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Renal Function–Based Contrast Dosing Predicts Acute Kidney Injury Following Transcatheter Aortic Valve Implantation

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Objectives This study sought to assess whether the volume of contrast media (CM) influences the occurrence of acute kidney injury (AKI) following transcatheter aortic valve implantation (TAVI).

Background The volume of CM has been shown to be associated with increasing risk of AKI; however, in a high-risk elderly TAVI population, the predictive value and optimal threshold of CM dose on AKI remain uncertain.

Methods Data of 415 consecutive transfemoral TAVI patients (age 83.6 ± 6.8 years, logistic EuroSCORE 23.0 ± 12.2%) were analyzed. AKI was defined by Valve Academic Research Consortium criteria. Based on a previous formula, the ratio of CM to serum creatinine (SCr) and body weight (BW) (CM × SCr/BW) was calculated as defining the degree of CM use. The association between CM dose and incidence of AKI, as well as predictive factors and prognosis of AKI, were investigated.

Results AKI occurred in 63 patients (15.2%). Cumulative 1-year mortality showed significant differences between the AKI and non-AKI groups (47.9% vs. 15.7%, $p < 0.001$). Mean CM × SCr/BW ratio was higher in the AKI group than in the non-AKI group (4.1 ± 2.9 vs. 2.9 ± 1.6, $p < 0.001$). By multivariate analysis, CM × SCr/BW per 1.0 increase, ejection fraction <40%, and transfusion were associated with the occurrence of AKI (odds ratio [OR]: 1.16; 95% confidence interval [CI]: 1.03 to 1.20; $p = 0.017$, OR: 3.01; 95% CI: 1.49 to 5.00; $p = 0.001$, OR: 2.73; 95% CI: 1.54 to 6.15; $p = 0.001$, respectively). A threshold value of CM × SCr/BW for predicting AKI was statistically identified as 2.7.

Conclusions Although mechanisms of AKI following TAVI are multifactorial, the present study identified a relationship between CM dose increment and high prevalence of AKI. Therapeutic efforts not to exceed the threshold value may reduce the risk of AKI. (J Am Coll Cardiol Intv 2013;6:479–86) © 2013 by the American College of Cardiology Foundation

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First introduced in 2002, transcatheter aortic valve implantation (TAVI) has emerged as a novel alternative procedure enabling catheter-based treatment of high surgical risk patients with symptomatic aortic stenosis) (1–5). Recent reports have shown that acute kidney injury (AKI) occurs in approximately 10% to 30% of patients undergoing TAVI and is associated with early and late mortality (6–11). AKI has been previously shown to increase midterm mortality in patients undergoing cardiac surgery or interventional cardiovascular procedures (12–16). The volume of contrast media (CM) is considered a major factor of AKI and the association between the occurrence of AKI and CM dosing has long been the subject of study (17–22). Several previous investigations have revealed that CM × serum creatinine (SCr) (in mg/dl)/body weight (BW) (in kg) over 5.0 is associated with an increased risk of kidney injury or of the need for dialysis after percutaneous coronary intervention (19–22). Another ratio, the total amount of CM volume divided by the estimated creatinine clearance (CCr), the CM/CCr ratio, is also considered a useful tool (23,24). Although efforts have been made to identify predictors of AKI in TAVI cohorts (6–11), there still exists a paucity of data due to the relatively small cohort size. Moreover, it remains unclear whether CM volume predicts AKI in this high-risk TAVI cohort composed of very elderly patients (6–11). The purpose of the study reported here was therefore to analyze the influence of renal function–based contrast dosing on AKI.

Abbreviations and Acronyms

AKI = acute kidney injury
AR = aortic regurgitation
BW = body weight
CCr = creatinine clearance
CI = confidence interval
CM = contrast media
Cr = creatinine
eGFR = estimated glomerular filtration rate
Euro SCORE = European System for Cardiac Operative Risk Evaluation
LVEF = left ventricular ejection fraction
OR = odds ratio
RBC = red blood cell
ROC = receiver-operating characteristic
SCr = serum creatinine
STS = Society of Thoracic Surgeons Predictive Risk of Mortality
TAVI = transcatheter aortic valve implantation

Methods

Study population. The study population comprised 446 consecutive patients with symptomatic aortic stenosis who underwent an elective transfemoral TAVI procedure in 2 French centers (n = 183, Henri Mondor University Hospital from December 2007 to January 2012; and n = 263, Jacques Cartier Institution Hospital from October 2006 to January 2012, respectively). Patients were selected for TAVI when considered unsuitable or high risk for surgical aortic valve replacement by consensus between individual centers and heart team discussion. The operative risk was calculated by using the logistic European System for Cardiac Operative Risk Evaluation (Logistic EuroSCORE) and Society of Thoracic Surgeons Predictive Risk of Mortality (STS) score. High surgical risk was defined as Logistic EuroSCORE >20% or STS score >10% and also assessed according to the presence of cardiac or noncardiac comorbidities (25). Thirty-one patients were excluded because they were not eligible to undergo assessment of the incidence of AKI: 12 patients were already receiving regular hemodialysis before TAVI, and 19 patients died within 72 h of TAVI. The analysis was performed in the 415 remaining patients. Clinical data, patient characteristics, echocardiographic data, procedural variables, length of hospital stay, and in-hospital and all-cause mortality rates were prospectively examined. Information about death was obtained from the treating hospital or by phoning the patient's family. The medical ethics committees at both hospitals approved this study protocol, and written informed consent was obtained from all patients before the TAVI procedure.

TAVI details and AKI analysis. TAVI procedures have already been described in detail (1–5,26–28). The Medtronic CoreValve Revalving System (Medtronic, Minneapolis, Minnesota) or the Edwards Sapien valve (Edwards Lifesciences, Irvine, California) were used. The femoral artery was mainly approached percutaneously using a pre-closing technique (ProStar XL, Abbott Laboratories, North Chicago, Illinois) (27). In the early phase of our experience, a surgical approach was chosen in both centers (26,27). The prosthesis size was determined from pre-procedural echocardiographic and multislice computed tomographic findings (28). Rapid right ventricular pacing (range 160 to 200 beats/min) was performed during balloon dilation for native aortic valves or implanted bioprosthetic valves. Iodixanol (320 mg of iodine/ml; 290 mOsm/kg of water [Visipaque, GE Healthcare, Buc, France])—a nonionic, iso-osmolar, dimetric type of CM—and iohexol (Omnipaque, GE Healthcare) or iomeprol (Iomeron, Bracco, Milano, Italy)—a nonionic, low-osmolar, monometric type of CM—were used. Catheterization or any other (invasive, significant) examinations requiring CM use were avoided for 72 h before TAVI. The estimated glomerular filtration rate (eGFR) value was calculated using the Modification of Diet in Renal Disease equation: eGFR (expressed in ml/min/1.73 m^2) = $186 \times SCr^{1.154} \times age^{0.203}$ (× 0.742 in the case of female patients) (29). The estimated CCr was calculated using the Cockcroft-Gault method: CCr (ml/min) = 140 − age (years) × BW (kg)/72 × SCr (mg/dl) × (0.85 in female patients) (29). Patients with impaired renal function (eGFR <60 ml/min/1.73 m^2) received hydration and/or pre-treatment drugs (e.g., *N*-acetylcysteine) before TAVI, depending on the physician's decision. The hydration regimens were administered according to previous recommendations: isotonic 0.9% saline was started with an infusion rate of 1 ml/kg of BW per h, 12 h before and continued 12 h after TAVI (30).

However, the hydration volume control varied in each patient due to the presence of multiple comorbidities (a wide age range, renal function, ejection fraction, pulmonary artery pressure, and combined valvular disease).

According to the Valve Academic Research Consortium criteria (31), AKI was defined as a change in SCr up to 72 h compared with baseline, categorized as follows: stage 1, 1.5- to 2-fold increase in SCr or an absolute increase in the highest value of SCr (delta creatinine [ΔCr]) of 0.3 mg/dl (26.4 μmol/l); stage 2, 2.0- to 3.0-fold increase in SCr or 0.3 mg/dl (≥26.4 μmol/l) ≤ ΔCr <4.0 mg/dl (<354 μmol/l); stage 3, ≥3.0-fold increase in SCr or ΔCr ≥4.0 mg/dl (≥354 μmol/l). Blood samples were obtained from the antecubital vein 24 h before and after TAVI and once daily for up to 72 h following TAVI. Other procedural complications during TAVI were also assessed based on the Valve Academic Research Consortium classification. The CM × SCr/BW and CM/CCr ratios were used to evaluate the degree of CM dose in individual patients according to the previous investigations (19–24).

Statistics and data analysis. All statistical analyses were performed using SPSS software, version 19 (SPSS, Chicago, Illinois). Continuous variables were expressed as mean ± SD or median, depending on variable distribution. Categorical data were expressed as percentages of the total. The 2 groups were compared using the chi-square test or the unpaired Student *t* test, as appropriate. A univariate logistic regression analysis was performed to obtain the odds ratio (OR) for AKI. Thereafter, a multivariate analysis was performed using the variables with p values <0.10 in the univariate analysis for examining their independent association with AKI. Receiver-operating characteristic (ROC) curve analyses were performed to examine the ability of the CM × SCr/BW and CM/CCr to identify the risk of AKI. The threshold value–predicted AKI incidence in overall patients was determined by the intersection of the sensitivity and specificity curves, if provided with statistically significant differences. Kaplan-Meier methods were used to estimate the cumulative survival rate in the AKI groups. Differences in survival in each group were compared with the log-rank test. All statistical tests were 2-sided, and a p value <0.05 was considered significant.

Results

Baseline and procedural patient characteristics. AKI occurred in 63 (15.2%) of the 415 study patients. Of these, 59 patients (93.7%) were categorized as AKI grade 2, and 4 other patients (6.3%) requiring hemodialysis during the index hospitalization were categorized as AKI grade 3. Baseline and procedural characteristics of patients according to occurrence of AKI are shown in Table 1. The baseline eGFR (49.3 ± 20.7 ml/min/1.73 m^2 vs. 57.3 ± 21.9 ml/min/1.73 m^2, p = 0.008) and left ventricular ejection fraction (LVEF) (45.2 ± 14.5% vs. 50.4 ± 14.5%, p = 0.009) were significantly lower in the AKI group than in the non-AKI. The degree of post-aortic regurgitation (AR) was higher in the AKI group (1.23 ± 0.82 vs. 1.01 ± 0.77, p = 0.041), and the prevalence of AR ≥ grade 2 tended to be higher in the AKI group (38.1% vs. 26.1%, p = 0.051). There was a trend toward higher prevalence of diabetes (30.2% vs. 20.5%, p = 0.086) and mean pulmonary artery pressure (53.1 ± 15.1 mm Hg vs. 49.4 ± 14.1 mm Hg, p = 0.079) in the AKI group compared with the non-AKI group. Procedural characteristics are shown in Table 2. The total amount of CM, the CM × SCr/BW ratio, and CM/CCr ratio were significantly higher in the AKI group than in the non-AKI group (187.3 ± 81.9 ml vs. 162.7 ± 76.9 ml; p = 0.023, 4.1 ± 2.9 vs. 2.9 ± 1.6; p < 0.001, 5.1 ± 2.9 vs. 3.9 ± 2.1; p < 0.001, respectively). The type of CM, iso-osmolar dimetric or low-osmolar monometric, had no influence on the occurrence of AKI (p = 0.47). Divided into quartile serial series of this study population, average CM dose showed a slight decrease across the 4 phases, although not statistically significant (172.8 vs. 170.5 vs. 163.4 vs. 159.7 ml, p = 0.59). The 30-day mortality rate was 5.8% and was higher in AKI patients than in non-AKI patients (15.9% vs. 4%, p = 0.001). In addition, the rates of major vascular complications (15.9% vs. 8%, p = 0.043) and red blood cell (RBC) transfusion (31.7% vs. 13.9%, p = 0.044) were higher in the AKI group than in the non-AKI group.

Predictors of AKI. The logistic regression analysis of the association between AKI and clinical findings is presented in Table 3. Predictive factors for AKI were eGFR (per 1 ml/min/1.73 m^2 increase), low LVEF (<40%), CM × SCr/BW (per 1.0 increase), post-AR (per 1 grade increase), RBC transfusion, and major vascular complication. In a multiple regression analysis (model 1), low LVEF, CM × SCr/BW, and RBC transfusion were the only independent predictive factors (OR: 2.73, 95% confidence interval [CI]: 1.40 to 5.00: p = 0.001; OR: 1.16, 95% CI: 1.03 to 1.20: p = 0.017; OR: 3.01, 95% CI: 1.54 to 6.15: p = 0.001; respectively). ROC analysis provided a modest discrimination with statistical significance in the CM × SCr/BW values (area under the curve: 0.630, 95% CI: 0.55 to 0.71, p = 0.001) and the threshold value of CM × SCr/BW was 2.7 for predicting AKI (OR: 1.77, sensitivity: 60.7%, specificity: 51.9%). Categories between CM × SCr/BW >2.7 and <2.7 were compared for high-risk subgroups with respect to the incidence of AKI (Fig. 1). Prevalence of AKI with CM × SCr/BW >2.7 was also significantly higher than that of AKI with CM × SCr/BW <2.7 in the subgroups of eGFR <60 ml/min/1.73 m^2 (26.1% vs. 11.9%, p = 0.036), LVEF <40% (30.8% vs. 15.2%, p = 0.033), and RBC transfusion (39.4% vs. 16.1%, p = 0.033). The other multivariate model using CM/CCr

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Table 1. Baseline Patient Characteristics

	Overall (N = 415)	AKI (n = 63)	Non-AKI (n = 352)	p Value
Baseline clinical characteristics				
Age, yrs	83.6 ± 6.8	83.2 ± 5.9	83.6 ± 6.9	0.67
Male	185 (44.6%)	33 (52.4%)	152 (43.2%)	0.18
Height, cm	162.8 ± 8.8	164.3 ± 9.1	162.6 ± 8.7	0.14
BW, kg	68.7 ± 14.1	70.6 ± 13.8	68.4 ± 14.2	0.25
Body mass index, kg/m^2	25.9 ± 4.7	26.2 ± 5.0	25.8 ± 4.6	0.58
Body surface area, m^2	1.7 ± 0.19	1.8 ± 0.19	1.7 ± 0.20	0.090
NYHA classification III/IV	321 (77.3)	53 (84.1)	268 (76.1)	0.16
COPD	132 (31.8)	22 (34.9)	110 (31.3)	0.57
Peripheral artery disease	85 (20.5)	14 (22.2)	71 (20.2)	0.71
Prior myocardial infarction	54 (13.0)	9 (14.3)	45 (12.8)	0.44
Prior PCI	127 (30.6)	19 (30.2)	108 (30.7)	0.93
Prior stroke	38 (9.2)	7 (11.1)	31 (8.8)	0.35
Prior cardiac surgery	67 (16.1)	7 (11.1)	60 (17.0)	0.16
Diabetes mellitus	91 (21.9)	19 (30.2)	72 (20.5)	0.086
Hypertension	306 (73.7)	47 (74.6)	259 (73.6)	0.87
Dyslipidemia	201 (48.4)	32 (50.8)	169 (48.0)	0.78
Smoking	39 (9.4)	8 (12.7)	31 (8.8)	0.22
CCr, ml/min.	43.8 ± 21.0	40.0 ± 18.1	43.8 ± 21.0	0.13
eGFR, ml/min./1.73 m^2	56.1 ± 21.8	49.3 ± 20.7	57.3 ± 21.9	0.008
eGFR ≥60 ml/min/1.73 m^2	149 (35.9)	17 (27.0)	132 (37.5)	
eGFR 45–60 ml/min/1.73 m^2	130 (31.3)	16 (25.4)	114 (32.4)	0.024
eGFR <45 ml/min/1.73 m^2	136 (32.8)	30 (47.6)	106 (30.1)	
LVEF <40%	131 (31.6)	30 (47.6)	101 (28.7)	0.003
Logistic EuroSCORE, %	21.0 (14.4–28.9)	21.4 (15.9–29.4)	21.0 (14.4–28.6)	0.63
STS score, %	7.4 (4.7–11.8)	8.6 (5.0–14.5)	7.2 (4.7–11.0)	0.39
Echocardiographic findings				
LVEF, %	49.6 ± 14.6	45.2 ± 14.2	50.4 ± 14.5	0.009
AVA, cm^2	0.64 ± 0.17	0.66 ± 0.16	0.64 ± 0.17	0.35
Mean aortic gradient, mm Hg	48.2 ± 17.9	44.3 ± 15.4	48.9 ± 18.3	0.065
AR grade 0–4	0.85 ± 0.73	0.83 ± 0.67	0.85 ± 0.74	0.83
MR grade 0–4	0.99 ± 0.69	0.11 ± 0.77	0.97 ± 0.68	0.19
Pulmonary artery pressure, mm Hg	49.9 ± 14.3	53.1 ± 15.1	49.4 ± 14.1	0.079
Post-procedural AVA, cm^2	1.9 ± 0.49	1.9 ± 0.66	1.9 ± 0.46	0.65
Post-mean aortic gradient, mm Hg	10.0 ± 4.4	10.4 ± 4.3	9.9 ± 4.5	0.47
Post-AR grade 0–4	1.04 ± 0.78	1.23 ± 0.82	1.01 ± 0.77	0.041
Post-AR ≥grade 2	116 (28.0)	24 (38.1)	92 (26.1)	0.051
Post-MR grade 0–4	0.93 ± 0.77	1.10 ± 0.75	0.91 ± 0.77	0.10

Values are mean ± SD, n (%), or median (interquartile range).

AKI = acute kidney injury; AR = aortic regurgitation; AVA = aortic valve area; BW = body weight; CCr = creatinine clearance; COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration rate; EuroSCORE = European System for Cardiac Operative Risk Evaluation; LVEF = left ventricular ejection fraction; MR = mitral regurgitation; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; STS score = Society of Thoracic Surgeons Predictive Risk of Mortality score.

(model 2) revealed that CM/CCr per 1.0 increase was also identified as an independent predictor of AKI (OR: 1.24, 95% CI: 1.05 to 1.47; p = 0.011) in addition to the other 2 predictors. ROC analysis also provided a modest discrimination in CM/CCr (area under the curve: 0.61, 95% CI: 0.57 to 0.92; p = 0.008) and a threshold value of CM/CCr was 3.7 (OR: 1.77, sensitivity: 59.0%, specificity: 55.1%).

Cumulative mortality and AKI. Clinical follow-up availability was 100%, and median follow-up was 334 days (interquartile range: 120 to 537 days). A total of 99 patients (23.9%) died; of these, 31 patients were in the AKI group. Kaplan-Meier analysis of cumulative mortality for the AKI groups is presented in Figure 2. The cumulative 1-year mortality was 45.7% in the AKI group and 15.7% in the non-AKI group, respectively. The probability of cumulative

Table 2. Procedural Patient Characteristics

	Overall (N = 415)	AKI (n = 63)	Non-AKI (n = 352)	p Value
Peri-procedural variables				
Procedure time, min	84.1 ± 42.1	91.5 ± 44.0	82.8 ± 41.7	0.20
Fluoroscopy time, min	20.1 ± 10.2	23.8 ± 10.1	19.5 ± 10.1	0.010
CM dose, ml	166.4 ± 78.1	187.3 ± 81.9	162.7 ± 76.9	0.023
Iso-osmolar dimetric CM	174 (41.9)	29 (16.6)	145 (41.2)	0.47
Low-osmolar monometric CM	241 (58.1)	34 (14.1)	207 (58.8)	
CM × SCr/BW ratio	3.1 ± 1.9	4.1 ± 2.9	2.9 ± 1.6	<0.001
CM/CCr ratio	4.1 ± 2.3	5.1 ± 2.9	3.9 ± 2.1	<0.001
Medtronic CoreValve	212 (51.2)	35 (55.6)	177 (50.3)	0.44
Edwards Sapien	203 (48.9)	28 (44.4)	175 (49.7)	
Post-procedural variables				
Length of stay in hospital, day	8.0 ± 7.7	9.6 ± 8.1	8.6 ± 5.8	0.55
Procedural success	396 (95.4)	56 (88.9)	340 (96.6)	0.015
30-day mortality	24 (5.8)	10 (15.9)	14 (4.0)	0.001
30-day combined safety endpoint	347 (83.6)	45 (71.4)	302 (85.8)	0.005
Myocardial infarction	2 (0.5)	1 (1.6)	1 (0.3)	0.28
Stroke	17 (4.1)	1 (1.6)	16 (4.5)	0.24
Major vascular complication	38 (9.2)	10 (15.9)	28 (8.0)	0.045
RBC transfusion	69 (16.6)	20 (31.7)	49 (13.9)	0.001
RBC transfusion ≥4 U	19 (4.6)	9 (14.3)	10 (2.8)	0.001
Two-valve implantation	9 (2.2)	2 (3.2)	7 (2.0)	0.41
New implantation of pacemaker	51 (12.3)	11 (17.5)	40 (11.4)	0.18
Cardiac tamponade	13 (3.1)	4 (6.3)	9 (2.6)	0.12
Surgery for vascular complication	15 (3.6)	4 (6.3)	11 (3.1)	0.18
Requirement of any cardiac surgery	6 (1.4)	1 (1.6)	5 (1.4)	0.92

Values are mean ± SD, n (%), or median.
CM = contrast media; RBC = red blood cell; SCr = serum creatinine; other abbreviations as in Table 1.

mortality over the entire follow-up period after TAVI significantly differed between the 2 groups (log-rank, $p < 0.001$).

Discussion

This study demonstrates that an increased CM × SCr/BW ratio and CM/CCr may influence the incidence of AKI following TAVI in a relatively large TAVI cohort of 415 patients. Low LVEF (<40%) and RBC transfusion were also significant predictive factors of AKI. The cumulative 1-year mortality rate in the AKI group showed a 3-fold increase compared with the non-AKI group (45.7% vs. 15.7%) and was consistent with previous reports (6–11). The ratio of CM × SCr/BW >2.7 and CM/CCr >3.7 for

Table 3. Multivariate Regression Analysis for the Predictive Factors of AKI

	Univariate Analysis			Multivariate Analysis (Model 1)			Multivariate Analysis (Model 2)		
	OR	95% CI	p Value	OR	95% CI	p Value	OR	95% CI	p Value
Diabetes	1.68	0.92–3.05	0.089						
eGFR (per 1 ml/min/1.73 m^2 increase)	0.98	0.97–0.99	0.008						
LVEF <40%	2.26	1.31–3.90	0.003	2.73	1.49–5.00	0.001	2.73	1.40–5.32	0.003
Pulmonary artery pressure	1.02	0.99–1.04	0.080						
CM × SCr/BW ratio (per 1.0 increase)	1.23	1.10–1.37	<0.001	1.16	1.03–1.20	0.017			
CM/CCr ratio (per 1.0 increase)	1.29	1.14–1.46	<0.001				1.24	1.05–1.47	0.011
Post-AR (per 1 grade increase)	1.43	1.01–2.02	0.043						
Red blood cell transfusion	2.88	1.56–5.30	0.001	3.01	1.54–6.15	0.001	3.01	1.41–6.49	0.005
Major vascular complication	2.18	1.00–4.75	0.049						

CI = confidence interval; OR = odds ratio; other abbreviations as in Tables 1 and 2.

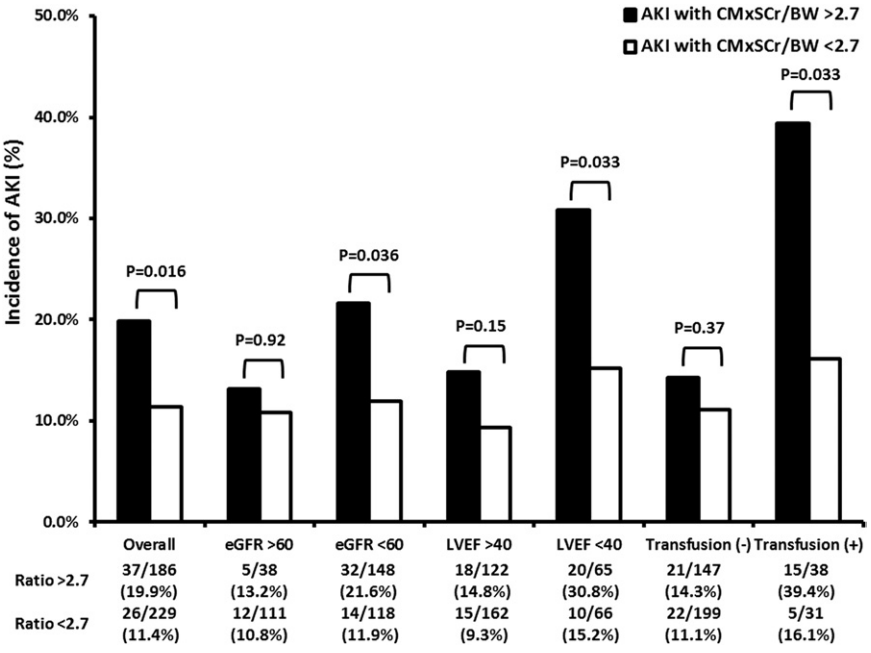

Figure 1. Patient Distribution of AKI

AKI incidence between CM × SCr/BW >2.7 and <2.7 for overall patients and for the patients of each subgroup are shown. AKI = acute kidney injury; BW = body weight; CM = contrast media; eGFR = estimated glomerular filtration rate; LVEF = left ventricular ejection fraction; SCr = serum creatinine.

predicting AKI could be considered threshold values to decrease the risk of AKI during TAVI. To the best of our knowledge, this is the first study to demonstrate that a simple formula integrating the amount of CM and renal function may predict the risk of AKI after TAVI.

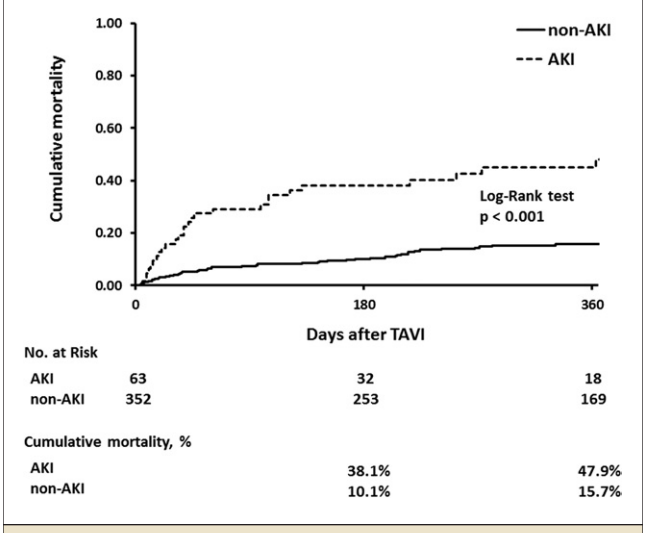

Figure 2. Time-To-Event Curves for Cumulative Mortality

Mortality rate was calculated using Kaplan-Meier methods and compared using the log-rank test according to the presence and absence of acute kidney injury (AKI).

Approximately 10% to 30% of patients undergoing TAVI sustain kidney injury arising from various factors. AKI, individually defined by elevations in SCr values, has been associated with early or late adverse events, even when kidney function damage was minimal (12–16). Although CM use was not identified as an independent predictor of AKI after TAVI in previous reports (6–11), it is still of the utmost importance to know whether CM use should be limited in TAVI procedures carried out in an elderly and high-risk cohort. The present study demonstrates the relationship between AKI and CM dose calculated by CM × SCr/BW and CM/CCr. Moreover, several factors may influence the occurrence of AKI, and these were classified into patient clinical characteristics and procedural complications (32). The AKI-related risk of low LVEF, hemodynamic instability, or hypotension with reduction in renal blood supply became more apparent during conventional catheter-based therapeutic procedures (17,18). A TAVI procedure carries an inherent risk of prolonged hypotension and hemodynamic changes due to rapid pacing during balloon valvuloplasty and bioprosthetic valve implantation. In addition, TAVI procedures in complex patients carry an increased risk of RBC transfusion, vascular complications, or other catastrophic complications compared with other catheter-based therapeutic strategies, all of which may potentially increase the risk of AKI. Several possible causes of AKI following TAVI should be taken into account. Our

data demonstrated that CM × SCr/BW was predictive of AKI, especially in the subgroups of low GFR, LVEF, and patients requiring transfusion, supporting the multifactorial pathogenesis of AKI after TAVI.

The BW- and baseline SCr-adjusted maximum CM dose (CM × SCr/BW) was established as a criterion for prevention of radiocontrast-induced nephropathy, and CM × SCr/BW >5.0 was shown to be a predictor for the occurrence of post-procedural kidney injury (19–22). The assessment of the CCr-adjusted maximum CM dose, CM/CCr, was also useful for risk stratification of post-procedural nephropathy and has been recommended to be kept under 3.7 or not to exceed 3.0 (23,24). After stratification for the CM × SCr/BW and CM/CCr factors, our data indicated that the threshold values using the ROC curve to predict AKI were 2.7 and 3.7, respectively. Although the cutoff value of CM/CCr was thought to be similar, CM × SCr/BW was lower in comparison with the previous threshold. This discrepancy may be explained by significant differences in the individual background of patients composing this very elderly TAVI population. In the current study, mean estimated eGFR and CCr values were 56.1 and 43.8 ml/min, respectively. The average CM dose was 166.4 ± 78.1 ml. By contrast, previous studies revealed that more than 70% of patients maintained the eGFR value or CCr >60 ml/min, with an average CM dose over 200 ml (20–24). This result means that similar CM value thresholds may be interpreted differently. Absolute CM dose should be more restricted in the TAVI cohort to stay under the previous recommended cutoff value. A reported study using transesophageal echocardiography revealed a significant volume reduction of CM during TAVI (33). We also show in the present study a slight reduction in average CM use (about 10 to 15 ml) in serial quartile study periods. Several possible approaches and device improvements may reduce the CM volume. It is noteworthy that CM overdosing may be a more powerful predictor of AKI when combined with other predictive factors of AKI, such as impaired renal function (eGFR <60 ml/min/1.73 m^2), LVEF <40%, and RBC transfusion. Classifying TAVI patients into high-risk categories and making all possible efforts to reduce the amount of CM used during TAVI procedures could prove clinically important. The outcome is widely known to be worse in patients with AKI. Our results demonstrated a finding that was in line with previous clinical studies (6–16). In order to improve prognosis, risk stratification is required to reduce the risk of subsequent AKI. Further investigations are warranted to establish whether use of limited CM doses may prevent or minimize AKI following TAVI.

Study limitations. Our study reports a prospective TAVI cohort from 2 centers in France that is not large enough to establish the definite cutoff point for CM dose. We opted to include recipients of both the Edwards valve and the CoreValve, as this mixed cohort reflected our real clinical experience. Although the CM dose was identified as one of the independent predictors of AKI, the incidence of AKI during TAVI can be multifactorial. Estimation of the renal function by using the Modification of Diet in Renal Disease equation or Cockcroft-Gault method in elderly patients is limited in terms of reliability (34). On the basis of the aforementioned limitations, the current limits of both CM × SCr/BW and CM/CCr ratios should not be considered a definitive threshold. In addition, the serial change in renal function is clinically important, especially in this group of patients with AKI after TAVI. Other factors confounding the association with AKI may have been neglected in this study. Although hemodynamic instability during the procedure is a well-known predictive factor for AKI (17,18), the precise degree of hemodynamic instability during TAVI is difficult to assess. Among the nineteen patients who died within 72 h of the procedure, the vast majority of them with cardiogenic shock, were excluded from the initial analysis.

Conclusions

Increasing CM dose as assessed by CM × SCr/BW or CM/CCr is associated with the occurrence of AKI following TAVI. The occurrence of AKI has become a strong factor of increased late mortality after TAVI. Therapeutic efforts to reduce the CM dose should be strongly encouraged for TAVI procedures.

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