Performance of Prediction Models for Contrast-Induced Acute Kidney Injury after Transcatheter Aortic Valve Replacement

Vitor E.E. Rosa^{a, b} Carlos M. Campos^{b, c} Antonio Bacelar^a
Alexandre A.C. Abizaid^b José A. Mangione^d Pedro A. Lemos^{a, b}
Vinicius Esteves^e Paulo Caramori^f Roney O. Sampaio^b Flávio Tarasoutchi^{a, b}
Roxana Mehran^g Fabio S. Brito Jr^{b, h}

^aHospital Israelita Albert Einstein, São Paulo, Brazil; ^bHeart Institute (InCor), University of São Paulo Medical School, São Paulo, Brazil; ^cInstituto Prevent Senior, São Paulo, Brazil; ^dHospital Beneficência Portuguesa, São Paulo, Brazil; ^eHospital Brasil – Rede D’Or, São Paulo, Brazil; ^fHospital São Lucas – PUCRS, Porto Alegre, Brazil; ^gMount Sinai Medical Center, New York, NY, USA; ^hHospital Sírio-Libanês, São Paulo, Brazil

Abstract

Background: Acute kidney injury (AKI) has shown to adversely affect outcomes in patients undergoing transcatheter aortic valve replacement (TAVR), and its correct risk estimation may interfere in procedural planning and strategies. The aim of the study was to test and compare 6 scores in predicting AKI after TAVR. **Methods:** We tested 6 scores (the contrast material limit score, volume-to-creatinine clearance ratio, ACEF, CR4EATME3AD3, Mehran model A, and Mehran model B) in a total of 559 consecutive patients included in the Brazilian TAVR registry. **Results:** All scores had a poor accuracy and calibration to predict the occurrence of AKI grade 1 or 2. All scores improved the accuracy of AKI risk prediction when stratified for AKI grade 2/3 and AKI grade 3 for all scores. The CR4EATME3AD3 was the best predictor of AKI stage 2/3 (AUC: 0.62; OR: 1.12; 95% CI 1.01–1.26; $p = 0.04$) and AKI stage 3 (AUC: 0.64; OR: 1.16; 95% CI 1.02–1.32; $p = 0.02$). Mehran models A and B were both good models for AKI stage 3 (AUC: 0.63; OR: 1.10; 95% CI 1.01–1.22; $p = 0.05$; and AUC: 0.62; OR: 1.10; 95% CI 1.00–1.21; $p = 0.05$, respectively). **Conclusions:** None of the current models demonstrated validity in detecting AKI when its lower grades were evaluated.

CR4EATME3AD3 was the best score in predicting moderate to severe AKI after TAVR. These findings suggest that contrast-induced AKI may not be the only factor related to kidney injury after TAVR.

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Introduction

The advent of transcatheter aortic valve replacement (TAVR) has been established as an alternative, less-invasive treatment for aortic stenosis. International guidelines recommend TAVR as a class I indication for symptomatic patients with severe aortic stenosis who have high-surgical risk or are not candidates for surgery [1, 2]. Recently, TAVR has been considered also for moderate- and low-risk patients [3–7].

Patients undergoing TAVR are commonly elderly with a high prevalence of comorbidities. Among these conditions, renal dysfunction is a relevant medical issue for elderly patients with severe aortic stenosis. Both baseline and post-procedural renal failure are risk factors for

Table 1. Risk scores for AKI after cardiac angiography and/or PCI

Risk score	Formula/variables	Prediction
Contrast material limit score	$(5 \times \text{body weight [kg]}) \div \text{serum creatinine (mg/dL)}$	Risk of AKI in patients with renal disease undergoing cardiac catheterization and angiography
Volume-to-creatinine clearance ratio	Contrast volume divided by creatinine clearance	Value >3.7 predicts an increase of creatinine in early-PCI patients (24–48 h)
ACEF score	$\text{Age/ejection fraction (\%)} + 1$ (if serum creatinine ≥ 2.0 mg/dL)	Risk of AKI within 72 h after coronary angiography with or without PCI: low risk (score <1.2), medium risk (1.2–1.5 score), and high risk (score >1.5)
CR4EATME3AD3	Contrast volume >200 mL (2 score), eGFR <60 mL/min/1.73 m ² (4 score), emergency PCI (2 score), age >70 years (2 score), hypotension (2 score), history of myocardial infarction (2 score), left ventricular ejection fraction $<45\%$ (3 score), anemia (2 score), and diabetes mellitus (3 score)	Risk of post-PCI AKI after 48–72 h of the procedure in patients older than 65 years: low risk (score ≤ 4), medium risk (5–8 score), high risk (9–12 score), and very high risk (score ≥ 13)
Mehran model A	Hypotension (5 score), intra-aortic balloon pump use (5 score), congestive heart failure (5 score), serum creatinine >1.5 mg/dL (4 score), age greater than 75 years (4 score), anemia (3 score), diabetes mellitus (3 score), and contrast volume (1 for 100 mL)	Risk of AKI after 48 h of PCI: low risk (score ≤ 5), medium risk (6–10 score), high risk (11–15 score), and very high risk (score ≥ 16)
Mehan model B	Congestive heart failure (5 score), hypotension (5 score), intra-aortic balloon pump use (5 score), age greater than 75 years (4 score), anemia (3 score), diabetes mellitus (3 score), contrast volume (1 for 100 mL), and eGFR (1 for 100 mL, 2 for 40–60 mL, 4 for 20–40 mL, and 6 for <20 mL)	Risk of AKI after 48 h of PCI: low risk (score ≤ 5), medium risk (6–10 score), high risk (11–15 score), and very high risk (score ≥ 16)

AKI, acute kidney injury; PCI, percutaneous coronary intervention; eGFR, estimated glomerular filtration rate.

increased mortality and complications after TAVR [8, 9]. Specifically, TAVR-related acute kidney injury (AKI) is frequently observed and is related to higher all-cause mortality, cardiovascular mortality, myocardial infarction, and life-threatening bleeding [10, 11]. However, current available risk scores for AKI have not been validated for patients undergoing TAVR. Thus, the aim of the present study was to test and compare the predictive performance of 6 scores for different grades of contrast-induced AKI after TAVR.

Methods

Study Population

From January 2008 to January 2015, 819 consecutive patients with symptomatic severe aortic stenosis underwent TAVR and were included in the multicentric TAVR Brazilian registry [12]. Patients with paradoxical aortic stenosis underwent calcium score computed tomography to confirm aortic stenosis severity. Twenty-two sites from different regions of Brazil participated in the study. For each patient, baseline characteristics, procedure details, and follow-up data were collected and recorded in a Web-based case report form designed especially for this registry. To better understand the risk of AKI following TAVR, we excluded 25 patients who died in the first 24 h after the procedure. Two hundred thirty-five participants did not have all the information that were necessary to calculate all 6 scores and were excluded from the present study. Ultimately, 559 subjects were included in this analysis. The estimated glomerular filtration rate was calculated using the Levey formula [13]. The study protocol was conducted in accordance with the Declaration of Helsinki and was approved by each institution's Ethics Committee under protocol number 05676012.4.1001.00701.

Procedure

TAVR procedures were performed according to standard techniques. The transfemoral vascular approach was the first choice of access. The self-expandable CoreValve (Medtronic, Minneapolis, MN, USA), the balloon-expandable SAPIEN XT (Edwards Life-

sciences, Irvine, CA, USA), and the balloon-expandable Inovare (Braile Biomedica, Sao Jose do Rio Preto, SP, Brazil) prostheses were used.

AKI Definitions

All outcomes were described according to the Valve Academic Research Consortium-2 (VARC-2) [10] criteria as follows

- Increase in serum creatinine to 150–199% ($1.5\text{--}1.99 \times$ increase compared with baseline) or increase of ≥ 0.3 mg/dL (≥ 26.4 mmol/L).
- Increase in serum creatinine to 200–299% ($2.0\text{--}2.99 \times$ increase compared with baseline).
- Increase in serum creatinine to $\geq 300\%$ ($>3 \times$ increase compared with baseline) or serum creatinine of ≥ 4.0 mg/dL (≥ 354 mmol/L) with an acute increase of at least 0.5 mg/dL (44 mmol/L).

Acute kidney recovery was defined as a 25% improvement in the glomerular filtration rate at 48 h after the procedure [14].

Risk Scores

We searched in PubMed (www.ncbi.nlm.nih.gov/pubmed/) using a combination of specific key words that included “acute kidney injury,” “contrast-induced nephropathy,” “contrast-induced acute kidney injury,” “creatinine increase,” “risk prediction,” “coronary catheterization,” and “percutaneous coronary intervention.” We found 6 scores, and they were tested and compared for the aforementioned grades of contrast-induced AKI after TAVR (Table 1): the contrast material limit score was calculated using the formula $(5 \times \text{body weight [kg]}) \div \text{serum creatinine (mg/dL)}$ [15]. The volume-to-creatinine clearance ratio evaluates the systemic exposure of the contrast [16]. The ACEF score (age, serum creatinine, and left ventricular ejection fraction) uses the formula $\text{age/ejection fraction (\%)} + 1$ (if serum creatinine ≥ 2.0 mg/dL) [17]. CR4EATME3AD3 uses a contrast volume >200 mL (2 points), estimated glomerular filtration rate <60 mL/min/1.73 m² (4 points), emergency procedure (2 points), age >70 years (2 points), hypotension (2 points), previous myocardial infarction (2 points), left ventricular ejection fraction $<45\%$ (3 points), anemia (2 points), and diabetes mellitus (3 points) [18]. The Mehran model A variables are hypotension (5 points), intra-aortic balloon pump use (5 points), congestive heart failure (5 points), serum creatinine >1.5 mg/dL (4 points), age over 75 years (4 points), anemia (3 points), diabetes mellitus (3 points), and contrast volume

(1 point for 100 mL) [19]. The Mehan model B is composed of congestive heart failure (5 points), hypotension (5 points), intra-aortic balloon pump use (5 points), age greater than 75 years (4 points), anemia (3 points), diabetes mellitus (3 points), contrast volume (1 point for 100 mL), and estimated glomerular filtration rate (1 point for 100 mL, 2 for 40–60 mL, 4 for 20–40 mL, and 6 for <20 mL) [19].

Data Analysis

Continuous variables were presented as mean $\pm$ standard deviation, and categorical variables were presented as frequencies. The first validation step consisted of assessing discrimination by the comparison of the area under the receiver operating characteristic curves. The second step was assessing calibration in the large, which compares the mean predicted probability and the mean observed frequency of AKI in the validation data. The ideal value is zero difference. Afterward, we performed graphical assessment in a calibration plot and estimation of a calibration slope. The last validation was estimating the predictor effects of each model in a univariate logistic regression model (using enter method). The scores of 30-day and overall mortality prediction were assessed using univariate and multivariate logistic regression and Cox regression, respectively. Variables with a p value ≤ 0.05 in the univariate model were included in the multivariate model. All probability values reported are 2-sided, and a probability value ≤ 0.05 was considered significant.

Results

Patient Characteristics

The baseline characteristics are shown in Table 2. The present study included 559 patients, with a mean age of 81.4 ± 7.3 years, 49.9% male and 81.6% with NYHA functional class III or IV. Chronic kidney disease, defined as an estimated glomerular filtration rate <60 mL/min/1.73 m², was found in 76.6% of patients, the mean creatinine was 1.28 ± 0.75 mL/dL, and the mean estimated glomerular filtration rate was 48.73 ± 22.43 mL/min/1.73 m². The mean logistic EuroSCORE was $20.06 \pm 14.24\%$ and STS PROM $20.06 \pm 14.24\%$.

Table 2 depicts baseline echocardiography and computerized tomography data. The mean aortic valve area was 0.67 ± 0.18 cm², mean transaortic gradient was 48.5 ± 15.6 mm-Hg, and left ventricular ejection fraction was $58.4 \pm 15.0\%$. The mean aortic valve diameter annulus was 23.02 ± 3.09 mm.

TAVR Procedure

Five hundred twenty-two patients (93.4%) underwent transfemoral access TAVR. The prostheses used were CoreValve (70.5%), SAPIEN XT (27.0%), and Inovare (2.5%). The mean contrast media volume during the procedure was 184.92 ± 103.65 mL, and 5% underwent percutaneous coronary intervention with the same procedure.

Table 2. Baseline characteristics

Characteristic	<i>n</i> = 559
Clinical data	
Age, years	81.4 $\pm$ 7.3
Body mass index, kg/m ²	26.3 $\pm$ 4.7
Male, <i>n</i> (%)	279 (49.9)
NYHA I/II, <i>n</i> (%)	103 (18.4)
NYHA III/IV, <i>n</i> (%)	456 (81.6)
Diabetes mellitus, <i>n</i> (%)	189 (33.8)
Hypertension, <i>n</i> (%)	426 (76.2)
Dyslipidemia, <i>n</i> (%)	278 (49.7)
COPD, <i>n</i> (%)	107 (19.1)
Coronary artery disease, <i>n</i> (%)	332 (59.4)
Peripheral arterial disease, <i>n</i> (%)	98 (17.5)
Porcelain aorta, <i>n</i> (%)	45 (8.1)
Previous stroke or TIA, <i>n</i> (%)	46 (8.2)
CKD (eGFR <60 mL/min/1.73 m ²), <i>n</i> (%)	428 (76.6)
Logistic EuroSCORE, %	20.06 $\pm$ 14.24
STS PROM, %	10.41 $\pm$ 7.8
Medications	
ACE inhibitors or ARB, <i>n</i> (%)	289 (51.7)
Diuretics, <i>n</i> (%)	362 (64.8)
Statins, <i>n</i> (%)	334 (59.7)
Laboratory data	
Hemoglobin, g/dL	11.8 $\pm$ 1.7
Platelet count, mm ³	201,290 $\pm$ 72,668
Creatinine, mg/dL	1.28 $\pm$ 0.75
eGFR, mL/min/1.73 m ²	48.73 $\pm$ 22.43
Echocardiographic data	
Aortic valve area, cm ²	0.67 $\pm$ 0.18
Left ventricular ejection fraction, %	58.4 $\pm$ 15.0
Left ventricular end-diastolic diameter, mm	51.2 $\pm$ 9.2
Peak transaortic gradient, mm-Hg	79.6 $\pm$ 23.5
Mean transaortic gradient, mm Hg	48.5 $\pm$ 15.6
CT data	
Aortic valve mean diameter annulus, mm	23.02 $\pm$ 3.09

Values are *n* (%) or mean ($\pm$ SD). ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CT, computerized tomography; eGFR, estimated glomerular filtration rate; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; TIA, transient ischemic attack.

Outcomes

According to VARC-2 definition, 17.9% patients ($n = 100$) had post-procedure AKI, 11.8% ($n = 66$) had AKI stage 1, 1.3% ($n = 7$) had AKI stage 2, and 4.8% ($n = 27$) had AKI stage 3.

Predictive Performance of Risk Scores

Figure 1 summarizes the metrics used in the present study to assess the performance of the risk models. All 6 scores had poor accuracy and calibration to predict the

Fig. 1. Predictive performance of risk scores for prediction of AKI after TAVR. Left panels show the ROC curves of the 6 scores for prediction of any AKI (a); AKI stage 2/3 (b), and AKI stage 3 (c). Right panels are calibration plots for % of predicted and observed risk among quintiles for the 6 tested scores. AUC, area under ROC curve; CI, confidence interval; CL, calibration in the large; Vol, volume (mL); Cr, creatinine (mg/dL); AKI, acute kidney injury; TAVR, transcatheter aortic valve replacement; ROC, receiver operating characteristic.

occurrence of any AKI (contrast material limit score 0.53, volume-to-creatinine clearance ratio 0.54, ACEF 0.51, CR4EATME3AD3 0.55, Mehran model A 0.53, and Mehran model B 0.55) (Fig. 1a). None of the models demon-

strated to have significant validity in predicting AKI stages 1, 2, and 3 (Table 3).

There was an improvement in AKI risk prediction when stratified for AKI grades 2/3 (Fig. 1b) for all

scores. The calibration in the large decreased for all scores, and the AUC also demonstrated higher accuracy. In the logistic regression analysis, only CR4EATME3AD3 was a predictor of AKI stages 2 or 3 (odds ratio: 1.12; 95% confidence interval 1.01–1.26; $p = 0.04$; Table 3).

For severe AKI (grade 3), the scores showed further improvement in their predictive performance when tested for AKI stage 3 for discrimination and calibration (Fig. 1c). CR4EATME3AD3, Mehran model A, and Mehran model B were able to predict AKI stage 3. CR4EATME3AD3 demonstrated to have the best numerical discrimination, and Mehran model B have the best calibration (higher slope and lower calibration in the large, Fig. 1c). Overall, the CR4EATME3AD3 score had the best performance as assessed by the combination of discrimination, calibration, and higher odds ratio coefficients.

General Anesthesia and Conscious Sedation

Forty-five patients (8.1%) underwent conscious sedation and 514 (91.9%) general anesthesia. General anesthesia was not a predictor of any AKI (odds ratio: 1.814; 95% confidence interval 0.697–4.718; $p = 0.222$) or severe AKI (grade 3) (odds ratio: 2.344; 95% confidence interval 0.311–17.689; $p = 0.409$).

Risk Scores Mortality Prediction

The contrast material limit score and volume-to-creatinine clearance ratio were the only 30-day mortality predictors in the univariate analysis (see online suppl. Table 1; for all online suppl. material, see www.karger.com/doi/10.1159/000517058). However, only the volume-to-creatinine clearance ratio remained an independent predictor in the multivariate analysis (odds ratio: 1.432; 95% confidence interval 1.037–1.977; $p = 0.029$; online suppl. Table 1). Regarding the overall mortality, none of the present scores was a predictor of long-term mortality. The median follow-up was 372 (89–730) days.

Acute Kidney Recovery

Forty-five patients (8.5%) had improvement in the glomerular filtration rate after TAVR. AKI was a predictor of overall mortality when compared to acute kidney recovery and unchanged glomerular filtration rate (odds ratio: 2.913; 95% confidence interval 1.972–4.302; $p < 0.001$ for AKI; odds ratio: 1.205; 95% confidence interval 0.598–2.425; $p = 0.602$ for acute kidney recovery; and unchanged glomerular filtration rate as reference).

Table 3. Logistic regression coefficients of risk models for different degrees of AKI after TAVR

	OR	p value
Any AKI		
Contrast material limit score	0.96 (0.88–1.04)	0.40
Volume-to-creatinine clearance ratio	0.98 (0.93–1.04)	0.68
ACEF	1.03 (0.74–1.43)	0.84
CR4EATME3AD3	1.06 (0.99–1.13)	0.10
Mehran model A	1.02 (0.97–1.08)	0.41
Mehran model B	1.04 (0.98–1.08)	0.16
AKI stage 2/3		
Contrast material limit score	1.02 (0.92–1.12)	0.68
Volume-to-creatinine clearance ratio	1.02 (0.96–1.10)	0.44
ACEF	1.40 (0.94–2.06)	0.10
CR4EATME3AD3	1.12 (1.01–1.26)	0.04
Mehran model A	1.06 (0.97–1.16)	0.21
Mehran model B	1.07 (0.99–1.17)	0.09
AKI stage 3		
Contrast material limit score	1.02 (0.91–1.14)	0.77
Volume-to-creatinine clearance ratio	1.02 (0.94–1.10)	0.61
ACEF	1.45 (0.95–2.19)	0.08
CR4EATME3AD3	1.16 (1.02–1.32)	0.02
Mehran model A	1.10 (1.01–1.22)	0.05
Mehran model B	1.10 (1.00–1.21)	0.05

AKI, acute kidney injury; TAVR, transcatheter aortic valve replacement.

Discussion

The main findings of our study were (1) all 6 scores had poor accuracy to predict the occurrence of AKI at earlier stages; (2) there was an improvement in their predictive performance for assessing advanced AKI; and (3) CR4EATME3AD3 had the best accuracy in prediction of AKI grade 2/3 and AKI grade 3.

The present work is the first study to assess and compare the predictive performance of previously validated scores (contrast material limit score; volume-to-creatinine clearance ratio; ACEF; CR4EATME3AD3; Mehran model A, and Mehran model B) for different grades of contrast-induced AKI in patients undergoing TAVR. This topic is of major clinical relevance since AKI after TAVR has marked prognostic implications [10].

It has been shown that significant AKI (stage 2 or 3) was associated with an increase in all-cause mortality, mainly in more advanced stages, including those who required dialysis [11, 20–22]. Thus, although the models had poor accuracy in detecting lower risk of AKI, stage 2/3 is the most clinically relevant. Furthermore, post-procedure AKI is also related to higher incidence of cardio-

Table 4. Risk categories of AKI according to the CR4EATME3AD3 score

	Low-risk (0–7 points) N = 181	Intermediate-risk (8–9 points) N = 170	High-risk (>10 points) N = 208	p value
Any AKI stage, %	14.9	16.5	21.6	0.19
AKI stages 2/3, %	2.2	7.6	8.2	0.03
AKI stage 3, %	1.7	5.9	6.7	0.05

AKI, acute kidney injury.

vascular mortality, cerebrovascular accidents, and myocardial infarction [11, 22]. Unexpectedly, only the volume-to-creatinine clearance ratio was an independent predictor of 30-day mortality. However, the volume-to-creatinine clearance ratio was not validated for mortality purpose, so this finding should be analyzed carefully. Besides, a previous study demonstrated that the impact of AKI on long-term mortality is limited, supporting the fact that no score predicted long-term mortality in our study [11].

Previous chronic kidney disease has uncertain impact on post-procedure AKI [23, 24]. In a previous study from the Brazilian registry, chronic kidney disease was not an independent predictor of AKI after TAVR [11]. However, all scores evaluated in our work included serum creatinine or the estimated glomerular filtration rate.

Choosing a risk score model is important to balance its statistical precision, clinical applicability, and computational readiness [25]. Numerically, CR4EATME3AD3 had the best accuracy in prediction of AKI grade 2/3 and AKI grade 3. Mehran models A and B also had fair accuracy in detecting AKI, but only in its severe state. CR4EATME3AD3 and Mehran models use similar variables as source for estimating the risk of AKI. However, CR4EATME3AD3 should also be considered because it is simpler to calculate.

CR4EATME3AD3 was developed to evaluate the risk of contrast-induced AKI 48–72 h post-percutaneous coronary intervention. This score system stratifies patients into low risk (score ≤ 4), medium risk (5–8 score), high risk (9–12 score), and very high risk (score ≥ 13) [18]. The present work is the first to validate CR4EATME3AD3 in a TAVR population. In the present population however, we propose to classify the patients in different categories: low risk of TAVR-related AKI (< 7 points), intermediate risk (8–9 points), and high risk (> 10 points). These categories were based on CR4EATME3AD3 tertiles and were able to discriminate different categories of AKI (Table 4).

None of the scores however had perfect calibration, that is, perfect correlation between the percentage of predicted and the percentage of observed risks among quintiles. Thus, the role of new renal biomarkers of AKI, such as N-acetyl- β -D-glucosaminidase, kidney injury molecule-1, neutrophil gelatinase-associated lipocalin, insulin-like growth factor-binding protein 7, and the tissue inhibitor of metalloproteinases-2, needs to be explored. N-acetyl- β -D-glucosaminidase, kidney injury molecule-1, and neutrophil gelatinase-associated lipocalin are good biomarkers of contrast-induced AKI, though in situations other than TAVR [26–29]. Until now, only 2 prospective studies addressed this issue in the TAVR population [30, 31]. Both evaluated insulin-like growth factor-binding protein 7 and tissue inhibitor of metalloproteinases-2 as tools for post-TAVR early AKI detection, but results were conflicting, and new studies are required to clarify the real predictive impact of these biomarkers.

Unlike other diagnostic or therapeutic procedures using iodine media and apart from the nephrotoxicity itself of the contrast, TAVR may provide an immediate hemodynamic improvement, with reduction in left ventricle afterload, with an ensuing increase in the cardiac index and in systemic perfusion [32–34]. The current models were not exclusively developed for TAVR. Thus, a score dedicated to these high-risk patients is welcome. Meanwhile, AKI preventive measures, such as low contrast volume, should be recommended. Prehydration should be performed with caution due to the risk of worsening heart failure, and acetylcysteine showed no benefit for the prevention of AKI [35].

Limitations

This is a multicentric observational study reported by the individual centers and has the limitations associated with retrospective analysis. So, a considerable number of

patients were excluded due to lack of data, and it can represent a selection bias. As other national registries, the data collection shares the weaknesses of the study design. Thus, potentially informative data including acetylcysteine administration, hydration, rapid pacing frequency, duration, and the pacing rate might not have been included, despite the possible impact of these measures [36]. However, self-expandable prostheses were implanted in 70.5% of patients, and it may have reduced the impact of rapid pacing on outcomes. Information on the amount of contrast used in computed tomography scan is also not included in the registry, but patients are usually submitted to computed tomography scan prior to hospitalizations. Nevertheless, this is a large study with real-world data. Also, our population was predominantly of high surgical risk, and our findings cannot be extrapolated to other surgical risk status.

Conclusion

None of the current models demonstrated validity in detecting AKI when its lower grades were evaluated. CR4EATME3AD3 was the best score in predicting moderate to severe AKI after TAVR. These findings suggest that contrast-induced AKI may not be the only factor related to kidney injury after TAVR.

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Statement of Ethics

The study protocol was conducted in accordance with the Declaration of Helsinki and was approved by each institution's Ethics Committee under protocol number 05676012.4.1001.00701. All patients have given their written informed consent to participate in the study.

Conflict of Interest Statement

José A. Mangione: proctor for Edwards Lifesciences and Medtronic. Fabio S. Brito Jr: proctor for Edwards Lifesciences and Medtronic. Alexandre A.C. Abizaid: proctor for Edwards Lifesciences and Boston Scientific. Paulo Caramori: proctor for Medtronic.

Funding Sources

The study was sponsored by Sociedade Brasileira de Hemodinâmica e Cardiologia Intervencionista, São Paulo, SP, Brazil.

Author Contributions

Vitor E.E. Rosa: design of the work; acquisition, analysis, interpretation of data, and drafting and revising the work. Carlos M. Campos: design of the work; acquisition, analysis, interpretation of data, and revising the work. Antonio Bacelar, José A. Mangione, Vinicius Esteves, and Paulo Caramori: acquisition of data and revising the work. Alexandre A.C. Abizaid and Pedro A. Lemos: interpretation of data and revising the work. Roney O. Sampaio, Flávio Tarasoutchi, and Roxana Mehran: revising the work. Fabio S. Brito Jr: design of the work, analysis and interpretation of data, and revising the work.

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