]
Orthopedics (*N* = 13,692)	10.4 [8.0-13.2]	13.4 [10.3-17.0]	5.8 [4.3-8.1]	0.23 [0.18-0.29]
Urologic surgery (*N* = 3148)	11.5 [9.6-13.7]	14.1 [11.8-16.7]	7.5 [5.8-9.5]	0.25 [0.21-0.29]
Continuous monitoring				
General surgery (*N* = 3360)	11.4 [9.8-13.4]	14.0 [12.1-16.2]	1.2 [1.0-1.5]	0.02 [0.02-0.03]
Neurosurgery (*N* = 1090)	10.3 [8.4-12.5]	12.8 [10.7-15.3]	1.5 [1.2-1.9]	0.02 [0.02-0.02]
Obstetrics and gynecology (*N* = 382)	10.7 [9.0-12.8]	13.2 [11.3-15.2]	1.3 [1.1-1.7]	0.02 [0.02-0.02]
Orthopedics (*N* = 593)	12.4 [10.2-14.7]	15.1 [12.7-18.0]	1.5 [1.2-1.9]	0.02 [0.02-0.03]
Thoracic surgery (lung) (*N* = 2010)	10.9 [9.4-12.8]	13.4 [11.6-15.4]	1.2 [1.0-1.4]	0.02 [0.02-0.02]
Intravenous blood pressure modifying agents				
SPARK-discovery				
Users (*N* = 4534)	12.1 [9.7-15.0]	14.5 [11.8-17.3]	6.3 [4.9-8.2]	0.09 [0.07-0.10]
Non-users (*N* = 40,986)	12.5 [9.9-15.4]	14.9 [12.1-18.1]	6.7 [5.1-8.6]	0.09 [0.07-0.11]
SPARK-validation				
Users (*N* = 11,370)	10.3 [8.0-13.0]	13.2 [10.3-16.7]	5.8 [4.4-7.9]	0.23 [0.18-0.29]
Non-users (*N* = 18,334)	11.3 [9.2-13.7]	14.0 [11.5-16.7]	7.4 [5.7-9.5]	0.25 [0.20-0.29]
Continuous monitoring cohort				
Users (*N* = 1547)	11.0 [9.2-13.1]	13.6 [11.6-16.0]	1.3 [1.0-1.7]	0.02 [0.02-0.03]
Non-users (*N* = 5888)	11.2 [9.5-13.3]	13.7 [11.7-16.0]	1.2 [1.0-1.6]	0.02 [0.02-0.03]
Surgery duration				
SPARK-discovery				
≥ 2.5 hours (*N* = 26,402)	12.3 [10.1-14.8]	14.9 [12.5-17.7]	6.7 [5.3-8.4]	0.09 [0.07-0.10]
< 2.5 hours (*N* = 19,118)	12.5 [0.7-15.8]	14.9 [11.7-18.4]	6.7 [4.9-8.7]	0.09 [0.07-0.11]
SPARK-discovery				
≥ 2.5 hours (*N* = 15,049)	10.9 [9.0-13.0]	13.6 [11.3-16.2]	6.9 [5.3-8.8]	0.24 [0.20-0.28]
< 2.5 hours (*N* = 14,655)	11.1 [8.4-14.1]	13.8 [10.6-17.4]	6.7 [4.7-9.3]	0.24 [0.18-0.30]
Continuous monitoring				
≥ 2.5 hours (*N* = 4906)	10.8 [9.2-12.7]	13.3 [11.5-15.3]	1.2 [1.1-1.6]	0.02 [0.02-0.02]
< 2.5 hours (*N* = 2529)	12.1 [10.0-14.4]	14.6 [12.4-17.3]	1.3 [1.1-1.6]	0.02 [0.02-0.03]
Presence of significant intraoperative hypotension (mean arterial pressure < 65 mmHg) [a]				
SPARK-discovery				
With mean arterial pressure < 65 mmHg (*N* = 32,101)	12.9 [10.4-15.8]	15.9 [13.2-19.0]	6.9 [5.4-8.8]	0.09 [0.08-0.11]
Without any mean arterial pressure < 65 mmHg (*N* = 13,419)	11.3 [8.6-14.2]	12.4 [9.7-15.2]	6.0 [4.4-7.9]	0.07 [0.06-0.09]
SPARK-validation				
With mean arterial pressure < 65 mmHg (*N* = 21,079)	11.5 [9.3-14.0]	14.8 [12.2-17.6]	7.2 [5.5-9.5]	0.26 [0.21-0.31]
Without any mean arterial pressure < 65 mmHg (*N* = 8625)	9.7 [7.5-12.1]	11.2 [8.8-13.7]	5.8 [4.3-7.7]	0.20 [0.16-0.25]

[a] The continuous monitoring cohort was not investigated for this subgroup analysis as most of the patients had a mean arterial pressure < 65 mmHg for at least several seconds because the cohort monitored mean arterial pressure values with second intervals.

Supplemental Table 2. The discriminative powers of the multivariable logistic regression models with inclusion of intraoperative hypotension parameters with different thresholds in SPARK-discovery cohort.

Outcome and exposure	Mean arterial pressure < 65 mmHg	Systolic BP < 90 mmHg	Diastolic BP < 55 mmHg	Mean arterial pressure ≥ 20% decrement
For postoperative AKI				
Time under threshold	0.818 (0.809-0.827)	0.818 (0.808-0.827)	0.817 (0.807-0.826)	0.816 (0.807-0.826)
Area under curve below threshold	0.817 (0.808-0.827)	0.818 (0.808-0.827)	0.816 (0.806-0.825)	0.816 (0.807-0.826)
For critical AKI				
Time under threshold	0.852 (0.836-0.869)	0.850 (0.833-0.867)	0.852 (0.836-0.869)	0.849 (0.832-0.866)
Area under curve below threshold	0.850 (0.833-0.867)	0.850 (0.833-0.867)	0.850 (0.833-0.867)	0.850 (0.833-0.867)

BP = blood pressure, AKI = acute kidney injury

The discriminative powers were the area under of the receiver-operating characteristic curve and confidence interval values of the multivariable logistic regression models including the variables in each row. The multivariable models were adjusted for age, sex, baseline eGFR, diabetes mellitus, surgery duration (continuous, hours), emergency operation, usage of renin-angiotensin aldosterone system blockades, dipstick albuminuria, anemia (< 13 g/dl for male, < 12 g/dl for female), hypoalbuminemia (< 3.5 g/dl), and hyponatremia (< 135 mEq/L), without missing values.

Supplemental Table 3. Sensitivity analysis for associations between intraoperative blood pressure variability and postoperative acute kidney injury risk with defining acute kidney injury with peak serum creatinine level within 7 days in the SPARK-discovery cohort.

Subgroup and exposure	Univariable model		Multivariable model 1 [c]		Multivariable model 2 [d]	
	sOR (95% CI)	P	Adjusted sOR (95% CI)	P	Adjusted sOR (95% CI)	P
Patients with available follow-up creatinine level within 7 days in the SPARK-discovery cohort [a]						
Standard deviation	1.19 (1.13-1.25)	< 0.001	1.13 (1.06-1.20)	< 0.001	1.18 (1.10-1.26)	< 0.001
Coefficient of variation	1.28 (1.21-1.35)	< 0.001	1.12 (1.05-1.20)	< 0.001	1.17 (1.09-1.26)	< 0.001
Average real variability	1.17 (1.11-1.23)	< 0.001	1.13 (1.06-1.19)	< 0.001	1.18 (1.10-1.25)	< 0.001
Variation independent of mean	1.26 (1.20-1.33)	< 0.001	1.13 (1.05-1.20)	< 0.001	1.17 (1.09-1.26)	< 0.001
In hypotension (+) patients [b]						
Standard deviation	1.19 (1.12-1.26)	< 0.001	1.17 (1.09-1.25)	< 0.001	1.22 (1.13-1.32)	< 0.001
Coefficient of variation	1.31 (1.23-1.39)	< 0.001	1.16 (1.08-1.25)	< 0.001	1.20 (1.11-1.31)	< 0.001
Average real variability	1.18 (1.11-1.24)	< 0.001	1.16 (1.09-1.24)	< 0.001	1.20 (1.12-1.29)	< 0.001
Variation independent of mean	1.29 (1.21-1.37)	< 0.001	1.16 (1.08-1.25)	< 0.001	1.21 (1.11-1.31)	< 0.001
In hypotension (-) patients [b]						
Standard deviation	1.08 (0.96-1.21)	0.18	1.02 (0.89-1.15)	0.81	1.06 (0.91-1.23)	0.42
Coefficient of variation	1.08 (0.95-1.22)	0.25	1.01 (0.87-1.17)	0.89	1.06 (0.89-1.26)	0.50
Average real variability	1.04 (0.92-1.17)	0.49	0.99 (0.87-1.13)	0.87	1.09 (0.93-1.26)	0.28
Variation independent of mean	1.08 (0.95-1.22)	0.23	1.01 (0.87-1.17)	0.87	1.06 (0.89-1.26)	0.48

sOR = standardized odds ratio, CI = confidence interval

All variability parameters were included in the regression model as continuous variables and standardized odds ratios for per 1 standard deviation increase are presented.

[a] The numbers of AKI events within 7 days were 1381 (5%) in the SPARK-discovery cohort with 30,102 patients who had available follow-up creatinine levels within 7 days from surgery.

[b] Subgroups were divided according to presence of any MAP < 65 mmHg during surgery. Hypotension (+) subgroup included 22,079 patients with 1088 (5%) AKI events. Hypotension (-) subgroup included 8023 patients with 293 (4%) AKI events.

[c] Multivariable model 1 was adjusted for preoperative risk factors; age, sex, eGFR (continuous, mL/min/1.73 m^2), diabetes mellitus, surgery duration (continuous, hours), emergency operation, usage of renin-angiotensin aldosterone system blockades, dipstick albuminuria, anemia (< 13 g/dl for male, < 12 g/dl for female), hypoalbuminemia (< 3.5 g/dl), hyponatremia (< 135 mEq/L), and hypotensive variables, including area under curve [minutes multiplied by subtraction (mmHg×min)] of mean arterial pressure under 65 mmHg, and the lowest mean arterial pressure value during surgery, without missing values.

[d] In multivariable model 2, estimated blood loss (mL) and red blood cell transfusion amount (mL) during surgery were added to the multivariable model 1. The model was constructed with 23,126 patients with existing estimated blood loss records, without missing values.

Supplemental Table 4. Comparisons of area-under-the-curve values of the postoperative AKI predictive models according to addition of blood pressure parameters.

Cohort and subgroup	Area under curve and 95% CI of model 1 [b] (base model)	Area under curve and 95% CI of model 2 [c] (+ hypotension)	Area under curve and 95% CI of model 3 [d] (+ hypotensive and variability)	P value between model 1 and 2 [e]	Difference in area under curves between model 1 and model 2 (95% CI)	P value between model 2 and 3 [e]	Difference in area under curves between model 2 and model 3 (95% CI)
SPARK-discovery	0.815 (0.806-0.825)	0.817 (0.808-0.826)	0.818 (0.809-0.827)	0.02	0.002 (0.0003-0.003)	0.10	0.001 (-0.0002-0.003)
Hypotension (+) [a]	0.821 (0.811-0.831)	0.824 (0.814-0.834)	0.826 (0.817-0.837)	<0.001	0.003 (0.001-0.005)	0.01	0.003 (0.001-0.005)
Hypotension (-) [a]	0.772 (0.749-0.795)	0.773 (0.750-0.796)	0.773 (0.751-0.796)	<0.001	0.001 (0.0006-0.002)	0.57	0.001 (-0.001-0.002)
SPARK-validation	0.750 (0.737-0.762)	0.750 (0.738-0.763)	0.751 (0.738-0.764)	0.34	0.001 (-0.001-0.002)	0.51	0.001 (-0.001-0.003)
Hypotension (+) [a]	0.756 (0.742-0.770)	0.757 (0.742-0.771)	0.757 (0.742-0.771)	0.37	0.001 (-0.001-0.003)	0.80	0.000 (-0.002-0.002)
Hypotension (-) [a]	0.727 (0.700-0.754)	0.726 (0.699-0.754)	0.736 (0.710-0.763)	0.66	-0.001 (-0.003-0.002)	0.03	0.010 (0.001-0.019)
Continuous-monitoring	0.747 (0.719-0.776)	0.759 (0.730-0.787)	0.769 (0.742-0.796)	0.004	0.011 (0.004-0.019)	0.02	0.010 (0.002-0.018)

CI = confidence interval

[a] Presence of intraoperative hypotension was defined when an experience of any intraoperative mean arterial pressure < 65 mmHg was present.

[b] Model 1 was a logistic regression model with postoperative AKI as the independent variables and with following explanatory variables: age, sex, baseline eGFR, diabetes mellitus, surgery duration (continuous, hours), emergency operation, usage of renin-angiotensin aldosterone blockades, dipstick albuminuria, anemia (< 13 g/dl for male, < 12 g/dl for female), hypoalbuminemia (< 3.5 g/dl), and hyponatremia (< 135 mEq/L).

[c] Model 2 was similar to model 1, with the addition of the lowest mean arterial pressure value and the area under the curve under 65 mmHg variable to the explanatory variables.

[d] Model 3 was similar to model 1, with the addition of the variability parameters (standard deviation, coefficient of variation, average real variability and variation independent of mean) to the explanatory variables.

[e] P values were calculated with DeLong's test.

Supplemental Table 5. Validation analysis regarding intraoperative hypotensive parameters in the SPARK-validation cohort.

Cohort, outcome, exposure, and subgroup	**Univariable model**		**Multivariable model 1** [c]	
	sOR (95% CI)	P	Adjusted sOR (95% CI)	P
SPARK-validation cohort [a]				
Postoperative AKI				
Mean arterial pressure (per 8.9 mmHg lower value)	1.25 (1.19-1.32)	< 0.001	1.04 (0.98-1.10)	0.19
In hypotension (+) patients [b]	1.45 (1.34-1.56)	< 0.001	1.12 (1.02-1.22)	0.01
In hypotension (-) patients [b]	0.91 (0.79-1.07)	0.25	0.96 (0.82-1.13)	0.64
Time with mean arterial pressure < 65 mmHg (per 43.9 minutes)	1.29 (1.24-1.33)	< 0.001	1.09 (1.05-1.14)	< 0.001
Area under curve < 65 mmHg (per 467.7 minute × mmHg)	1.27 (1.22-1.32)	< 0.001	1.10 (1.06-1.14)	< 0.001
Critical AKI				
Mean arterial pressure (per 8.9 mmHg lower value)	1.40 (1.27-1.54)	< 0.001	1.07 (0.97-1.19)	0.15
In hypotension (+) patients [b]	1.76 (1.54-2.00)	< 0.001	1.23 (1.07-1.42)	0.004
In hypotension (-) patients [b]	0.71 (0.55-0.92)	0.008	0.80 (0.61-1.06)	0.11
Time with mean arterial pressure < 65 mmHg (per 43.9 minutes)	1.33 (1.26-1.39)	< 0.001	1.06 (0.99-1.14)	0.07
Area under curve < 65 mmHg (per 467.7 minutes × mmHg)	1.24 (1.19-1.30)	< 0.001	1.06 (1.00-1.12)	0.03

AKI = acute kidney injury, sOR = standardized odds ratio, CI = confidence interval

All hypotensive parameters were included as 1 standard deviation in the regression models; 8.9 mmHg for lowest mean arterial pressure values, 43.9 minutes for time under 65 mmHg, and 467.7 minute × mmHg for area under curve under 65 mmHg.

[a] Total number of patients in the SPARK-validation cohort was 29,704, including 1552 (5%) AKI and 411 (1%) critical AKI events, respectively.

[b] Subgroups were divided according to presence of any mean arterial pressure < 65 mmHg during surgery. Hypotension (+) subgroup included 21,079 patients with 1182 (6%) AKI and 347 (2%) critical AKI events, respectively. Hypotension (-) subgroup included 8625 patients with 370 (4%) AKI and 97 (1%) critical AKI events, respectively.

[c] Multivariable model 1 was adjusted for age, sex, eGFR, diabetes mellitus, surgery duration (continuous, hours), emergency operation, usage of renin-angiotensin aldosterone system blockades, dipstick albuminuria, anemia (< 13 g/dl for male, < 12 g/dl for female), hypoalbuminemia (< 3.5 g/dl), and hyponatremia (< 135 mEq/L), without missing values.

Supplemental Table 6. Validation analysis results in the subgroups of SPARK-validation cohort with the variability parameters.

Cohort, subgroup, outcome, and exposure	**Univariable model**		**Multivariable model 1** [c]	
	sOR (95% CI)	P	Adjusted sOR (95% CI)	P
SPARK-validation cohorts [a]				
In hypotension (+) patients [b]				
Postoperative AKI				
Standard deviation	1.13 (1.07-1.20)	< 0.001	1.12 (1.05-1.20)	< 0.001
Coefficient of variation	1.18 (1.12-1.25)	< 0.001	1.14 (1.06-1.22)	< 0.001
Average real variability	1.15 (1.09-1.21)	< 0.001	1.10 (1.03-1.17)	< 0.001
Variation independent of mean	1.17 (1.10-1.24)	< 0.001	1.13 (1.06-1.21)	< 0.001
Critical AKI				
Standard deviation	1.16 (1.05-1.28)	< 0.001	1.17 (1.03-1.31)	0.01
Coefficient of variation	1.24 (1.12-1.37)	< 0.001	1.16 (1.02-1.31)	0.02
Average real variability	1.25 (1.14-1.37)	< 0.001	1.25 (1.12-1.39)	< 0.001
Variation independent of mean	1.22 (1.10-1.34)	< 0.001	1.16 (1.03-1.31)	0.02
In hypotension (-) patients [b]				
Postoperative AKI				
Standard deviation	1.14 (1.02-1.26)	0.01	1.11 (0.99-1.25)	0.06
Coefficient of variation	1.16 (1.03-1.31)	0.01	1.18 (1.03-1.35)	0.02
Average real variability	1.15 (1.02-1.28)	0.02	1.11 (0.98-1.24)	0.09
Variation independent of mean	1.15 (1.03-1.29)	0.01	1.16 (1.02-1.31)	0.03
Critical AKI				
Standard deviation	0.90 (0.72-1.11)	0.32	0.89 (0.70-1.12)	0.33
Coefficient of variation	0.88 (0.68-1.12)	0.31	0.93 (0.70-1.22)	0.61
Average real variability	0.99 (0.78-1.23)	0.91	0.96 (0.75-1.21)	0.75
Variation independent of mean	0.88 (0.69-1.12)	0.31	0.92 (0.70-1.18)	0.51

sOR = standardized odds ratio, CI = confidence interval, AKI = acute kidney injury

All variability parameters were included in the regression model as continuous variables and standardized odds ratios for per 1 standard deviation higher are presented. In the SPARK-validation cohort, one standard deviation value was 3.7 mmHg, 4.4%, 3.1 mmHg/measurement, and 0.08 unit for standard deviation, coefficient of variation, average real variability, and variation independent of mean parameters, respectively.

[a] Total number of patients in the SPARK-validation cohort was 29,704, including 1552 (5%) AKI and 444 (2%) critical AKI events, respectively.

[a] Subgroups were divided according to presence of any mean arterial pressure < 65 mmHg during surgery. Hypotension (+) subgroup included 21,079 patients with 1182 (6%) AKI and 347 (2%) critical AKI events, respectively. Hypotension (-) subgroup included 8625 patients with 370 (4%) AKI and 97 (1%) critical AKI events, respectively.

[b] Multivariable model 1 was adjusted for preoperative risk factors; age, sex, eGFR (continuous, mL/min/1.73 m^2), diabetes mellitus, surgery duration (continuous, hours), emergency operation, usage of renin-angiotensin aldosterone system blockades, dipstick albuminuria, anemia (< 13 g/dl for male, < 12 g/dl for female), hypoalbuminemia (< 3.5 g/dl), hyponatremia (< 135 mEq/L), and hypotensive variables, including area under curve [minutes multiplied by subtraction (mmHg×min)] of mean arterial pressure under 65 mmHg, and the lowest mean arterial pressure value during surgery, without missing values.

Supplemental Table 7. Validation analysis regarding intraoperative hypotensive parameters in the continuous-monitoring cohort.

Cohort, outcome, and exposure	Univariable model		Multivariable model 1 [b]	
	sOR (95% CI)	P	Adjusted sOR (95% CI)	P
Continuous monitoring cohort [a]				
Postoperative AKI				
Mean arterial pressure (per 10.3 mmHg lower value)	1.02 (0.89-1.18)	0.80	1.00 (0.87-1.17)	0.95
Time with mean arterial pressure < 65 mmHg (per 1387.8 seconds)	1.46 (1.35-1.57)	< 0.001	1.24 (1.14-1.36)	< 0.001
Area under curve < 65 mmHg (per 8103.4 second × mmHg)	1.46 (1.35-1.58)	< 0.001	1.45 (1.28-1.65)	< 0.001
Critical AKI				
Mean arterial pressure (per 10.3 mmHg lower value)	1.36 (0.91-2.16)	0.16	1.30 (0.87-2.06)	0.24
Time with mean arterial pressure < 65 mmHg (per 1387.8 seconds)	1.64 (1.47-1.81)	< 0.001	1.45 (1.28-1.65)	< 0.001
Area under curve < 65 mmHg (per 8103.4 second × mmHg)	1.52 (1.37-1.68)	< 0.001	1.31 (1.16-1.47)	< 0.001

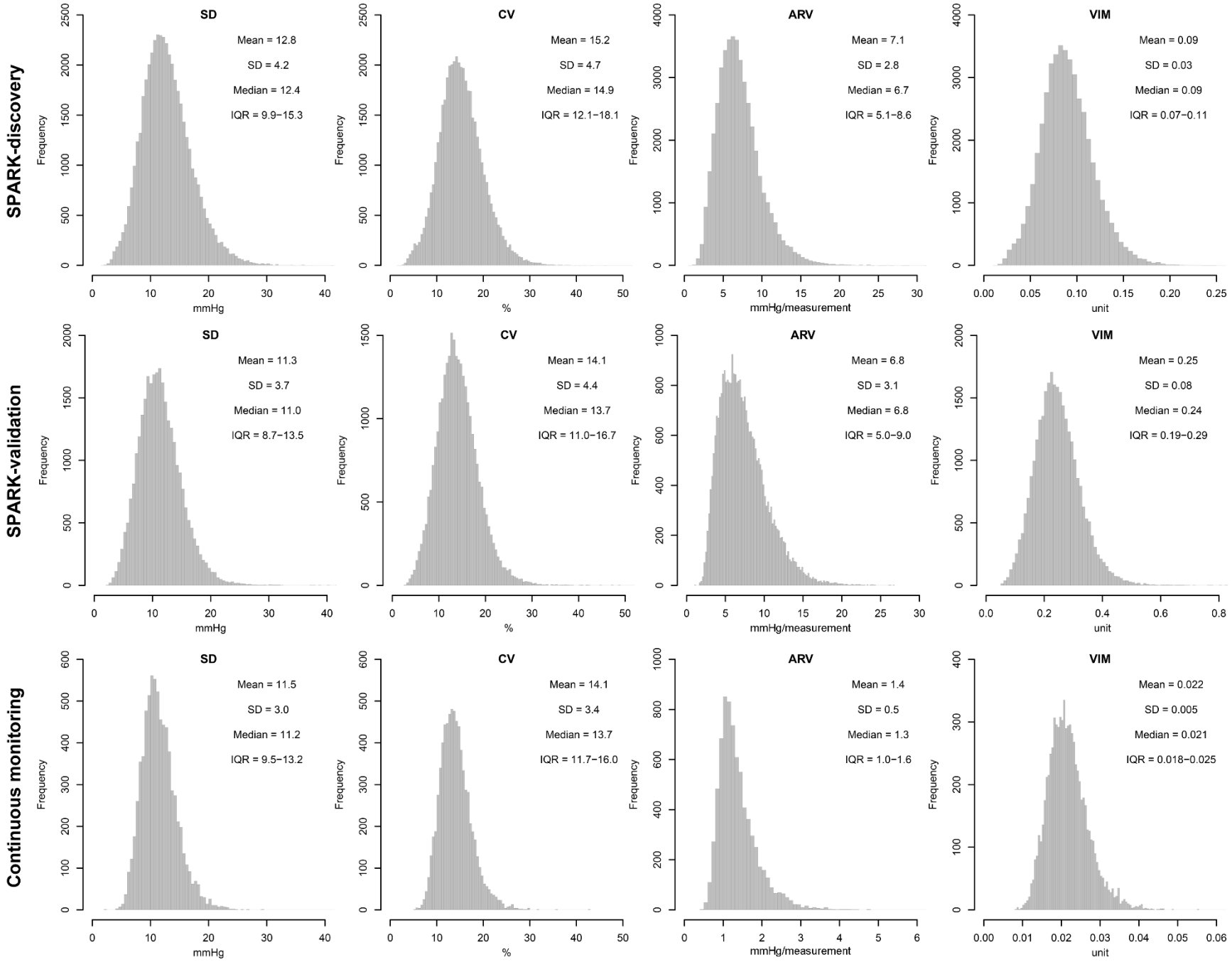
AKI = acute kidney injury, sOR = standardized odds ratio, CI = confidence interval

All blood pressure parameters were included in the regression model as continuous variables and standardized odds ratios for per 1 standard deviation higher are presented; 1 standard deviation values were 10.3 mmHg for lowest mean arterial pressure values, 1387.8 seconds for time under 65 mmHg, and 8103.4 second × mmHg for area under curve under 65 mmHg, respectively.

[a] There were 300 (4%) and 91 (1%) patients with postoperative AKI and critical AKI events, respectively, in the continuous monitoring cohort with number of 7435 patients.

[b] Multivariable model 1 was adjusted for age, sex, eGFR, diabetes mellitus, surgery duration (continuous, hours), emergency operation, usage of renin-angiotensin aldosterone system blockades, dipstick albuminuria, anemia (< 13 g/dl for male, < 12 g/dl for female), hypoalbuminemia (< 3.5 g/dl), and hyponatremia (< 135 mEq/L), without missing values.

Supplemental Figure 1. Distribution of the variability parameters and their descriptive statics.

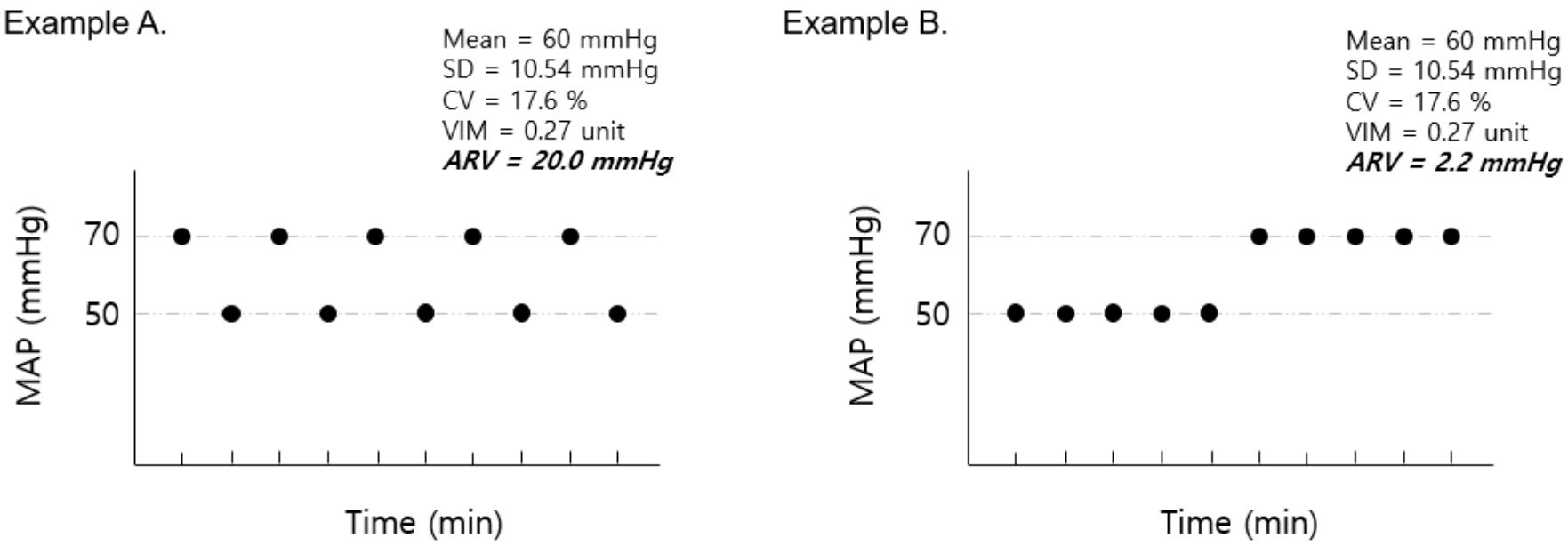


SD = standard deviation, CV = coefficient of variation, ARV = average real variability, VIM = variation independent of mean, IQR = interquartile range

Supplemental Figure 2. Correlation between preoperative clinical variables and variability parameters in the study population.

Correlation analysis was done with Spearman's test, and the squares show the correlation index between the variables according to row and column. The significant correlations ($P < 0.05$) were colored, with red showing positive correlations and blue showing negative correlations. SD = standard deviation, CV = coefficient of variation, ARV = average real variability, VIM = variation independent of mean, DM = diabetes mellitus, RAASB = renin-angiotensin-aldosterone system blockade, eGFR = estimated glomerular filtration rate, Hb = hemoglobin, Alb = albumin, Na = sodium

Supplemental Figure 3. Example cases showing the advantage of average real variability parameter which reflects the orders and differences between the adjacent values.

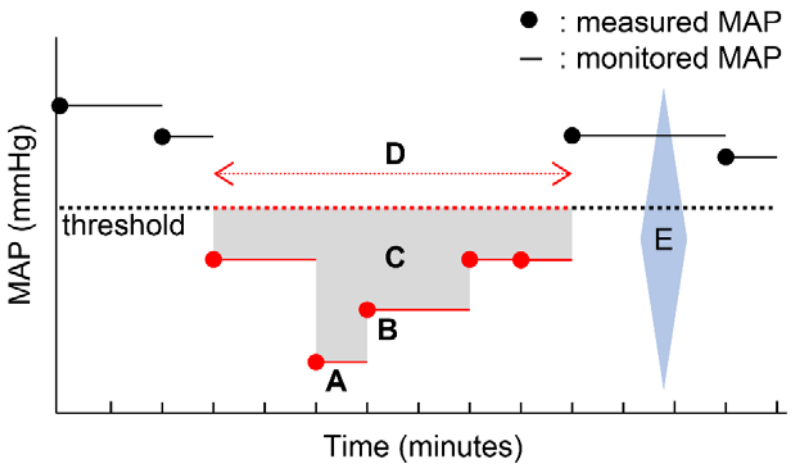


Example cases with the same mean, standard deviation, coefficient of variation, and variation independent of mean values. However, as average real variability can reflect the orders and differences between the adjacent values, the parameter represented the differences between the example cases. Variation independent of mean was calculated within the SPARK-discovery cohort. MAP = mean arterial pressure, SD = standard deviation, CV = coefficient of variation, VIM = variation independent of mean, ARV = average real variability

Supplemental Method 1. The studied mean arterial pressure parameters.

We defined an artifactual blood pressure (BP) value when (1) only systolic or diastolic BP was measured, (2) systolic BP was >10 times that of diastolic BP, (3) systolic BP > 300 mmHg or diastolic BP > 200 mmHg was measured, (4) systolic BP < 30 mmHg or diastolic BP < 20 mmHg was measured, or (5) diastolic BP was > 95% of the systolic BP. The main BP variable studied, mean arterial pressure, was calculated from the results of one-third of systolic BP plus two-thirds of diastolic BP.

Regarding the hypotension-related parameters, the graphical description of the studied mean arterial pressure variables in the SPARK-discovery cohort, which were initially investigated, are shown below. The mean arterial pressure values were measured intermittently, and we collected the "measured mean arterial pressure" values as the main variable. The empty intervals were filled with previously measured mean arterial pressure values, which appeared on the patient monitor ("monitored mean arterial pressure"). Regarding parameters indicative of hypotension, the lowest mean arterial pressure values for certain cumulative times were first collected. As the previous study robustly identified the threshold value associated with an increased risk of postoperative AKI in noncardiac surgery (1), we used aspects of their methods to confirm whether 65 mmHg was a valid cutoff. Then, the cumulative time under the threshold was collected. Additionally, the area under the curve below the threshold level was calculated by summing the multiplication of time and the subtraction of the monitored mean arterial pressure with the threshold value (mmHg×min).



A : Lowest MAP, cumulative 1 minute
B : Lowest MAP, cumulative 2 minute
C : Area under curve (AUC) below threshold
D : Time under threshold
E : Variability (SD, CV, ARV, and VIM)

1. Salmasi V, Maheshwari K, Yang D, et al. Relationship between Intraoperative Hypotension, Defined by Either Reduction from Baseline or Absolute Thresholds, and Acute Kidney and Myocardial Injury after Noncardiac Surgery: A Retrospective Cohort Analysis. *Anesthesiology.* 2017;126:47-65.

Supplemental Method 2. Equations for calculation of the variability parameters from measured *n* number of BP values ($x_1, x_2, ...x_n$) with mean value ($\bar{x}$).

Name	**Abbreviation**	**Equation**
Standard deviation	SD	$\sqrt{\frac{\sum_{i=1}^{n}(x_i - \bar{x})^2}{(n-1)}}$
Coefficient of variation	CV	SD/ $\bar{x}$
Average real variability	ARV	$\frac{1}{n-1}\sum_{i=1}^{n-1}\lvert x_{i+1} - x_i\rvert$
Variation independent of mean	VIM	k x SD/ $\bar{x}^m$

For VIM, linear regression fitting log (SD) with log ($\bar{x}$) was performed. The “k” was the exponential of β0 and the “m” was the β1 of the linear regression model.

Supplemental Method 3. Details of the statistical analysis.

Continuous variables are presented as median values [interquartile ranges], and categorical variables are shown as numbers (percentages). The associations between BP parameters and the risk of the study outcomes were investigated using multivariable logistic regression analysis. The standardized odds ratios per 1 standard deviation increment were calculated when continuous BP parameters were included in the regression models. As our previous SPARK study identified 11 preoperative variables that were the most significantly associated with postoperative AKI and critical AKI risks in our study hospitals, we adjusted the variables in the first multivariable model: age (continuous, years), sex, diabetes mellitus, usage of renin-angiotensin-aldosterone system blockades, surgery duration (continuous, hours), emergency operation, preoperative estimated glomerular filtration rate (eGFR, continuous, mL/min/1.73 m^2), presence of dipstick albuminuria, anemia, hypoalbuminemia, and hypoalbuminemia. However, as this study was conducted to investigate intraoperative insults, actual surgery durations were included in the multivariable models rather than the previously suggested expected surgery duration in the SPARK study. When investigating the clinical significance of the intraoperative mean arterial pressure variability, the second multivariable model was constructed with the addition of the area under curve under threshold mean arterial pressure and the lowest mean arterial pressure measured in the operating room. The third multivariable model was constructed to consider intraoperative blood loss with the addition of estimated blood loss (mL) and transfused amounts of packed red blood cells (mL). The third model was analyzed for patients with this information available only in the SPARK-discovery cohort. Subgroups were divided according to presence of any intraoperative mean arterial pressure <65 mmHg. In the SPARK-discovery cohort, additional subgroup analysis was performed by dividing the cohort according to presence of significant intraoperative hypotension (mean arterial pressure <65 mmHg) and high BP variability (average real variability in the upper quartile range). We used generalized additive models to investigate the overall association between the BP parameters and the risks of study outcomes in the SPARK-discovery cohort. The predicted values of the generalized additive models were from the smoothing functions with the BP parameters as the explanatory variable. The area under curve of the receiver operating characteristics curves were used to compare the discriminative power with P values and confidence intervals calculated by Delong's test. Spearman's test was used to calculate the P values of the correlation between the clinical characteristics and the variability parameters. All statistical analyses were performed with R software version 3.4.3 (The R foundation, Vienna, Austria), and two-sided P values <0.05 were considered statistically significant.