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ORIGINAL RESEARCH

Evidence-to-Practice Gap for Preventing Procedure-Related Acute Kidney Injury in Patients Undergoing Percutaneous Coronary Intervention

Satoshi Shoji, MD; Mitsuaki Sawano, MD; Alexander T. Sandhu, MD; Paul A. Heidenreich, MD; Yasuyuki Shiraishi, MD; Shigetaka Noma, MD; Masahiro Suzuki, MD; Yohei Numasawa, MD; Keiichi Fukuda, MD; Shun Kohsaka, MD

BACKGROUND: Acute kidney injury (AKI) is a common complication of percutaneous coronary intervention. This risk can be minimized with reduction of contrast volume via preprocedural risk assessment. We aimed to identify quality gaps for implementing the available risk scores introduced to facilitate more judicious use of contrast volume.

METHODS AND RESULTS: We grouped 14 702 patients who underwent percutaneous coronary intervention according to the calculated NCDR (National Cardiovascular Data Registry) AKI risk score quartiles (Q1 [lowest]–Q4 [highest]). We compared the used contrast volume by the baseline renal function and NCDR AKI risk score quartiles. Factors associated with increased contrast volume usage were determined using multivariable linear regression analysis. The overall incidence of AKI was 8.9%. The used contrast volume decreased in relation to the stages of chronic kidney disease (168 mL [SD, 73.8 mL], 161 mL [SD, 75.0 mL], 140 mL [SD, 70.0 mL], and 120 mL [SD, 73.7 mL] for no, mild, moderate, and severe chronic kidney disease, respectively; $P<0.001$), albeit no significant correlation was observed with the calculated NCDR AKI risk quartiles. Of the variables included in the NCDR AKI risk score, anemia (7.31 mL [1.76–12.9 mL], $P=0.01$), heart failure on admission (10.2 mL [6.05–14.3 mL], $P<0.001$), acute coronary syndrome presentation (10.3 mL [7.87–12.7 mL], $P<0.001$), and use of an intra-aortic balloon pump (17.7 mL [3.9–31.5 mL], $P=0.012$) were associated with increased contrast volume.

CONCLUSIONS: The contrast volume was largely determined according to the baseline renal function, not the patients' overall AKI risk. These findings highlight the importance of comprehensive risk assessment to minimize the contrast volume used in susceptible patients.

Key Words: acute kidney injury ■ acute kidney injury risk score ■ contrast volume ■ percutaneous coronary intervention

See Editorial by Carhart et al.

Acute kidney injury (AKI) after percutaneous coronary intervention (PCI) is a common complication associated with increased mortality and morbidity.[1–5] Decreasing the contrast volume during PCI is the most effective strategy for preventing subsequent AKI.[6–8] Therefore, the clinical practice guidelines recommend preprocedural risk assessment for AKI using validated risk-prediction models for all PCI procedures to alter the contrast volume on the basis of the individual patient profile.[9–11] Recently, the NCDR (National Cardiovascular Data Registry) CathPCI registry developed an AKI prediction model that was designed to promote minimization of contrast volume to the lowest feasible level, especially in high-risk patients.[12,13]

Correspondence to: Shun Kohsaka, MD, Department of Cardiology, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan. E-mail: sk@keio.jp

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CLINICAL PERSPECTIVES

What Is New?

- Acute kidney injury (AKI) is a common complication of percutaneous coronary intervention and can be minimized with reduction of contrast volume via preprocedural risk assessment using validated risk-prediction models.
- Our study demonstrated that the contrast volume was largely determined according to the baseline renal function, not the patients' overall AKI risk as estimated by a validated risk-prediction model.
- Furthermore, the presence of baseline anemia, recent heart failure, acute coronary syndrome, and the use of an intra-aortic balloon pump were associated with increased contrast volume usage, despite the fact that these variables are known risk factors for AKI and are included in the actual prediction model.

What Are the Clinical Implications?

- This suggests an important evidence–practice gap in the use of comprehensive preprocedural AKI risk models.
- Modification of contrast volume based on a complete preprocedural risk assessment may prevent subsequent AKI in susceptible patients.

Nonstandard Abbreviations and Acronyms

AKI	acute kidney injury
CGS	cardiogenic shock
IABP	intra-aortic balloon pump
JCD-KiCS	Japan Cardiovascular Database-Keio Interhospital Cardiovascular Studies
NCDR	National Cardiovascular Data Registry

However, whether these guideline recommendations are reflected in routine clinical practice remains unclear. Despite concerns that the baseline renal function would be the major driving factor regarding the contrast volume, the comprehensive preprocedural AKI risk scores are not weighted enough in relation to the contrast volume used.[14] Although risk factors other than the parameters of renal function are included in the NCDR AKI risk scores, previous studies have not reported that the contrast volume was adjusted for in the presence of these risk factors.

Here, we aimed to investigate the distribution of contrast volume in a PCI registry. We evaluated the association between contrast volume and overall preprocedural AKI risk, along with the relationship between contrast volume and the nonrenal AKI risk factors in the NCDR AKI risk score.

METHODS

This article adheres to the American Heart Association journals' implementation of the Transparency and Openness Promotion Guidelines. The data and materials used to conduct this research are available to researchers for purposes of reproducing the results or replicating the procedure on request. The procedure does need to follow the Act on the Protection of Personal Information Law (as of May 2017) and the Ethical Guidelines for Medical and Health Research Involving Human Subjects (as of March 2015) in Japan.

Study Design

The JCD-KiCS (Japan Cardiovascular Database-Keio Interhospital Cardiovascular Studies) is a large, ongoing, multicenter retrospective cohort study of clinical data collected from consecutive patients undergoing PCI for both acute and elective indications in 13 participating facilities.[15] Clinical variables collected in the JCD-KiCS were defined according to those in the American College of Cardiology–sponsored NCDR CathPCI registry, enabling comparative research between the data from the United States and Japan to investigate disparities in PCI management.[15]

All 17 360 consecutive patients who underwent PCI during July 2008 to March 2018, including acute and elective cases as per the JCD-KiCS, were eligible for this study (Figure 1). Patients with insufficient baseline demographic information (n=85, 0.5%), those who underwent multiple PCIs during a single hospitalization (n=876, 5.0%), those who tested positive for acetylcholine provocation indicating possible vasospastic angina (n=600, 3.5%), those on hemodialysis (n=824, 4.7%), and those who underwent salvage PCI (n=273, 1.6%) were excluded. Patients who were in cardiogenic shock when PCI was started and who underwent salvage PCI were excluded, because contrast volume reduction to minimize AKI is given a lower priority because of the patients' overall high rate of periprocedural morbidity. The final study population comprised 14 702 patients (acute coronary syndrome [ACS], 6271 patients; elective PCI, 8376 patients).

Patients' data were collected from medical records by onsite clinical research coordinators and were entered into an electronic data-capturing system, and data quality was validated using a robust data-query engine. To ensure the accuracy of recorded adverse events, complex JCD-KiCS PCI data were reviewed by an events committee that included board-certified

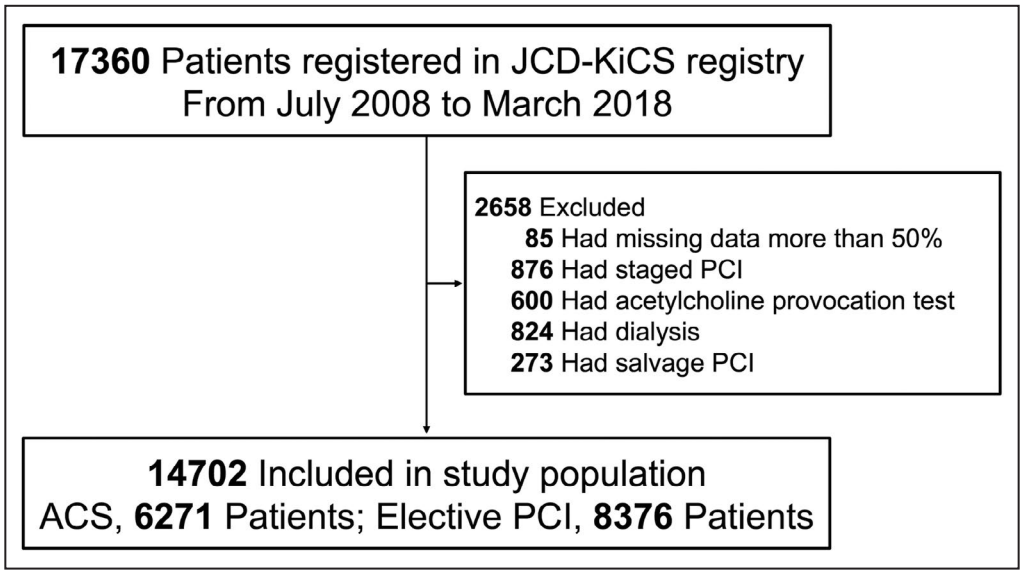

Figure 1. Study flowchart.
ACS indicates acute coronary syndrome; JCD-KiCS, Japan Cardiovascular Database-Keio Interhospital Cardiovascular Studies; and PCI, percutaneous coronary intervention.

cardiologists, who adjudicated on major procedural complications (eg, death, bleeding complications, cardiac and cerebrovascular events). Initially, all procedural complications were reviewed by a trained clinical research coordinator under supervision of the project coordinator and were categorized as those in need of adjudication and those exempt from it. One member from the events committee reviewed the abstracted record, and a second or third adjudicator was called upon in the event of disagreement between the opinions of the project coordinator and the first adjudicator. In patients with history of prolonged hospitalization, we restricted coding of the postprocedural events to 30 days after the last procedure, in accordance with the definition provided by the NCDR.[15] Recording of the contrast volume is strongly recommended in the Japanese Circulation Society Guidelines, and its registration had become mandatory for the nationwide PCI registration system after 2019.[16]

This study followed the Strengthening the Reporting of Observational Studies in Epidemiology reporting guidelines. This study was conducted according to the principles of the Declaration of Helsinki and was approved by each participating hospital's ethics review board. Each patient provided written informed consent.

Definition of AKI

We calculated the estimated glomerular filtration rate (eGFR) (mL/min per 1.73 m^2) using the Modification of Diet in Renal Disease equation and classified patients as having normal baseline renal function (eGFR >60 mL/min per 1.73 m^2), mild (45 mL/min per 1.73 m^2 < eGFR <60 mL/min per 1.73 m^2), moderate (30 mL/min per 1.73 m^2 < eGFR <45 mL/min per 1.73 m^2), or severe chronic kidney disease (CKD; eGFR <30 mL/min per 1.73 m^2).

AKI was defined as (1) >0.3 mg/dL absolute or >1.5-fold relative increase in post-PCI creatinine level, as compared with the baseline value, or (2) new initiation of dialysis.[17] Postprocedural creatinine was defined as the highest value within 30 days after the index procedure, based on the definition used by the NCDR CathPCI registry. Therefore, if >1 postprocedural creatinine level was measured in this period, the highest value was used for determining whether the patient had AKI. Clinical research coordinators collected all creatinine values from within 30 days after PCI, from both in-hospital and outpatient medical records, which guaranteed an adequate sampling of creatinine values for determining AKI. Postprocedural creatinine level was reported to be the highest on the day after PCI, as demonstrated in previous studies[13,18]; thus, our definition of AKI was comparable with that of the Kidney Disease: Improving Global Outcomes consensus, which is the most recent and widely accepted definition.[19–21] AKI requiring dialysis was identified using the predefined JCD-KiCS criteria for acute or worsening renal failure requiring initiation of dialysis after PCI.[13] Patients with AKI requiring dialysis were also included in the AKI group.

Calculation of the NCDR AKI Risk Score

The preprocedural AKI risk was calculated using the previously validated NCDR AKI risk assessment model.[12] Accordingly, the following 11 variables were

used for predicting AKI: (1) age, (2) baseline renal impairment (categorized as mild, moderate, and severe CKD), (3) prior cerebrovascular disease, (4) prior heart failure, (5) heart failure occurring in the 2 weeks before PCI, (6) presenting with non–ST-segment–elevation myocardial infarction/unstable angina versus ST-segment–elevation myocardial infarction, (7) diabetes mellitus, (8) history of cardiogenic shock, (9) prior cardiac pulmonary arrest, (10) anemia (preprocedural hemoglobin <10 mg/dL), and (11) use of an intra-aortic balloon pump (IABP). Using the aforementioned criteria for defining clinical parameters in this study, we could calculate the NCDR AKI risk score for each patient from the JCD-KiCS data set. With no universal criterion for stratifying the NCDR AKI score according to the level of risk,[12] we defined and categorized patients into 4 quartiles according to the severity of the predicted risk as follows: Q1, Q2, Q3, and Q4 included those who scored 0 to 8 (n=3524, 23.9%), 9 to 14 (n=3715, 25.2%), 15 to 22 (n=3730, 25.3%), and ≥23 (n=3753, 25.5%) points on the NCDR AKI risk assessment scale, respectively (Figure 2). Accordingly, patients predicted to be at the highest risk of AKI constituted the last quartile (Q4).

Statistical Analysis

Baseline demographic characteristics and outcomes were compared among the 4 quartile groups. Normally distributed continuous variables are expressed as mean with SD. Statistical comparisons between baseline characteristics were performed using ANOVA for continuous variables with normal distribution. The Pearson χ^2 test or Fisher exact test was used, as appropriate, for categorical variables.

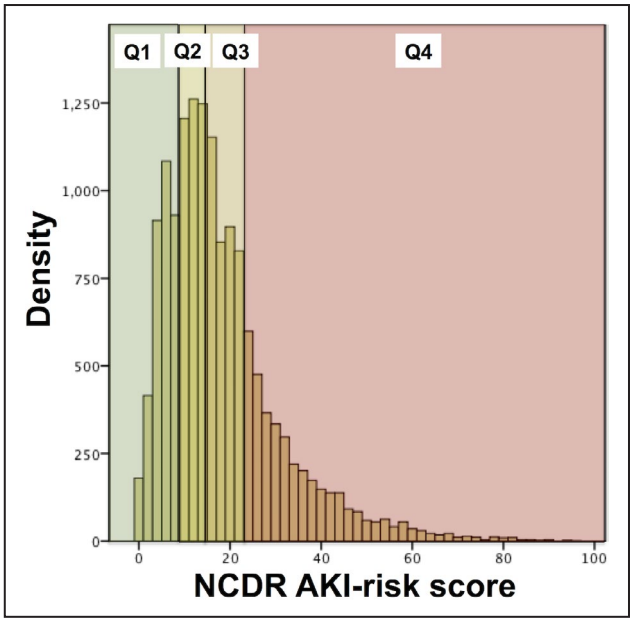

Figure 2. Patient distribution by NCDR (National Cardiovascular Data Registry) acute kidney injury (AKI) risk score quartiles.
Q1, 0 to 8 points; Q2, 9 to 14 points; Q3, 15 to 22 points; Q4, ≥23 points. Q indicates quartile.

First, we plotted the contrast volume used and the rate of AKI occurrence by participating hospitals, to ascertain unadjusted variations in these parameters. Next, we evaluated contrast volume and AKI incidence in the entire study population and in representative subgroups (ACS and elective PCI).

Second, we evaluated the contrast volume used in relation to stages of CKD and the NCDR AKI risk score quartiles, using ANOVA with post hoc Holm correction for multiple comparisons. Furthermore, the contrast volume was compared among stages of CKD and NCDR AKI risk score quartiles using ANCOVA–adjusted variables from the NCDR AKI risk model.[12]

We identified nonrenal risk factors for AKI associated with use of increased contrast volume using multivariable linear regression analysis. The covariates incorporated in this analysis were the complexity of coronary lesions (left main trunk lesion, multivessel PCI in the same procedure, type C lesion, chronic total occlusion, and bifurcation lesion) and variables from the NCDR AKI risk model.[12] We also performed subgroup analyses of (1) ACS, (2) ACS complicated by cardiogenic shock, and (3) elective PCI cases separately. In these models, participating hospitals were included as a random effect to account for clustering of patients by site.

Finally, we evaluated the association between contrast volume used and observed AKI incidence, using multivariable logistic regression analysis. The incorporated covariates were variables from the NCDR AKI risk model.[12] We also performed similar multivariable logistic regression analysis of (1) ACS, (2) ACS complicated by cardiogenic shock, and (3) elective PCI cases separately. In these models, participating hospitals were included as a random effect to account for clustering of patients by site.

Baseline data were missing for <1% of the patients (except for that of body mass index [n=200, 1.4%]). A single mean imputation was used to account for missing data. All *P* values were 2-sided. Results were considered statistically significant at $P<0.05$, except for in multiple testing. The Holm method was used to adjust the *P* values in multiple testing. All statistical analyses were performed using SPSS version 26.0.0 (IBM, Armonk, NY). Data analysis was conducted in July 2020.

RESULTS

Baseline Characteristics

Table summarizes baseline characteristics of the study cohort, divided into quartiles as per NCDR AKI risk

scores. Patients' mean age was 68.7 years (SD, 11.1 years), and 79.1% were men. Patients in the highest quartile of the NCDR AKI risk score (Q4) were more likely to be older, women, present with ACS, have comorbidities, and have reduced eGFR.

Variations in the Contrast Volume and AKI Incidence

We observed significant variations in contrast volume used across the hospitals among the entire cohort (range, 132–258 mL), as well as among patients presenting with ACS (range, 134–259 mL) and patients who underwent elective PCI (range, 132–259 mL) (Figure S1). We also observed wide variations in AKI incidence across participating hospitals among the entire cohort, ranging from 4.3% to 14.1%, as well as among patients presenting with ACS (range, 5.3%–21.4%) and patients who underwent elective PCI (range, 2.5%–7.1%) (Figure S2).

Overall, 1127 (8.9%) study patients, including 750 (21.1%) in Q4, developed AKI. Among patients who underwent elective PCI, 258 (3.9%) developed AKI, and 103 (11.8%) developed AKI in the Q4 group. Of the patients with ACS, 858 (14.2%) developed AKI, and 638 (24.0%) developed AKI in the Q4 group.

Variables Associated With Contrast Volume

The mean contrast volume used was 161 mL (SD, 74.8 mL). Figure 3 shows the contrast volume in relation to the CKD stages and the NCDR AKI risk score quartiles. According to the Holm adjustment, the contrast volume during PCI decreased with increasing CKD stage (168 mL [73.8 mL], 161 mL [75.0 mL], 140 mL [70.0 mL]; 120 mL [73.7 mL] in no, mild, moderate, and severe CKD, respectively; $P<0.001$ for ANOVA, $P<0.001$ for Q1 versus Q2, $P<0.001$ for Q2 versus Q3, $P<0.001$ for Q3 versus Q4). However, the contrast volume was not significantly correlated with the overall NCDR AKI risk score (168 mL [80.1 mL], 161 mL [71.0 mL], 161 mL [71.1 mL], and 157 mL [76.2 mL] in Q1, Q2, Q3, and Q4, respectively; $P<0.001$ for ANOVA, $P<0.001$ for Q1 versus Q2, $P=0.999$ for Q2 versus Q3, $P=0.049$ for Q3 versus Q4). Further adjustment for known confounding variables showed that the contrast volume decreased with increasing CKD stage (184 mL [95% CI, 176–194 mL]; 179 mL [95% CI, 170–188 mL]; 158 mL [95% CI, 149–168 mL]; 134 mL [95% CI, 124–144 mL] in no, mild, moderate, and severe CKD). However, the contrast volume was not significantly correlated with the overall NCDR AKI risk score (181 mL [95% CI, 169–191 mL], 175 mL [95% CI, 164–185 mL], 172 mL [95% CI, 162–182 mL], and 166 mL [95% CI, 157–175 mL] in Q1, Q2, Q3, and Q4), respectively.

Significant predictors of decreased contrast volume usage were high CKD stage (−49.0 mL [95% CI, −55.2 to −42.7 mL], −26.8 mL [95% CI, −30.7 to −22.8 mL], −6.46 mL [95% CI, −9.33 to −3.60 mL] in severe, moderate, and mild CKD compared with no CKD, respectively; $P<0.001$), cardiac pulmonary arrest (−13.5 mL [95% CI, −25.0 to −1.88 mL], $P=0.023$), prior heart failure (−6.41 mL [95% CI, −10.8 to −1.98 mL], $P=0.001$), diabetes mellitus (−4.26 mL [95% CI, −6.77 to −1.74 mL], $P=0.001$), and age (−0.42 mL [95% CI, −0.54 to

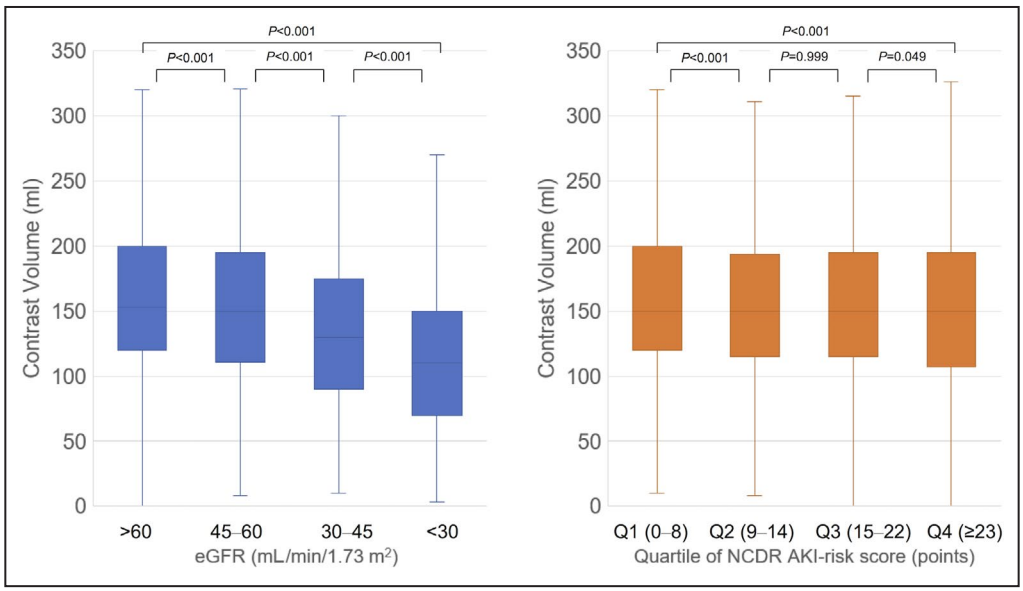

Figure 3. Contrast volume used according to estimated glomerular filtration rate (eGFR) and NCDR (National Cardiovascular Data Registry) acute kidney injury (AKI) risk scores.
Boxplot with whiskers with maximum 1.5 interquartile range. Q indicates quartile.

–0.31 mL], *P*<0.001). Conversely, preprocedural anemia (7.31 mL [95% CI, 1.76–12.9 mL], *P*=0.01), heart failure occurring within 2 weeks before PCI (10.2 mL [95% CI, 6.05–14.3 mL], *P*<0.001), ACS (10.3 mL [95% CI, 7.87–12.7 mL], *P*<0.001), and preprocedural IABP application (17.7 mL [95% CI, 3.9–31.5 mL], *P*=0.012) were significant predictors of increased contrast volume (Figure 4).

Sensitivity analyses of patients with ACS demonstrated that heart failure occurring within 2 weeks before PCI (8.69 mL [95% CI, 3.39–14.0 mL], *P*=0.001) and preprocedural IABP application (22.2 mL [95% CI, 6.91–37.5 mL], *P*=0.004) were significant predictors of increased contrast volume (Figure S3). Conversely, high CKD stage (–37.3 mL [95% CI, –45.2 to –29.4 mL], –20.0 mL [95% CI, –25.7 to –14.4 mL], –5.17 mL [95% CI, –9.30 to –1.05 mL] in severe, moderate, and mild CKD compared with no CKD, respectively; *P*<0.001), and cardiac pulmonary arrest (–12.9 mL [95% CI, –24.9 to –0.80 mL], *P*=0.023) were significant predictors of decreased contrast volume (Figure S3). Further analyses of patients with ACS complicated by cardiogenic shock demonstrated that cerebrovascular disease (23.6 mL [95% CI, 3.10–44.0 mL]; *P*=0.024) and preprocedural IABP use (31.3 mL [95% CI, 5.79–56.8 mL], *P*=0.016) were significant predictors of increased contrast volume (Figure S4). Conversely, high CKD stage (–28.1 mL [95% CI, –50.0 to –6.16 mL], –40.8 mL [95% CI, –59.3 to –22.2 mL], –22.7 mL [–40.2 to –5.15 mL] in severe, moderate, and mild CKD compared with no CKD, respectively; *P*<0.001) was a significant predictor of decreased contrast volume (Figure S4). Finally, the subgroup analyses for patients who underwent elective PCI revealed that heart failure occurring within 2 weeks before PCI (11.4 mL [95% CI, 4.91–17.9 mL], *P*=0.001), and preprocedural anemia (13.5 mL [95% CI, 5.74–21.2 mL], *P*=0.001) were significant predictors of increased contrast volume usage (Figure S5). Conversely, high CKD stage (–61.7 mL [95% CI, –71.5 to –51.9 mL], –31.7 mL [–37.1 to –26.3 mL], –7.25 mL [95% CI, –11.2 to –3.32 mL] in severe, moderate, and mild CKD compared with no CKD, respectively; *P*<0.001), prior heart failure (–7.60 mL [95% CI, –12.9 to –2.26 mL], *P*=0.001), diabetes mellitus (–5.27 mL [95% CI, –8.60 to –1.94 mL], *P*=0.001), and age (–0.55 mL [95% CI, –0.72 to –0.37 mL], *P*<0.001) were significant predictors of decreased contrast volume (Figure S5).

Increased contrast volume was associated with AKI incidence in the entire study population (odds ratio [OR], 1.003 per mL increase in volume; 95% CI, 1.003–1.004, *P*<0.001) and in those with ACS (OR, 1.003 per mL increase in volume; 95% CI, 1.002–1.004, *P*<0.001), ACS complicated by cardiogenic shock (OR, 1.007 per mL increase in volume; 95% CI, 1.003–1.011, *P*=0.001), and in elective PCI (OR, 1.005 per mL increase in volume; 95% CI, 1.003–1.006, *P*<0.001) cases.

DISCUSSION

AKI is considered a preventable complication of PCI. We demonstrated that the contrast volume for PCI is largely influenced by the patient's stage of renal function. Furthermore, the presence of baseline anemia, recent heart failure, ACS presentation, and IABP application were independent predictors associated with

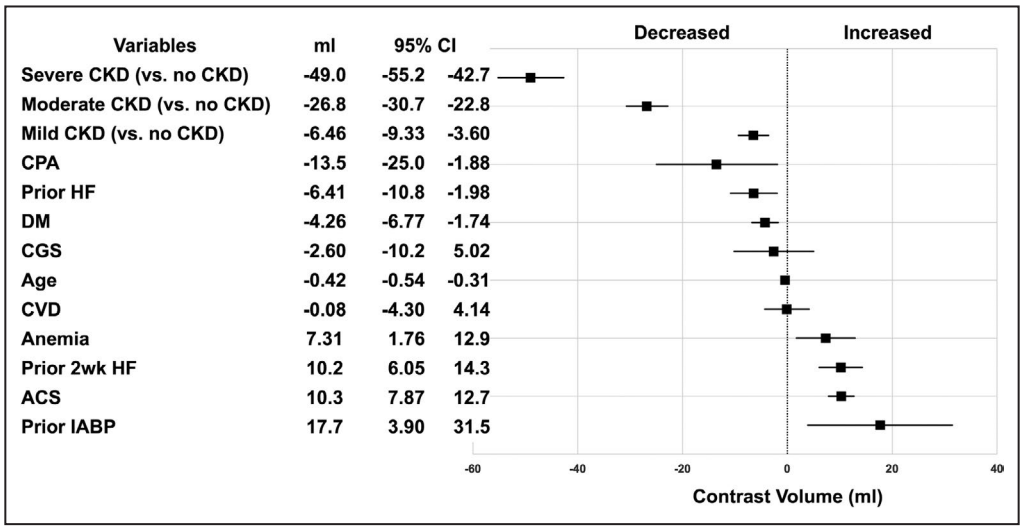

Figure 4. Predictors associated with increased contrast volume usage among entire population (N=14 702).
ACS indicates acute coronary syndrome; CGS, cardiogenic shock; CKD, chronic kidney disease; CPA, cardiac pulmonary arrest; CVD, cerebrovascular disease; DM, diabetes mellitus; HF, heart failure; and IABP, intra-aortic balloon pump.

Table. Baseline Characteristics of the Patients Undergoing PCI Stratified by the Quartiles of the NCDR AKI Risk Score

Characteristics	Total	Q1 0–8	Q2 9–14	Q3 15–22	Q4 ≥23	*P* Value
	n=14 702	n=3515	n=3710	n=3727	n=3750	
Age, y	68.7 (11.1)	63.8 (10.9)	68.7 (8.5)	68.5 (11.7)	73.6 (10.8)	<0.001
Men	11 642 (79.2)	2963 (84.3)	3032 (81.7)	2966 (79.6)	2675 (71.3)	<0.001
Body mass index, kg/m^2	24.3 (3.7)	24.8 (3.5)	24.6 (3.5)	24.5 (3.7)	23.4 (3.8)	0.001
Mean eGFR	64.2 (20.9)	73.5 (14.1)	67.1 (18.0)	65.4 (21.1)	51.5 (2.5)	<0.001
Normal: eGFR ≥60	8536 (58.6)	3030 (88.0)	2310 (62.9)	2010 (54.1)	1186 (31.6)	
Mild: eGFR 45–60	3783 (26.0)	412 (12.0)	1180 (32.2)	1206 (32.5)	985 (26.3)	
Moderate: eGFR 30–45	1624 (11.1)	2 (0.1)	180 (4.9)	483 (13.0)	959 (25.6)	
Severe: eGFR <30	634 (4.3)	0	0	13 (0.4)	621 (16.6)	
Prior 2-wk heart failure	1504 (10.2)	0	12 (0.3)	213 (5.7)	1279 (34.1)	<0.001
Prior heart failure	1335 (9.1)	49 (1.4)	171 (4.6)	342 (9.2)	773 (20.6)	<0.001
Diabetes mellitus	4910 (33.4)	69 (2.0)	1636 (44.1)	1508 (40.5)	1697 (45.3)	<0.001
Cerebrovascular disease	1244 (8.5)	76 (2.2)	225 (6.1)	379 (10.2)	564 (15.0)	<0.001
CAD presentation						<0.001
Stable angina	8388 (57.2)	3162 (89.9)	2716 (73.2)	1524 (41.0)	986 (26.5)	
NSTE-ACS	3198 (21.8)	355 (10.1)	992 (26.8)	980 (26.4)	871 (23.4)	
STEMI	3081 (21.0)	0	0	1211 (32.6)	1870 (50.2)	
Hemoglobin	13.4 (2.1)	14.0 (1.8)	13.6 (1.6)	13.8 (2.0)	12.6 (2.5)	<0.001
Hemoglobin <10 mg/dL	865 (6.1)	0	22 (0.6)	136 (3.8)	707 (19.0)	<0.001
Previous myocardial infarction	3582 (24.3)	1047 (29.7)	992 (26.7)	786 (21.1)	757 (20.2)	<0.001
Previous PCI	5944 (40.4)	1793 (50.9)	1858 (50.0)	1293 (34.7)	1000 (26.7)	<0.001
Previous CABG	717 (4.9)	144 (4.1)	185 (5.0)	184 (4.9)	204 (5.4)	0.060
Hypertension	11 215 (76.2)	2619 (74.3)	2884 (77.7)	2785 (74.7)	2927 (78.0)	<0.001
Dyslipidemia	9867 (67.0)	2556 (72.5)	2632 (70.9)	2458 (65.9)	2221 (59.2)	<0.001
Chronic obstructive pulmonary disease	491 (3.3)	92 (2.6)	122 (3.3)	134 (3.6)	143 (3.8)	0.027
Current smoking	4652 (31.6)	1172 (33.3)	1114 (30.0)	1260 (33.8)	1106 (29.5)	<0.001
Peripheral artery disease	1281 (8.7)	250 (7.1)	359 (9.7)	316 (8.5)	356 (9.5)	<0.001
Atrial fibrillation	995 (8.8)	152 (5.5)	224 (7.6)	244 (8.6)	375 (13.6)	<0.001
Cancer	724 (4.9)	143 (4.1)	199 (5.4)	178 (4.8)	204 (5.4)	0.024
Transradial intervention	8739 (59.4)	2388 (67.8)	2493 (67.1)	2209 (59.3)	1649 (44.0)	<0.001
Out-of-hospital cardiac pulmonary arrest	195 (1.3)	0	3 (0.1)	6 (0.2)	186 (5.0)	<0.001
Cardiogenic shock	407 (2.8)	0	0	2 (0.1)	405 (10.8)	<0.001
VA-ECMO	86 (0.6)	0	2 (0.1)	2 (0.1)	82 (2.2)	<0.001
Preprocedural intra-aortic balloon pumps	126 (0.9)	0	10 (0.3)	10 (0.3)	106 (2.8)	<0.001
Intravascular ultrasound	12 051 (82.0)	2954 (85.1)	3027 (85.3)	3086 (83.7)	2914 (79.0)	<0.001

Values are expressed as mean (SD) or number (percent). AKI indicates acute kidney injury; CABG, coronary artery bypass grafting; CAD, coronary artery disease; eGFR, estimated glomerular filtration rate (mL/min per 1.73 m^2); NCDR, National Cardiovascular Data Registry; NSTE-ACS, non–ST-segment–elevation acute coronary syndrome; PCI, percutaneous coronary intervention; Q, quartile; STEMI, ST-segment–elevation myocardial infarction; and VA-ECMO, venoarterial extracorporeal membrane oxygenation.

increased contrast volume usage, despite the fact that these variables are associated with the occurrence of AKI, and are included in AKI risk assessment models. This suggests an important evidence–practice gap in the use of comprehensive preprocedural AKI risk models. There appears to be an opportunity to optimize

contrast volume and reduce the incidence of PCI-related renal damage.

Because contrast volume reduction is the most effective strategy for preventing AKI,[22] using preprocedural comprehensive risk assessment to identify patients at high risk of AKI is of paramount importance.[12] Previously, Amin et al demonstrated that the contrast volume used was not reduced for patients at high risk of AKI.[14] We provide further evidence that the contrast volume for PCI is mostly adjusted according to the patient's eGFR or CKD stage at the time of the procedure. Other risk factors for postprocedural AKI were associated with similar or higher contrast volumes. These findings suggest that risk factors accounted for in the risk model represent either a lack of awareness or are heavily associated with the complexity of the PCI procedure (eg, it may be difficult to avoid higher contrast volume use in some cases). Importantly, in elective PCI, anemia and recent heart failure were associated with higher contrast volume after adjusting for the complexity of the PCI procedure. This finding underscores the importance in recognizing these variables as potential candidates for developing AKI in elective PCI, where physicians typically have time to comprehensively evaluate the AKI risk before the procedure.

Our findings on the association between the contrast volume used and subsequent AKI were consistent with those in the existing literature. Marenzi et al reported that increased contrast volume is associated with AKI in patients undergoing primary PCI, whereas Laskey et al demonstrated the utility of the ratio of contrast volume administered to the estimated creatine clearance for the predictive assessment of AKI.[23,24] The consistency of our findings with those of earlier studies, even in the contemporary era of evolved PCI, could help implement measures to reduce the incidence of subsequent preventable AKI.

Models predicting the risks of various outcomes and complications of PCI are increasingly used to facilitate clinical decision making and improve the quality of the procedure.[25,26] However, contrary to the expected role of the AKI risk models, we found that some nonrenal AKI risk factors, incorporated as part of the NCDR risk model (baseline anemia, recent heart failure, ACS presentation, and IABP) were associated with increased contrast volume usage. Because it is inevitable and considerable to use a relatively large volume of contrast media for patients with ACS or in the setting of using an IABP, the association in this critical situation appears to be merely descriptive. However, we observed a substantial variation among hospitals in the contrast volume administered among patients presenting with ACS, suggesting room for improvement in the volume of contrast media used even in this critical situation. The presence of baseline anemia and recent heart failure may be modifiable factors by recognizing that those who have these factors have a higher risk of AKI. Moreover, anemia is an independent predictor of AKI,[27] and risk of renal damage correlates with severity of anemia.[28] Furthermore, periprocedural blood loss is an independent risk factor in patients developing AKI, which can be potentially reduced by recognizing and actively managing pre- or periprocedural bleeding.[29] Although evidence from prospective clinical studies is required to support blood transfusion in high-risk patients for AKI prevention, our findings emphasize the importance of recognizing baseline anemia before performing PCI. As for recent heart failure, although the European Society of Cardiology guidelines recommend adequate pre- and postprocedural hydration with saline (at a rate of 0.5 mL/kg per hour), this might be associated with the risk of worsening acute heart failure.[9] Given their increased risk of AKI, cardiologists should focus on minimizing contrast volume in such cases to prevent subsequent AKI.

Finally, our finding highlights the need for developing evidence-based strategies within routine clinical practice to reduce the incidence of subsequent AKI. One demonstrative example of such a quality improvement program showed that implementation of an individual bleeding risk estimation tool was associated with the increased use of bleeding avoidance strategies (bivalirudin, transradial intervention, and vascular closure devices), resulting in a lower rate of bleeding events for patients undergoing PCI.[30] A nonrandomized hospital-level study demonstrated a broad quality improvement program intended to reduce the risk of procedural AKI reduced the risk by 21%, but there is still a lack of high-quality evidence for the use of risk scores in supporting clinical decisions.[31] Currently, a randomized stepped-wedge trial is testing an evidence-based multifaceted intervention to reduce the incidence of AKI.[32] The intervention includes automated identification of high-risk patients using a validated risk score, point-of-care recommendations on safe contrast volume targets, personalized recommendations for hydration, and appropriate outpatient follow-up timing according to patients' risk.

Limitations

The study results should be interpreted within the context of several potential limitations. First, AKI has multifactorial causes (hemodynamic, ischemic, nephrotoxic, or atheroembolic), and the precise pathophysiology of postprocedural AKI could not be identified. Second, although JCD-KiCS is a large, representative registry that reflects current Japanese

practice patterns, it does not include all hospitals conducting PCI in Japan. However, an earlier comparative analysis found comparable baseline characteristics between the JCD-KiCS and the Japanese national PCI registry, indicating generalizability of the findings of the former across Japan.[13] Third, NCDR AKI risk models have been developed based on clinical practices in the United States. Given the racial and ethnic differences between Japanese and Western patient characteristics and treatment strategies, the validity of the model should be confirmed before applying it to the Japanese cohort. However, we previously externally and internationally validated the NCDR AKI risk score using our registry, which supports the international applicability of our study findings.[13] Fourth, because we did not collect clinical data on urine output (also not collected by the NCDR CathPCI registry), we might have underestimated the postprocedural incidence of AKI. Fifth, CKD is defined as structural or functional abnormalities of the kidneys for ≥3 months, as manifested by markers of kidney damage such as proteinuria, in addition to decreased eGFR. We had no data on the presence of proteinuria, which may have led to underestimation of CKD. Sixth, we did not evaluate the use of contrast volume separately between diagnostic coronary angiography and that following PCI. We also did not collect the data for the proportion of ad hoc PCIs among elective PCIs. Seventh, although the NCDR AKI risk models were developed in 2014, we applied these models to the patients who were enrolled before this year. However, given the fact that the association of AKI development with an increased dose of contrast volume was clearly demonstrated and recognized before 2014, possibly going back to 2004,[33–35] we believe that inclusion of patients who underwent PCI before 2014 would not have had a major effect on our results. Finally, there is a concern that anemia and recent heart failure were associated with a higher volume of contrast media. Patients with anemia and with recent heart failure were more likely to have angiographically complicated lesions and severe comorbid diseases compared with patients without anemia and recent heart failure; thus, cardiologists might use comparable contrast volume for patients with anemia and with recent heart failure. Given the increased risk of AKI in such patients, cardiologists should focus on minimizing contrast volume in such cases to prevent subsequent AKI.

CONCLUSIONS

In our study of a large contemporary cohort of patients who underwent PCI, we identified that contrast volume was associated with the severity of concomitant renal disease, and not on the overall risk of developing AKI, as estimated by a comprehensive risk-scoring system. This illustrates that an important evidence–practice gap exists. Modification of contrast volume based on a complete preprocedural risk assessment may prevent subsequent AKI in susceptible patients.

ARTICLE INFORMATION

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Affiliations

Department of Cardiology (S.S., M.S., Y.S., K.F., S.K.), Department of Medicine, Division of Cardiovascular Medicine (A.T.S., P.A.H.), Medical Service (P.A.H.), Department of Cardiology, Saiseikai Utsunomiya Hospital, Tochigi, Japan (S.N.); Department of Cardiology, National Hospital Organization Saitama Hospital, Saitama, Japan (M.S.); and Department of Cardiology, Japanese Red Cross Ashikaga Hospital, Tochigi, Japan (Y.N.).

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Supplementary Material

Figures S1–S5

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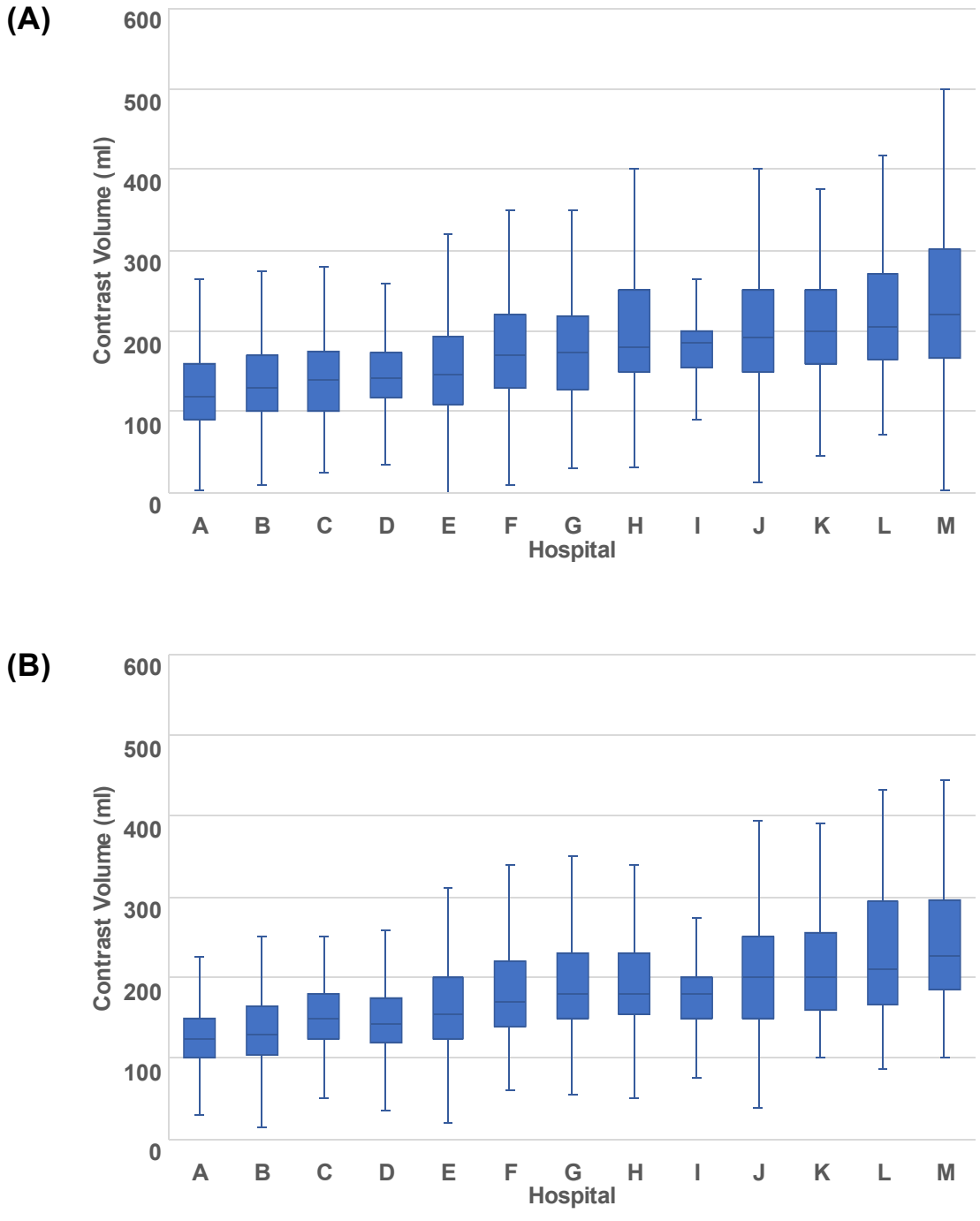
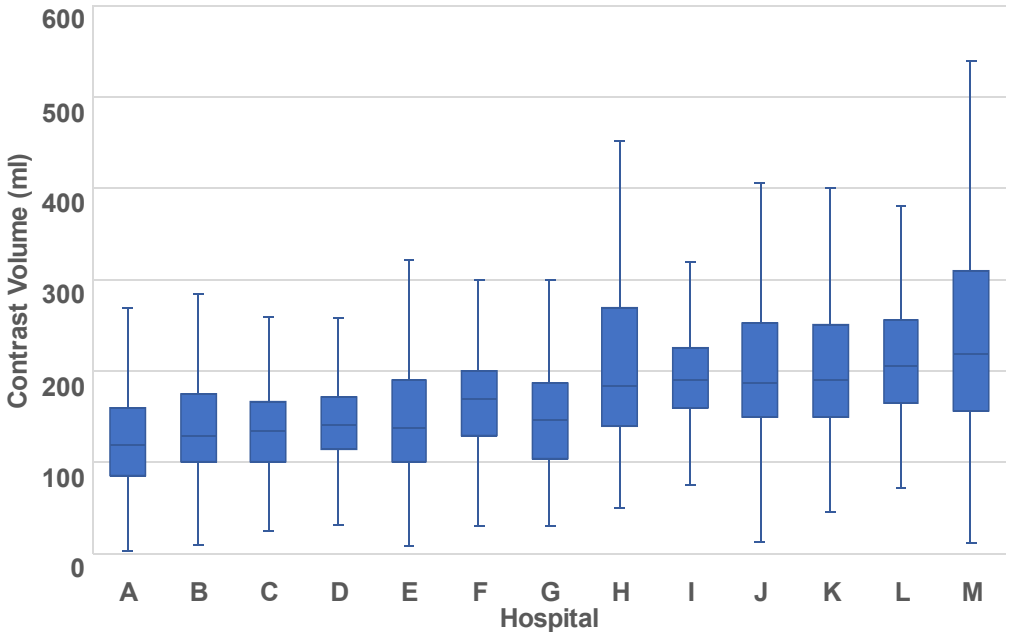
Supplemental Material

Figure S1. Variations in contrast volume used across participating hospitals in (A) the entire cohort, (B) patients presenting with acute coronary syndrome, and (C) patients who underwent elective percutaneous coronary intervention.

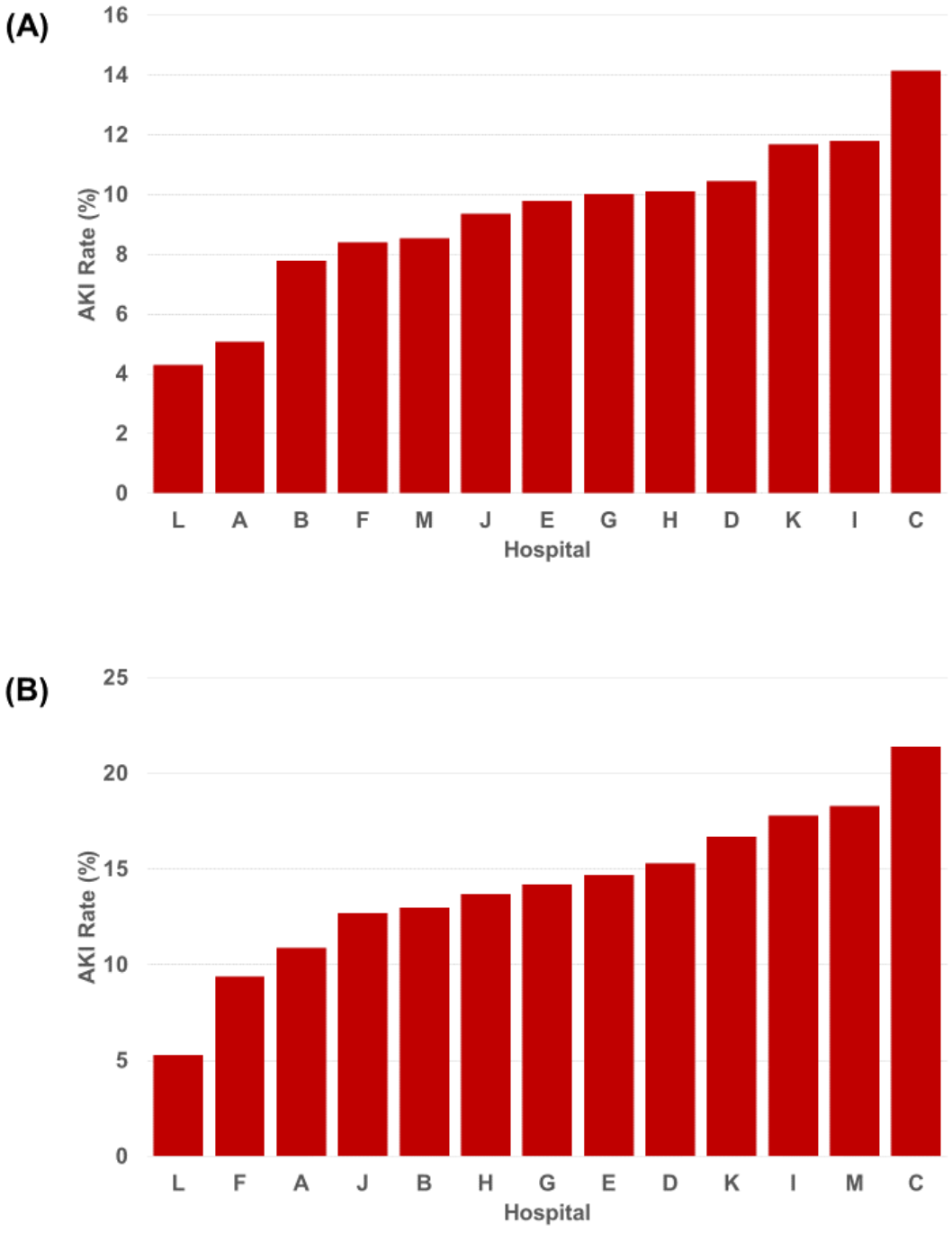


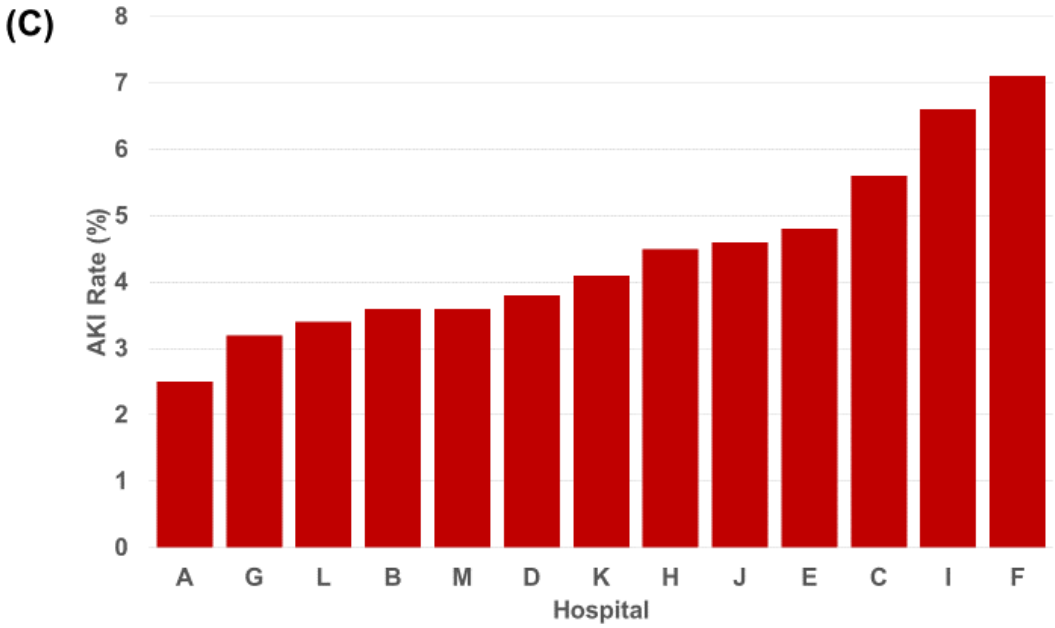
(C)



Boxplot with whiskers with maximum 1.5 interquartile range. Participating hospitals (on the X-axis) are listed in ascending order according to the median contrast volume used.

Figure S2. Variations in the incidence of acute kidney injury across participating hospitals in (A) the entire cohort, (B) patients presenting with acute coronary syndrome and (C) patients who underwent elective percutaneous coronary intervention.

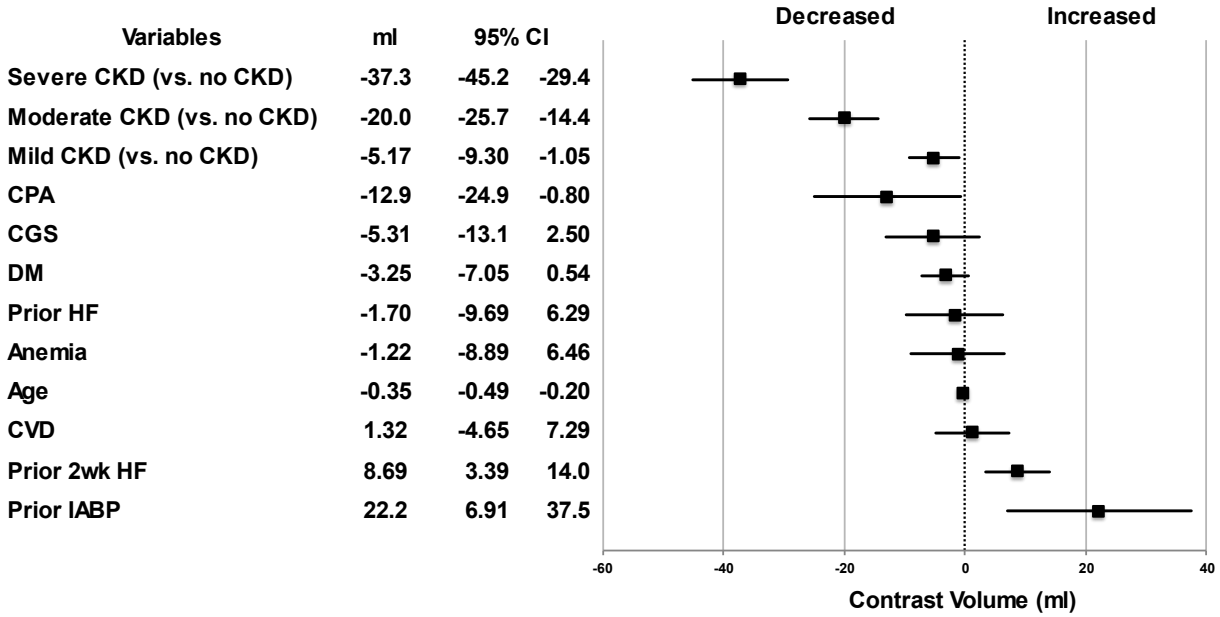




Participating hospitals (on the X-axis) are listed in ascending order according to their incidence of acute kidney injury.

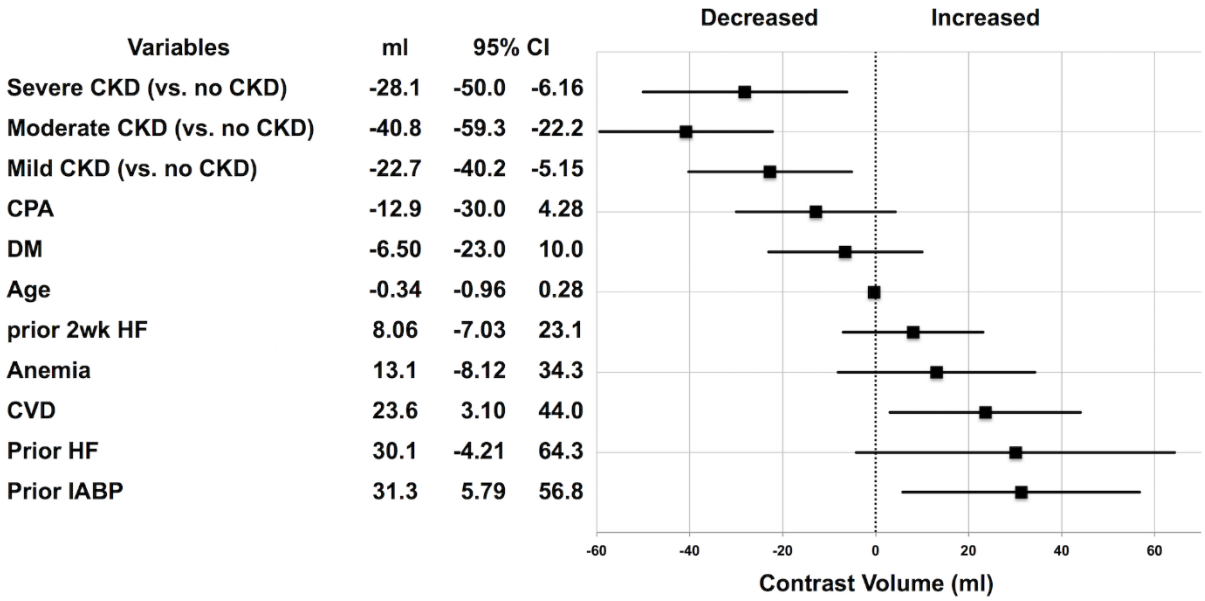
AKI, acute kidney injury.

Figure S3. Predictors associated with increased contrast volume used among patients with acute coronary syndrome (N=6,271).



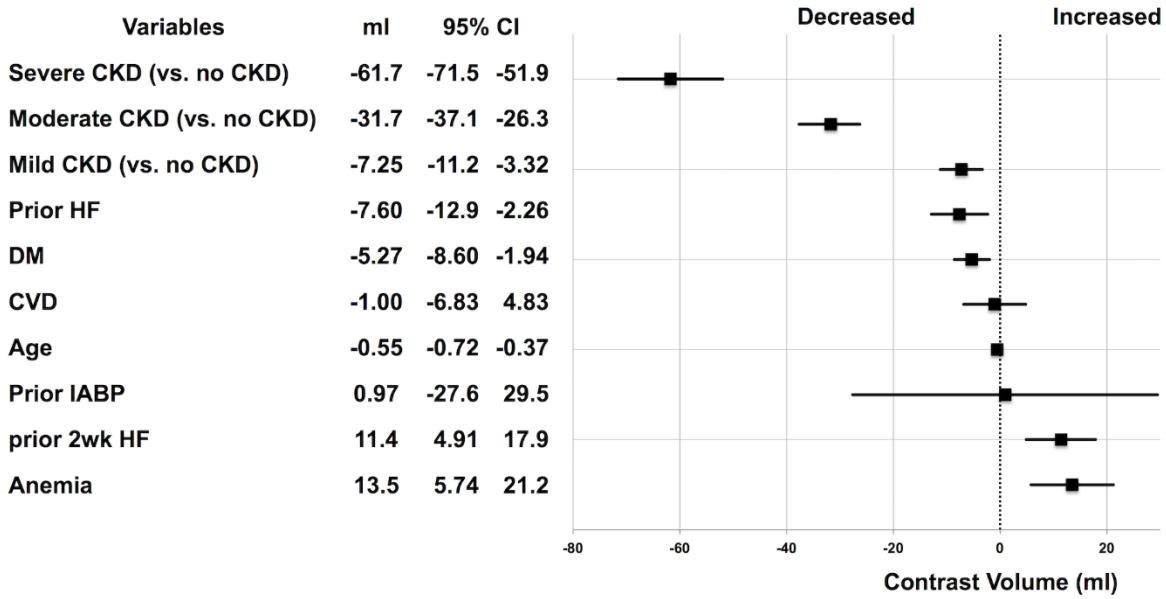
CI, confidence interval; CKD, chronic kidney disease; CPA, cardiac pulmonary arrest; CGS, cardiogenic shock; CVD, cerebrovascular disease; DM, diabetes mellitus; HF, heart failure; IABP, intra-aortic balloon pump.

Figure S4. Predictors associated with increased contrast volume used among patients with acute coronary syndrome complicating cardiogenic shock (N=385).



CI, confidence interval; CKD, chronic kidney disease; CPA, cardiac pulmonary arrest; CVD, cerebrovascular disease; DM, diabetes mellitus; HF, heart failure; IABP, intra-aortic balloon pump.

Figure S5. Predictors associated with increased contrast volume used among the patients undergoing elective percutaneous coronary intervention (N=8,376).



CI, confidence interval; CKD, chronic kidney disease; CVD, cerebrovascular disease; DM, diabetes mellitus; HF, heart failure; IABP, intra-aortic balloon pump.