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Relationship between Minute-to-minute Variability of Intraoperative Arterial Blood Pressure and Postoperative Acute Kidney Injury in Patients Undergoing Noncardiac Surgery

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Abstract

Aim: To investigate the effects of minute-to-minute variability of intraoperative arterial blood pressure (BP) on development of postoperative acute kidney injury (AKI) in patients undergoing noncardiac surgery.

Methods: This is retrospective observational study, in which a total 2411 patients aged ≥20 years) who underwent noncardiac surgery with general anesthesia at Fukuoka University Hospital from 2017 to 2019 were included in the present analysis. Minute-to-minute variability of intraoperative systolic BP based on continuous invasive BP measurement using an arterial catheter was estimated using standard deviation (SD) and coefficient of variation (CV). Postoperative AKI was defined as an increase serum creatinine level by more than 0.3 mg/dL or 1.5 times from preoperation within 48 hours after surgery.

Results: A total of 123 (5.10%) cases developed AKI postoperatively. Incidence of AKI was lowest in the first quartile of SD of intraoperative systolic BP (2.65%) compared with the others (7.48% in the second quartile, 5.14% in the third quartile, and 5.14% in the highest quartile). Similarly, the incidence of AKI was also lowest in the first quartile group of CV of intraoperative systolic BP: 2.82%, 6.63%, 5.64% and 5.31% in first to fourth quartile groups, respectively. These associations were significant after adjustment for other risk factors.

Conclusions: In a large-scale observational study who underwent non-cardiac surgery, the lowest risks of postoperative AKI was observed among patients who achieved small minute-to-minute variability in intraoperative systolic BP measurements using an arterial catheter. These results suggest that stable control of intraoperative BP may provide protection against postoperative AKI.

Key words: blood pressure variability, minute-to-minute variability, acute kidney injury, perioperative period, observational study

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Introduction

The most common cause of acute kidney injury (AKI) is sepsis, whereas the second most common cause is surgery. Postoperative AKI is a major complication of surgery. It is known that the incidence of AKI is particularly high after cardiac surgery, but a systematic review of major abdominal surgery showed that the incidence of AKI was 13% in this patient population[1)-4)]. Postoperative AKI has been shown to be associated with long-term adverse events of surgery such as chronic kidney disease and late mortality, and to long-term decline in glomerular filtration rate even after temporary recovery of renal function at discharge[5),6)]. Therefore, prevention of postoperative AKI may provide improvement of long-term prognosis after surgery.

Appropriate blood pressure (BP) control, fluid management, and use of vasopressor during surgery are recommended for the prevention of postoperative AKI[7)]. With regard to intraoperative BP control, intraoperative BP variability has been suggested to be associated with increased risks of postoperative AKI among patients who underwent noncardiac surgery[8),9)] or coronary artery bypass surgery[10)]. However, most previous studies used BP variability based on non-invasive BP measured every 5 minutes or longer[11)], and uncertainty remains surrounding the association between intraoperative BP variability based on invasive BP measurements with short interval and postoperative AKI, particularly among Japanese.

In the present large-scale observational study, we examined the effects of minute-to-minute variability of intraoperative systolic BP on incidence of postoperative AKI among patients who underwent noncardiac surgery.

Materials and Methods

Study design and participants

This is a hospital-based retrospective observational study. A total of 14,479 consecutive cases underwent surgeries with general anesthesia in Fukuoka University Hospital between January 2017 and December 2019. After exclusion of patients aged under 20 years old (n=2180), those on dialysis (n=268), those with missing information on pre- and/or post-operative serum creatinine data (n=2729), those who underwent surgery with less than 60 minutes of anesthesia (n=191) or those without continuous invasive arterial BP measurement (n=6,192), and those with less than 50 continuous invasive arterial BP measurements (n=34), or those who underwent cardiovascular surgery (n=474), 2411 were included in this study. This study was approved by the Fukuoka University Medical Ethics Committee (No. H19-12-006).

Risk factors

During general anesthesia, invasive arterial BP was continuously measured through 22-gauge catheters (20-gauge for limited cases), which was inserted to the radial artery (except for special circumstances), and recorded every minute using automated devise (Life Scope series, Nihon Kohden, Tokyo, Japan). Extreme values in arterial BP (i.e. systolic pressure ≥300 mmHg or ≤35 mmHg and diastolic pressure ≥225 mmHg or ≤5 mmHg) were regarded as inaccurate measurements (due to artifacts etc.) and were excluded from the analysis. Minute-to-minute variability of systolic BP during anesthesia was estimated using standard deviation (SD) and coefficient of variation (CV). Average values of systolic BP during anesthesia were also estimated.

Data collection

Age, gender, smoking history, hypertension, diabetes, heart failure, ischemic heart disease, stroke, proteinuria (Semi-quantitative test ≧ 30 mg/dl), body mass index (BMI), blood test results (hemoglobin level, albumin level, estimated glomerular filtration rate [eGFR]), duration of anesthesia, and type of surgery (urology, cranial nerve, head and neck, orthopedic, general surgery, gynecology, plastic, thoracic, emergency, other) were extracted from the hospital electronic medical records.

Outcome

Postoperative AKI was defined as an increase serum creatinine of ≥0.3 mg/dL or 1.5 times within 48 hours postoperatively from the preoperative serum creatinine level based on the criteria of the Kidney Disease Improving Global Outcomes (KDIGO) guidelines[12)].

Statistical analysis

Continuous variables were shown as mean ± SD, and trends across quartile groups were tested using simple regression models. Categorical variables were shown as the number of participants (percentage), and trends across quartile groups were tested using

Table 1 Baseline characteristics according to quartile of the arterial systolic blood pressure standard deviation

	arterial systolic blood pressure standard deviation				
	quartile1 ≤20.0	quartile2 20.1-27.2	quartile3 27.3-38.2	quartile4 ≥38.3	p value for trend
Age, mean (SD), years	62.6 (15.0)	67.4 (13.4)	67.7 (12.9)	66.7 (14.0)	<0.001
Male, N (%)	318 (52.7)	338 (56.2)	339 (56.2)	326 (54.1)	0.655
Smoking, N (%)	111 (19.2)	121 (20.5)	106 (18.0)	94 (16.3)	0.116
Body mass index, mean (SD), kg/m^2	22.3 (7.6)	21.9 (4.0)	22.4 (8.5)	22.5 (7.1)	0.29
Hypertension, N (%)	293 (48.6)	332 (55.1)	333 (55.2)	325 (54.0)	0.078
Diabetes mellitus, N (%)	183 (30.4)	187 (31.1)	226 (37.5)	200 (33.2)	0.083
Heart failure, N (%)	50 (8.3)	70 (11.6)	71 (11.8)	57 (9.5)	0.512
Ischemic heart disease, N (%)	89 (14.8)	106 (17.6)	104 (17.3)	100 (16.8)	0.45
Stroke, N (%)	110 (18.2)	104 (17.3)	104 (17.3)	121 (20.1)	0.439
Proteinuria, N (%)	103 (17.1)	146 (24.3)	143 (23.7)	112 (18.6)	0.594
Hemoglobin, mean (SD), g/dL	12.60 (1.90)	12.21 (2.02)	12.55 (2.02)	12.71 (1.95)	0.06
Albumin, mean (SD), g/dL	3.84 (0.63)	3.70 (0.65)	3.84 (0.58)	3.90 (0.56)	0.006
eGFR, mean (SD), mL/min	73.13 (22.73)	70.45 (25.52)	67.60 (21.23)	69.14 (19.55)	<0.001
Anesthesia duration (SD), minute	422 (194)	415 (199)	399 (172)	345 (154)	<0.001
Intraoperative mean systolic blood pressure (SD), mmHg	103.3 (12.1)	107.0 (11.5)	109.1 (11.8)	117.3 (15.9)	<0.001
Surgical type, N (%)					
Urologic 116	24 (4.0)	29 (4.8)	27 (4.5)	36 (6.0)	0.993
Neurologic 546	170 (28.2)	122 (20.3)	124 (20.6)	130 (21.6)	
Head and neck 65	19 (3.2)	19 (3.2)	15 (2.5)	12 (2.0)	
Orthopedic 119	22 (3.7)	25 (4.2)	38 (6.3)	34 (5.6)	
General 864	176 (29.2)	241 (40.0)	234 (38.8)	213 (35.3)	
Gynecologic 127	36 (6.0)	32 (5.3)	32 (5.3)	27 (4.5)	
Plastic 22	10 (1.7)	6 (1.0)	5 (0.8)	1 (0.2)	
Thoracic 385	85 (14.1)	73 (12.1)	102 (16.9)	125 (20.7)	
Emergency 137	56 (9.3)	47 (7.8)	19 (3.2)	15 (2.5)	
Other 30	5 (0.8)	8 (1.3)	7 (1.2)	10 (1.7)	

logistic regression models. The effects of intraoperative BP variability on incidence of postoperative AKI was evaluated using logistic regression models with/without covariates and presented as odds ratios (ORs) with 95% confidence intervals (95% CI). A two-sided p-value of <0.05 was considered statistically significant. All data analyses were performed using SAS version 9.4.

Results

Table 1 shows baseline characteristics according to quartile groups of SD of arterial systolic BP measurements using an arterial catheter. Patients with higher SD levels were older and had lower levels of preoperative eGFR, higher intraoperative mean systolic BP, and shorter duration of anesthesia time. Similar findings were observed for quartile groups of CV of arterial systolic BP (Table 2).

Of the 2411 subjects, 123 (5.10%) developed postoperative AKI. Table 3 shows the risks of postoperative AKI according to quartile of SD of intraoperative arterial systolic BP. Incidence of AKI was lowest in the first quartile of SD of intraoperative systolic BP (2.65%) compared with the others (7.48% in the second quartile, 5.14% in the third quartile, and 5.14% in the highest quartile). This association did not change after adjustment for other risk factors, including gender, age, smoking history, BMI, comorbidities (hypertension, diabetes, heart failure, ischemic heart disease stroke and proteinuria), blood tests (hemoglobin level, albumin level and eGFR), anesthesia duration, intraoperative mean systolic BP and type of surgery (urology, cranial nerve, head and neck, orthopedic, and general surgery, gynecology, plastic, thoracic, emergency, and other): multivariable-adjusted odds ratio 3.01 [95% CI 1.54-5.89] for the second quartile, 2.32 [95% CI 1.14-4.70] for the third quartile and 2.79 for the fourth

Table 2 Baseline characteristics according to quartile of the arterial systolic blood pressure coefficient of variation

	arterial systolic blood pressure coefficient of variation				
	quartile1 ≤0.18	quartile2 0.19-0.25	quartile3 0.26-0.35	quartile4 ≥0.36	p value for trend
Age, mean (SD), years	63.2 (15.4)	67.4 (12.8)	66.8 (13.7)	66.6 (13.7)	<0.001
Male, N (%)	318 (52.8)	338 (56.1)	340 (56.4)	325 (53.9)	0.696
Smoking, N (%)	114 (19.7)	114 (19.4)	110 (18.8)	94 (16.2)	0.122
Body mass index, mean (SD), kg/m²	22.3 (7.6)	21.9 (4.1)	22.6 (10.3)	22.2 (4.0)	0.772
Hypertension, N (%)	301 (50.0)	343 (56.9)	309 (51.2)	330 (54.7)	0.348
Diabetes mellitus, N (%)	177 (29.4)	213 (35.3)	204 (33.8)	202 (33.5)	0.208
Heart failure, N (%)	57 (9.5)	67 (11.1)	64 (10.6)	60 (10.0)	0.865
Ischemic heart disease, N (%)	99 (16.5)	112 (18.6)	88 (14.6)	100 (16.6)	0.598
Stroke, N (%)	113 (18.8)	103 (17.1)	101 (16.8)	122 (20.2)	0.564
Proteinuria, N (%)	107 (17.8)	147 (27.4)	133 (22.06)	117 (19.4)	0.731
Hemoglobin, mean (SD), g/dL	12.54 (2.00)	12.24 (1.95)	12.57 (2.05)	12.72 (1.93)	0.018
Albumin, mean (SD), g/dL	3.83 (0.62)	3.71 (0.65)	3.82 (0.59)	3.91 (0.56)	0.001
eGFR, mean (SD), mL/min	72.96 (23.27)	69.74 (25.19)	68.27 (21.47)	69.35 (19.18)	<0.001
Anesthesia duration (SD), minute	421 (194)	416 (197)	397 (176)	347 (153)	<0.001
Intraoperative mean systolic blood pressure (SD), mmHg	106.8 (14.0)	107.2 (10.9)	109.5 (11.6)	113.1 (17.3)	<0.001
Surgical type, N (%)					
Urologic 116	27 (4.5)	25 (4.2)	31 (5.1)	33 (5.5)	0.912
Neurologic 546	155 (25.8)	130 (21.6)	128 (21.2)	133 (22.1)	
Head and neck 65	20 (3.3)	18 (3.0)	15 (2.5)	12 (2.0)	
Orthopedic 119	25 (4.2)	25 (4.2)	35 (5.8)	34 (5.6)	
General 864	182 (30.2)	245 (40.6)	234 (38.8)	203 (33.7)	
Gynecologic 127	36 (6.0)	30 (5.0)	34 (5.6)	27 (4.5)	
Plastic 22	11 (1.8)	5 (0.8)	5 (0.8)	1 (0.2)	
Thoracic 385	78 (13.0)	80 (13.3)	91 (15.1)	136 (22.6)	
Emergency 137	60 (10.0)	39 (6.5)	23 (3.8)	15 (2.5)	
Other 30	8 (1.3)	6 (1.0)	7 (1.2)	9 (1.5)	

quartile [95% CI 1.32-5.90] compared with the reference group of the lowest quartile (Table 3).

Table 4 shows the risks of postoperative AKI according to quartile of CV of intraoperative arterial systolic BP. The incidence of AKI was also lowest in the first quartile group of CV of intraoperative systolic BP: 2.82%, 6.63%, 5.64% and 5.31% in first to fourth quartile groups, respectively. This association did not change after adjustment for other risk factors: multivariable-adjusted odds ratio 2.85 [95% CI 1.42-5.70] for the second quartile, 2.86 [95% CI 1.41-5.80] for the third quartile and 2.71 for the fourth quartile [95% CI 1.29-5.66] compared with the reference group of the lowest quartile (Table 4).

Discussion

In the present large-scale observational study of our institution, the lowest risks of postoperative AKI was observed among patients who achieved small minute-to-minute variability in intraoperative systolic BP measurements using an arterial catheter among Japanese patients who underwent non-cardiac surgery. These findings were significant after adjustment for other risk factors such as gender, age, smoking history, BMI, comorbidities (hypertension, diabetes, heart failure, ischemic heart disease stroke and proteinuria), blood tests (hemoglobin level, albumin level and eGFR), anesthesia duration, mean intraoperative systolic BP and type of surgery (urology, cranial nerve, head and neck, orthopedic, and general surgery, gynecology, plastic, thoracic, emergency, and other).

Few papers have examined short-interval intraoperative BP variability and postoperative AKI in noncardiac surgery[11]. Using data from several Korean hospitals,

Table 3 Risk of AKI according to quartile of the arterial systolic blood pressure standard deviation

	arterial systolic blood pressure standard deviation				
	quartile1 ≤20.0	quartile2 20.1-27.2	quartile3 27.3-38.2	quartile4 ≥38.3	p value for trend
N of events / person	16/603	45/602	31/603	31/603	
Incidence rate	2.65%	7.48%	5.14%	5.14%	
Crude hazard ratio (95% confidence interval)	1 (Reference)	2.96 (1.66-5.31)	1.99 (1.08-3.67)	1.99 (1.08-3.67)	0.201
Adjusted hazard ratio* (95% confidence interval)	1 (Reference)	3.01 (1.54-5.89)	2.32 (1.14-4.70)	2.79 (1.32-5.90)	0.34

*Adjusted for gender, age, smoking history, BMI, comorbidities (hypertension, diabetes, heart failure, ischemic heart disease stroke and proteinuria), blood tests (hemoglobin level, albumin level and eGFR), anesthesia duration, intraoperative mean systolic BP and type of surgery (urology, cranial nerve, head and neck, orthopedic, and general surgery, gynecology, plastic, thoracic, emergency, and other)

Table 4 Risk of AKI according to quartile of the arterial systolic blood pressure coefficient of variation

	arterial systolic blood pressure standard deviation				
	quartile1 ≤0.18	quartile2 0.19-0.25	quartile3 0.26-0.35	quartile4 ≥0.36	p value for trend
N of events / person	17/602	40/603	34/603	32/603	
Incidence rate	2.82%	6.63%	5.64%	5.31%	
Crude hazard ratio (95% confidence interval)	1 (Reference)	2.45 (1.37-4.36)	2.06 (1.14-3.72)	1.93 (1.06-3.51)	0.109
Adjusted hazard ratio* (95% confidence interval)	1 (Reference)	2.85 (1.42-5.70)	2.86 (1.41-5.80)	2.71 (1.29-5.66)	0.02

*Adjusted for gender, age, smoking history, BMI, comorbidities (hypertension, diabetes, heart failure, ischemic heart disease stroke and proteinuria), blood tests (hemoglobin level, albumin level and eGFR), anesthesia duration, intraoperative mean systolic BP and type of surgery (urology, cranial nerve, head and neck, orthopedic, and general surgery, gynecology, plastic, thoracic, emergency, and other)

Kim et al[8] showed a significant association between intraoperative BP variability with time intervals of 5 minutes, 3 minutes, and 2 seconds and increased risk of postoperative AKI in 82,659 patients. The present study confirmed the findings of previous studies and clearly demonstrated an association between short-interval intraoperative BP variability (based on SD and CV of systolic BP) and the development of postoperative AKI.

It is not well understood why intraoperative BP variability affects postoperative AKI. A possible mechanism is a temporary decrease in glomerular filtration rate due to intraoperative hypotension caused by the surgical procedure, blood loss, anesthetic management, or increased aortic stiffness etc[13),14)]. Another possible mechanism is that sympathetic nerve activation, which is closely associated with increased BP variability, may temporarily decrease glomerular filtration rate due to excessive constriction of afferent glomerular arteriole[15),16)].

This is a large-scale observational study which demonstrated the association between intraoperative minute-to-minute BP variability and incidence of postoperative AKI who underwent noncardiac surgery. However, there are several limitations which should be discussed. First, as this is a single-center, retrospective study is subject, findings of this study may be affected by selection bias and may not be generalizable to total Japanese patients. Second, selection bias might have affected the findings of this study because intraoperative use of an arterial catheter was on the discretion of anesthesiologist. Third, other indexes of BP variability such as minimum BP, average real variability (ARV) and difference between highest and lowest mean arterial pressure (MAP) were not used in the present analysis. Fourth, information on intraoperative bleeding, intraoperative infusion, depth of anesthesia, intraoperative use of vasopressor, and background use of beta-blockers and/or calcium channel blockers, which might be associated with BP variability and/or AKI, was missing in the present analysis. Fifth, we do not have information on detailed causes of BP variability (elevated arterial stiffness of the participants, unstable BP control of participants which is attributable to skills of anesthesiologists etc.), Future research is required to investigate cause-specific variability of intraoperative BP and incidence of postoperative AKI.

In conclusion, small minute-to-minute variability in intraoperative systolic BP measurements using an arterial catheter was associated with lower risks of postoperative AKI in a large-scale observational study of Japanese patients who underwent non-cardiac surgery. These results suggest that stable control of intraoperative BP may provide protection against postoperative AKI.

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