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Original Article

Early acute kidney injury after transcatheter aortic valve implantation: predictive value of currently available risk scores

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ABSTRACT

Background: Acute kidney injury (AKI) after transcatheter aortic valve implantation (TAVI) is a frequent complication associated with adverse outcomes and mortality. Various scores have been developed to predict this complication in the coronary setting. However, none have ever been tested in a large TAVI population. This study aimed to evaluate the power of four different scores in predicting AKI after TAVI.
Methods: Overall, 1535 consecutive TAVI patients from the observational multicentric "Magna Graecia" TAVI registry were included in the analysis. Of the study population, 235 (15.31%) developed AKI early. The Mehran, William Beaumont Hospital, $CR_4EATME_3AD_3$, and ACEF scores were calculated retrospectively.
Results: The patients who developed TAVI-related AKI had significantly higher absolute values of all risk scores than those who did not. The receiver-operating characteristic analysis also showed a significant correlation between these four scores and AKI, but without a significant difference among all of them (p value = 0.176). Nevertheless, based on their area under the curve values ($\leq$0.604 for all), none had adequate diagnostic accuracy in predicting TAVI-related AKI. Importantly, multivariate analysis identified myocardial revascularization close to the TAVI procedure and implantation of self-expanding prostheses,

Abbreviations: TAVI, transcatheter aortic valve implantation; AKI, acute kidney injury; CM, contrast medium; WBH, William Beaumont Hospital; $CR_4EATME_3AD_3$, contrast medium volume, estimated glomerular filtration rate, emergency procedure, age, hypotension, myocardial infarction, left ventricular ejection fraction, anemia, and diabetes; ACEF, age, serum creatinine, and left ventricular ejection fraction; AUC, area under the curve; CKD, chronic kidney disease; SCr, serum creatinine; LVEF, left ventricular ejection fraction; eGFR, estimated glomerular filtration rate; CrCl, creatinine clearance; LOCM, low-osmolar contrast media; UO, urine output; PAD, peripheral arterial disease; CI, confidence interval; OR, odds ratio; EuroSCORE, european system for cardiac operative risk evaluation; STS-PROM, Society of Thoracic Surgery predictive risk of mortality.

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as well as atrial fibrillation, low-osmolar contrast media administration, corrected contrast medium volume, and any transfusion (p value < 0.05 for all) as independent risk factors for AKI.
Conclusions: Although high values of current AKI risk scores are significantly associated with the development of this complication, these are not sufficiently accurate. Further studies are needed so that a TAVI-dedicated AKI risk score may be created.

1. Introduction

Although, according to the latest guidelines on valvular heart disease[1], surgical valve replacement is still considered the most effective treatment for aortic stenosis in low-risk patients, the transcatheter approach seems to become increasingly spread worldwide, leading its past limitations to be overcome in this patient setting as well[2].

The population of patients undergoing transcatheter aortic valve implantation (TAVI) is quite different from that of patients undergoing coronary catheterization: comorbidities play a major role in the pathogenesis of acute kidney injury (AKI), and thus the mechanisms underlying the development of this complication after TAVI are still a matter of debate. Certainly, renal injury is not only related to contrast-induced nephropathy because of contrast medium (CM) amount[3] and osmolality[4], but it could also depend on patients' comorbidities, and procedure-related and periprocedural factors that may affect renal perfusion.

There is no consensus on preventing AKI in patients undergoing cardiac catheterization procedures; hence, identifying and limiting risk factors are currently critical. So far, most risk factors have been organized to develop different coronary-specific AKI risk scores; some of the most commonly used are the Mehran score[5], the William Beaumont Hospital (WBH) score[6], and the CM volume, estimated glomerular filtration rate, emergency procedure, age, hypotension, myocardial infarction, left ventricular ejection fraction, anemia, and diabetes ($CR_4EATME_3AD_3$) score[7]. Another score, the age, serum creatinine, and left ventricular ejection fraction (ACEF) score[8], has been established as an effective predictor of mortality in patients undergoing elective cardiac surgery but has also proven to be an independent and potentially useful predictor of CM-induced nephropathy in patients undergoing coronary angiography[9].

The Mehran, $CR_4EATME_3AD_3$, and ACEF scores have already been tested in the prediction of TAVI-related AKI in small populations, but they were proven to underperform compared with the coronary field[10-12]. Therefore, the main aim of our retrospective analysis was to investigate the predictive performance of these four coronary-specific AKI risk scores in a large TAVI cohort.

2. Methods

2.1. Study population

All consecutive patients undergoing TAVI at four of the Italian heart centers involved in the "Magna Graecia" TAVI registry were evaluated. This multicentric prospective observational all-comers registry was first approved by the Independent Ethics Committee (study number 6244) of the Policlinico University Hospital of Bari, Italy, in accordance with the Declaration of Helsinki; all patients provided written informed consent at enrollment.

The exclusion criteria were chronic kidney disease (CKD) requiring hemodialysis treatment, pre-TAVI acute renal failure, unavailable serum creatinine (SCr) concentration before and/or after TAVI, administration of iodinated CMs and/or nephrotoxic agents within 5 days before and/or 72 hours after TAVI, contraindications to the placement of a Foley catheter in the bladder, and intraprocedural death according to Valve Academic Research Consortium-2 criteria[13]; after excluding 226 patients, the final study population consisted of 1535 patients implanted between March 2011 and December 2021 (Supplementary Fig. 1).

In diabetic patients on metformin treatment, this drug was suspended 48 hours before and readministered 48 hours after TAVI. All patients had intravenous hydration therapy for 24 hours before the procedure and continued for 48 hours after TAVI: 1 mL/kg/h of 0.9% NaCl solution, at a rate of 40 to 100 mL/h, depending on left ventricular ejection fraction (LVEF) and New York Heart Association functional class. The decision to administer or withhold diuretics preoperatively was individualized for each patient, aiming for a euvolemic state.

All demographic, clinical, laboratory, echocardiographic, intraprocedural, and postprocedural data and hospital outcomes were collected prospectively from each patient's medical record, whereas the analysis was performed retrospectively. Pre-TAVI mortality and AKI risk scores were calculated retrospectively online using official websites. Data on events occurring after discharge and rehospitalizations for all causes were obtained from follow-up outpatient visits or telephone interviews.

2.2. Renal function assessment and definitions

Baseline SCr was defined as the SCr measured before and closest to the time of the TAVI procedure. In line with the provisions of the Mehran[5], WBH[6], and $CR_4EATME_3AD_3^7$ scores, estimated glomerular filtration rate (eGFR) and creatinine clearance (CrCl) at baseline were calculated with the simplified Modification of Diet in Renal Disease[14] and the Cockcroft–Gault formula, respectively, from the steady-state SCr. For the present analysis, CKD was defined as an eGFR baseline of <60 mL/min/1.73 m^2.

Iodixanol was the only iodinated iso-osmolar non-ionic dimeric CM administered; the other monomeric low-osmolar contrast media (LOCM) used for the procedure were iopromide, iobitridol, iohexol, and iomeprol. The amount of CM was recorded during all TAVI procedures. According to previous investigations, the CM volume × SCr/body weight, CM volume/CrCl, and CM volume/eGFR ratios were used to assess the degree of CM dose in individual patients.

As suggested by the Valve Academic Research Consortium consensus documents[13,15] to unify the definition across trials, AKI stages were defined by the AKI Network from the SCr- and urine output (UO)-based criteria[16]. According to the system described above, AKI stages were defined as follows.

- Stage 1: increase in SCr of 150–199% (1.5–1.99 × increase compared with baseline) or increase of ≥0.3 mg/dL (≥26.4 mmol/L) or UO <0.5 mL/kg/h for >6 h but <12 h;
- Stage 2: increase in SCr of 200–299% (2.0–2.99 × increase compared with baseline) or UO <0.5 mL/kg/h for >12 h but <24 h;
- Stage 3: increase in SCr of ≥300% (>3 × increase compared with baseline) or SCr of ≥4.0 mg/dL (≥354 mmol/L) with an acute

increase of at least 0.5 mg/dL (44 mmol/L) or UO <0.3 mL/kg/h for ≥24 h or anuria for ≥12 h or renal replacement therapy administration (irrespective of other criteria).

If more than one post-TAVI measurement was available, the greater SCr value within 48 hours was included in the analysis; UO was evaluated until at least 72 hours after TAVI or until hospital discharge if it occurred before 72 hours after TAVI. According to the World Health Organization, preprocedural anemia was defined if hemoglobin was <12 g/dL for women and <13 g/dL for men[17]; nadir hemoglobin was defined as the lowest hemoglobin measured after TAVI until discharge. All other complications and composite endpoints were also defined according to the Valve Academic Research Consortium-2 consensus document[13].

2.3. AKI risk scores

Among several coronary-specific AKI predictive scores, we chose to retrospectively calculate four ones whose variables are also suitable for the TAVI setting: Mehran, WBH, $CR_4EATME_3AD_3$, and ACEF score.

The Mehran score includes eight different variables, both patient- and procedure-related: eGFR (up to 6 points), hypotension (5 points), intra-aortic balloon pump use (5 points), congestive heart failure (5 points), age >75 years (4 points), anemia (3 points), diabetes mellitus (3 points), and increasing volumes of CM (1 point for each 100 mL). The patients are usually divided as follows: low (≤5), moderate (6–10), high (11–15), and very high (≥16) risk of developing AKI; the values of the area under the receiver-operating characteristic curve (AUC) were 0.70 and 0.67 in the development and coronary validation cohorts, respectively[5].

The WBH score uses CrCl <60 mL/min (2 points), intra-aortic balloon pump use (2 points), urgent/emergency procedure (2 points), diabetes mellitus (1 point), congestive heart failure (1 point), hypertension (1 point), peripheral arterial disease (PAD) (1 point), and CM amount >260 mL (1 point). The risk is considered low if the WBH score is ≤4, moderate if it is 5–6, high if it is 7–8, and very high if it is ≥9; its AUC value was 0.89 in the validation coronary cohort[6].

The $CR_4EATME_3AD_3$ score considers a scoring system based on CKD (4 points), LVEF <45% (3 points), diabetes mellitus (3 points), CM volume >200 mL (2 points), emergency procedure (2 points), age >70 years (2 points), hypotension (2 points), history of acute myocardial infarction (2 points), and anemia (2 points). Based on this score, patients are considered at low risk of developing AKI if it is ≤4 points, moderate risk if it is 5–8 points, high risk if it is 9–12 points, and very high risk if it is ≥13 points; its AUC value was 0.79 in the coronary validation cohort[7].

The ACEF score uses the formula age/LVEF (%) + 1 (if SCr ≥2.0 mg/dL); its AUC value was 0.71 in the first development cohort after coronary catheterization[9], while no validation has been performed so far.

2.4. Statistical methods

Statistical analysis was performed using SigmaStat 3.5, SPSS 25.0, and STATA 13.0 software. Continuous variables were expressed as mean ± standard deviation and median (interquartile ranges) of absolute numbers; categorical variables were expressed as frequencies and percentages. Comparisons were made by the t test, Mann–Whitney's U-test, Fisher's exact test, or $\chi 2$ test, as appropriate. The normal distribution was assessed using Kolmogorov–Smirnov tests. A propensity score-matching analysis was performed to eliminate possible selection bias between prostheses subgroups; all tested valve-type variables were entered as covariates to calculate propensity scores, and TAVI-related AKI was used as the outcome.

Subsequently, a receiver-operating characteristic curve analysis was performed to validate the already known threshold levels of risk scores that provided the best cut-off for AKI in the coronary care setting. AUC values were calculated with confidence intervals (CIs) through concordance statistics as a measure of test accuracy. DeLong test was used to identify AUC standard errors. The calibrations of these AKI risk models were evaluated by comparing the mean predicted probability and the mean observed frequency of AKI with goodness-of-fit R-squared and Cochran–Armitage tests, calibration plots, and estimation of a calibration slope. Thereafter, new optimal cut-off points were selected to predict TAVI-related AKI using Youden's tests, reporting Youden's indexes. The sensitivity, specificity, accuracy, and positive and negative likelihood ratios were evaluated according to these new cut-off points. All AUCs of AKI risk scores were then compared using the receiver-operating characteristic regression test.

Finally, AKI predictors were tested in a univariate logistic regression model; all variables with a p value <0.05 at univariate regression were tested for multicollinearity in a stepwise multivariate model: only variables with a variance inflation factor <4 were incorporated in the multivariate logistic regression model. The odds ratios (ORs) with 95% CIs were estimated.

All statistical tests were two-sided. For all tests, a p value <0.05 was considered statistically significant.

3. Results

3.1. AKI incidence and outcomes

TAVI-related AKI was observed in 235 patients (15.31%), with only one meeting AKI criteria by UO alone. Of these, 80.43% were categorized as stage 1, 11.49% as stage 2, and 8.08% as stage 3. The need for transient and chronic dialysis occurred in 21 (8.94%) and 1 (0.43%) out of these 235 patients with AKI, respectively. However, 4 patients requiring dialysis were classified in the non-AKI group because they worsened their renal function parameters more than 48 hours after TAVI (Table 1).

Compared with non-AKI patients, those who developed AKI were older (81.91 ± 5.32 vs 80.83 ± 5.65 years, p value = 0.007), more frequently with CKD (52.77 vs 38.46%, p value <0.001), PAD (35.32 vs 25.92%, p value = 0.004), with elevated pulmonary artery systolic pressure (41.95 ± 14.34 vs 38.58 ± 13.41 mmHg, p value <0.001), and with recent myocardial revascularization (21.70 vs 14.85%, p value = 0.011) (Table 1 and Supplementary Table 1). As a result, AKI patients were more likely to have higher logistic european system for cardiac operative risk evaluation (EuroSCORE), EuroSCORE II, and the Society of Thoracic Surgery predictive risk of mortality (STS-PROM) scores (p value <0.001). As shown in Supplementary Table 1, CM volume corrected for CrCl and eGFR – CM volume/CrCl (3.44 vs 2.88 min, p value = 0.020) and CM volume/eGFR (2.81 vs 2.33 min × 1.73 m^2, p value = 0.004) - was significantly higher in AKI patients. In addition, iso-osmolar CM administration had a protective effect against TAVI-related AKI (14.72 vs 29.04%, p value <0.001).

A self-expanding bioprosthesis implantation was significantly associated with a higher rate of AKI (p value <0.001), even after propensity score matching; however, these patients had a lower STS-PROM score (p value = 0.036) than those implanted with a balloon-expandable valve (Supplementary Table 2).

Table 1 also describes a comparison of procedural outcomes according to AKI onset. AKI patients exhibited worse outcomes, including a higher rate of bleeding, transfusion, and vascular complications (p value <0.001). Besides a longer postprocedural hospital

Table 1
Baseline characteristics and outcomes of the study population according to AKI incidence (n = 1535).

Variable	All	AKI		p value
		Yes (n = 235)	No (n = 1300)	
Patient characteristics				
Age (years)	80.01 ± 5.62	81.91 ± 5.32	80.83 ± 5.65	**0.007**
Male	679 (44.23%)	103 (43.83%)	576 (44.31)	0.949
Body mass index (kg/m^2)	27.47 ± 4.54	27.63 ± 4.94	27.44 ± 4.46	0.576
Hypertension	1461 (95.18%)	228 (97.02%)	1233 (94.85%)	0.205
Diabetes mellitus	469 (30.55%)	82 (34.89%)	387 (29.77%)	0.136
Insulin dependent	179 (38.17%)	37 (45.12%)	142 (36.69%)	0.193
Dyslipidemia	986 (64.23%)	159 (67.66%)	827 (63.61%)	0.264
Smoking	101 (6.58%)	22 (9.36%)	79 (6.08%)	0.084
CKD	624 (40.65%)	124 (52.77%)	500 (38.46%)	**<0.001**
Anemia	821 (53.48%)	133 (56.60%)	688 (52.92%)	0.333
COPD	403 (26.25%)	59 (25.11%)	344 (26.46%)	0.723
PAD	420 (27.36%)	83 (35.32%)	337 (25.92%)	**0.004**
Carotid stenosis ≥50%	276 (17.98%)	51 (21.70%)	225 (17.31%)	0.128
Critical preoperative state	52 (3.39%)	11 (4.68%)	41 (3.15%)	0.320
CAD history	374 (24.36%)	62 (26.38%)	312 (24.00%)	0.484
Prior myocardial infarction	187 (12.18%)	37 (15.74%)	150 (11.54%)	0.088
Prior cardiac surgery	212 (13.81%)	26 (11.06%)	186 (14.31%)	0.221
Residual significant CAD during TAVI	203 (13.22%)	44 (18.72%)	159 (12.23%)	**0.009**
NYHA functional class III-IV	1406 (91.60%)	216 (91.91%)	1190 (91.54%)	0.949
Mortality risk scores				
Logistic EuroSCORE (%)	15.74 ± 11.83	18.04 ± 12.67	15.33 ± 11.63	**<0.001**
EuroSCORE II (%)	5.79 ± 5.43	7.04 ± 6.32	5.56 ± 5.22	**<0.001**
STS-PROM (%)	4.62 ± 3.07	5.33 ± 3.46	4.49 ± 2.97	**<0.001**
AKI risk scores				
Mehran score	12.51 ± 3.44	13.23 ± 3.39	12.37 ± 3.43	**<0.001**
WBH score	3.74 ± 1.31	4.14 ± 1.29	3.66 ± 1.30	**<0.001**
$CR_4EATME_3AD_3$ score	6.54 ± 3.27	7.45 ± 3.28	6.37 ± 3.24	**<0.001**
ACEF score	1.63 ± 0.51	1.71 ± 0.57	1.62 ± 0.50	**0.012**
Complications and outcomes (VARC-2)				
AKI	235 (15.31%)			
Stage 1	189 (12.31%)			
Stage 2	27 (1.76%)			
Stage 3	19 (1.24%)			
CVVH	23 (1.50%)	21 (8.94%)	2 (0.15%)	**<0.001**
Chronic hemodialysis	3 (0.20%)	1 (0.43%)	2 (0.15%)	0.939
Bleeding	446 (29.05%)	99 (42.13%)	347 (26.69%)	**<0.001**
Minor	102 (6.64%)	17 (7.23%)	85 (6.54%)	0.801
Major	308 (20.06%)	61 (25.96%)	247 (19.00%)	**0.018**
Life threatening	36 (2.34%)	21 (8.94%)	15 (1.15%)	**<0.001**
Need of transfusion	225 (14.67%)	63 (26.81%)	162 (12.47%)	**<0.001**
1 unit	107 (6.97%)	24 (10.21%)	83 (6.39%)	**0.048**
2 units	83 (5.41%)	16 (5.16%)	67 (6.81%)	0.383
>2 units	35 (2.28%)	23 (9.79%)	12 (0.92%)	**<0.001**
Vascular complications	247 (16.09%)	59 (25.11%)	188 (14.46%)	**<0.001**
Minor	161 (10.49%)	34 (14.47%)	127 (9.77%)	**0.041**
Major	86 (5.60%)	25 (10.64%)	61 (4.69%)	**<0.001**
Moderate-to-severe residual aortic regurgitation	107 (7.43%)	18 (7.96%)	89 (7.33%)	0.845
Permanent pacemaker implantation	163 (12.10%)	38 (19.79%)	125 (10.82%)	**<0.001**
ECM/cardiac arrest	19 (1.24%)	4 (1.70%)	15 (1.15%)	0.705
New-onset atrial fibrillation/flutter	130 (10.08%)	25 (13.37%)	105 (9.53%)	0.139
Acute myocardial infarction	8 (0.52%)	3 (1.28%)	5 (0.38%)	0.209
Stroke/TIA	28 (1.82%)	8 (3.40%)	20 (1.54%)	0.089
Hospital length of stay (days)	5.37 ± 3.89	6.69 ± 4.25	5.13 ± 3.78	**<0.001**
Device success	1381 (89.97%)	213 (90.64%)	1168 (89.85%)	0.799
Periprocedural mortality	16 (1.04%)	6 (2.55%)	10 (0.77%)	**0.033**
Early safety*	1363 (88.79%)	159 (67.66%)	1204 (92.61%)	**<0.001**

AKI = acute kidney injury; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; PAD = peripheral arterial disease; TAVI = transcatheter aortic valve implantation; NYHA = New York Heart Association; EuroSCORE = european system for cardiac operative risk evaluation; STS-PROM = Society of Thoracic Surgery predictive risk of mortality; WBH = William Beaumont Hospital; $CR_4EATME_3AD_3$ = contrast medium volume, estimated glomerular filtration rate, emergency procedure, age, hypotension, myocardial infarction, left ventricular ejection fraction, anemia, and diabetes; ACEF = age, serum creatinine, and left ventricular ejection fraction; VARC = Valve Academic Research Consortium; CVVH = continuous venovenous hemofiltration; ECM = external cardiac massage; TIA = transient ischemic attack.

* Short-term composite endpoint of the VARC-2 consensus document, combining all-cause mortality, all stroke, life-threatening bleeding, stage 2 or 3 AKI, coronary artery obstruction requiring intervention, and valve-related dysfunction requiring another aortic valvular procedure within 30 days after TAVI[13].

stay observed in AKI patients (6.69 vs 5.13 days, p value <0.001), the incidence of AKI was also associated with higher periprocedural mortality (2.55 vs 0.77%, p value = 0.033) and lower early safety (67.66 vs 92.61%, p value <0.001); no significant differences were observed between the two groups in terms of device success.

3.2. AKI risk scores

All AKI risk scores were significantly higher, as absolute values, in the AKI group (Fig. 1); in fact, we found that a significant proportion of patients at higher AKI risk develop any stage of AKI compared with

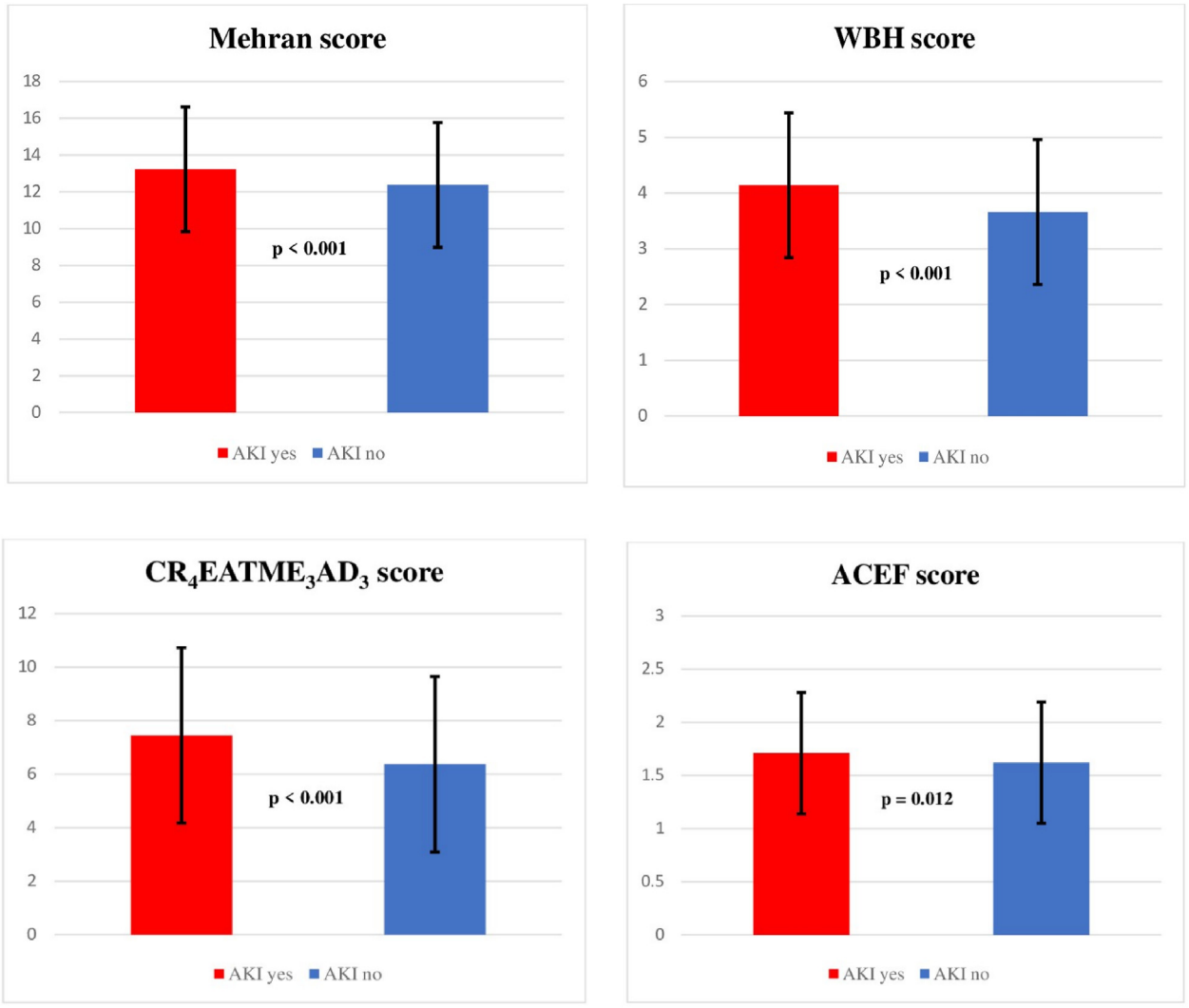

Figure 1. Calculated currently available risk scores in patients who did and did not develop TAVI-related AKI. AKI = acute kidney injury; WBH = William Beaumont Hospital; $CR_4EATME_3AD_3$ = contrast medium volume, estimated glomerular filtration rate, emergency procedure, age, hypotension, myocardial infarction, left ventricular ejection fraction, anemia, and diabetes; ACEF = age, serum creatinine, and left ventricular ejection fraction.

those at lower AKI risk. These four scores were associated with TAVI-related AKI only using logistic regression analysis, but they were not incorporated in the multivariate logistic regression model because their variance inflation factor was not <4. The receiver-operating characteristic analysis also showed a significant correlation between these scores and worsening renal function after TAVI (see results in Supplementary Table 1) but without a significant difference among them (p value = 0.176). Nevertheless, based on the AUC of the new cut-off values established with the higher Youden's indexes, none of the risk scores was significantly performant in detecting TAVI-related AKI (Mehran score: AUC 0.576, 95% CI 0.55–0.60, sensitivity 50%, specificity 65%, and accuracy 62%, p value <0.001; WBH score: AUC 0.604, 95% CI 0.58–0.63, sensitivity 41%, specificity 74%, and accuracy 69%, p value <0.001; $CR_4EATME_3AD_3$ score: AUC 0.597, 95% CI 0.57–0.62, sensitivity 63%, specificity 53%, and accuracy 54%, p value <0.001; ACEF score: AUC 0.551, 95% CI 0.52–0.58, sensitivity 28%, specificity 82%, and accuracy 74%, p value = 0.012) (Fig. 2 and Table 2).

3.3. AKI predictors

Univariate and multivariate analysis models were built using logistic regression; several baseline and procedural parameters, i.e. age, PAD, close to TAVI myocardial revascularization, pre-TAVI CKD, chronic or persistent atrial fibrillation, pulmonary artery systolic pressure, all AKI and mortality risk scores, predilation and post-dilation of a self-expanding prosthesis, corrected CM volume, LOCM use, post-TAVI bleedings, red blood cell transfusions, and vascular complications, were found to be significantly associated with AKI. Nevertheless, only myocardial revascularization close to TAVI (OR 1.48; 95% CI 1.02 to 2.17; p value = 0.041), persistent or permanent atrial fibrillation (OR 1.52; 95% CI 1.03 to 2.23, p value = 0.033), implantation of self-expanding valves (OR 1.50; 95% CI 1.08 to 2.09; p value = 0.016), LOCM administration (OR 2.30; 95% CI 1.49 to 3.57; p value <0.001), CM volume/CrCl (OR 1.15; 95% CI 1.06 to 1.25, p value = 0.001), any transfusion (OR 1.77; 95% CI 1.09 to 2.31, p value = 0.019), and any vascular complication (OR 1.59; 95% CI 1.09 to 2.31; p value = 0.015) remained independently associated with AKI (Table 3).

4. Discussion

The main findings of our study were (1) the incidence of AKI, based on the greater SCr value in the first 48 hours after TAVI, in our population was 15.31%; (2) short-term complications, as well as

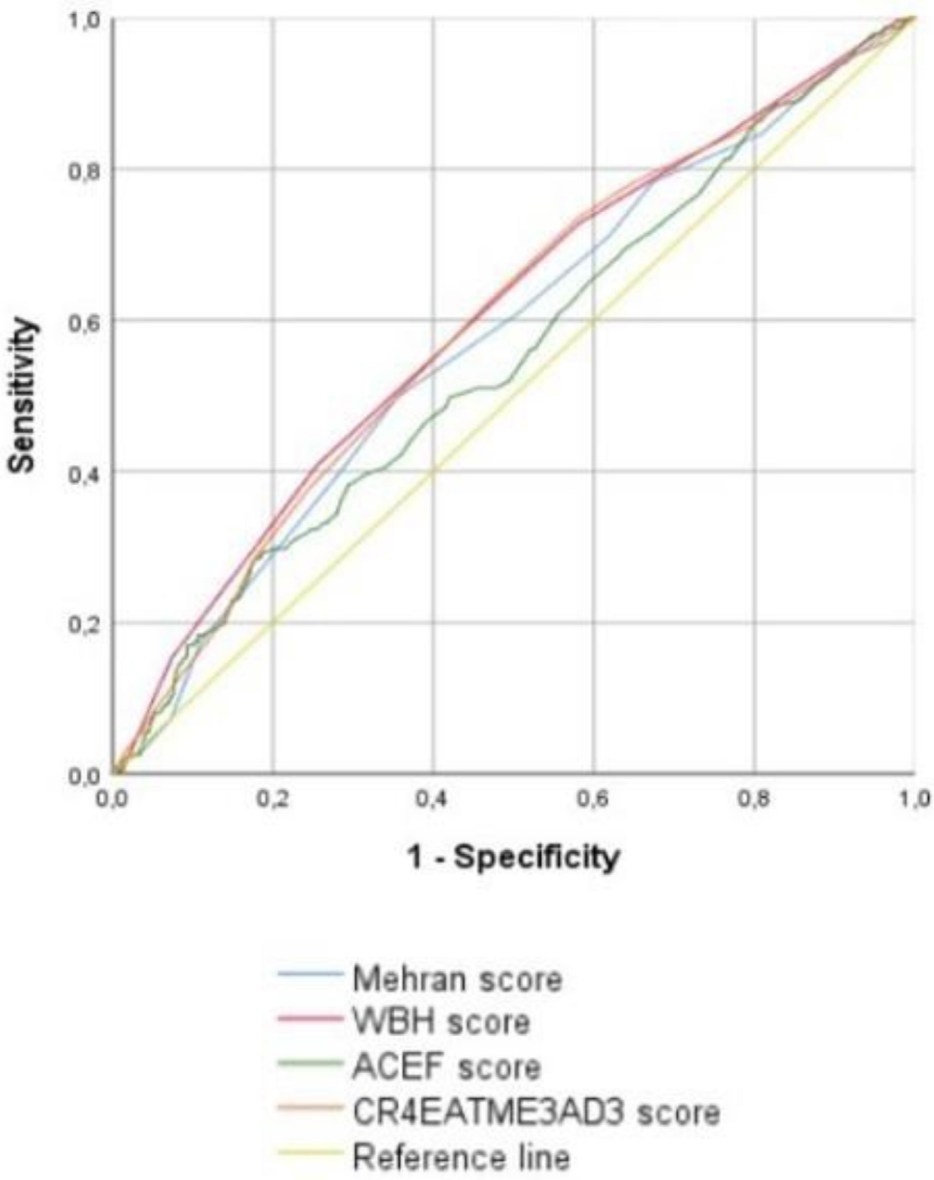

Figure 2. ROC curve analysis for current AKI risk scores predictive power in TAVI patients. ROC = receiver-operating characteristic; WBH = William Beaumont Hospital; ACEF = age, serum creatinine, and left ventricular ejection fraction; $CR_4EATME_3AD_3$ = contrast medium volume, estimated glomerular filtration rate, emergency procedure, age, hypotension, myocardial infarction, left ventricular ejection fraction, anemia, and diabetes.

periprocedural mortality, were higher in AKI patients; (3) besides those already known, self-expanding prostheses and LOCM use could be considered as new independent predictors of TAVI-related AKI; (4) although all AKI risk scores had significantly higher absolute values in patients who developed AKI, they did not have adequate diagnostic accuracy in predicting the occurrence of AKI.

4.1. AKI post-TAVI: incidence, predictors, and relation to outcomes

Given the use of different definitions of AKI and different patient and procedure characteristics, the incidence of this complication is disparate across various series: in our population, this incidence based on a single definition was 15.31%, thus within the reported limits of 8.3% to 57%[18]. Previous studies have shown worse outcomes in TAVI patients who develop AKI after the procedure[19-21]. This group of patients is burdened with more comorbidities, such as higher preoperative SCr concentration, PAD, and atrial fibrillation, which represent independent predictors of AKI development after TAVI[21-23]. In addition, in our population, patients who developed AKI had higher pulmonary artery systolic pressure, which may lead to kidney dysfunction through increased central venous pressure mediated by right ventricular dysfunction; the latter may induce increased kidney venous pressures and decreased effective kidney perfusion[24]. The presence of CKD can exacerbate the mechanisms responsible for elevated pulmonary artery systolic pressure, causing a vicious circle of worsening kidney function because of volume overload, endothelial dysfunction, vascular calcification, and arterial stiffening[25]. Finally, patients undergoing myocardial revascularization no more than 1 month prior to TAVI showed a statistically significant increase in the incidence of AKI, although a recent meta-analysis[26] showed only a trend toward significance; this could likely correlate with some delayed effect of CM administration.

The use of self-expanding prostheses was associated with a higher incidence of AKI in our TAVI population; this different

Table 2
ROC analysis for the prediction of AKI by dedicated scores.

	Mehran score	WBH score	$CR_4EATME_3AD_3$ score	ACEF score
AUC (DeLong standard error)	0.576 ± 0.020	0.604 ± 0.020	0.597 ± 0.020	0.551 ± 0.021
95% CI	0.55-0.60	0.58-0.63	0.57-0.62	0.52-0.58
Asymptotic significance	**<0.001**	**<0.001**	**<0.001**	**0.012**
CL	−0.001	−0.001	−0.001	−0.001
Slope	1.001	0.988	0.981	0.922
Cut-off	13	4	6	1.86
Youden's index	0.143	0.153	0.155	0.105
Sensitivity (%)	50	41	63	28
Specificity (%)	65	74	53	82
Accuracy (%)	62	69	54	74
LR^-/LR^+	0.78-1.40	0.79-1.60	0.71-1.33	0.87-1.59

ROC = receiver-operating characteristic; AKI = acute kidney injury; WBH = William Beaumont Hospital; $CR_4EATME_3AD_3$ = contrast medium volume, estimated glomerular filtration rate, emergency procedure, age, hypotension, myocardial infarction, left ventricular ejection fraction, anemia, and diabetes; ACEF = age, serum creatinine, and left ventricular ejection fraction; AUC = area under the curve; CI = confidence interval; LR = likelihood ratio; CL = calibration in the large.

finding from the current literature[27,28] could probably be related to the fact that their deployment usually requires longer periods of extreme hypotension compared with balloon-expandable valves, but it surely needs to be confirmed by further clinical studies.

Certainly, an important role in the development of AKI is played by the type and volume of CM administered. Furthermore, in our study, patients receiving a lower corrected amount of CM[29,30] showed a favorable impact on post-TAVI renal function, emphasizing the importance of minimizing the CM dose during TAVI to <100 mL. Interestingly, our results identified LOCM use as an independent AKI predictor, as previously reported in another single study[4]. Because of their hyperosmolality relative to plasma, LOCM could determine greater degrees of intra-renal vasoconstriction, activating tubuloglomerular feedback or increasing tubular hydrostatic pressure; all of these adaptations would result in worsening medullary hypoxemia[31].

Table 3
AKI predictors.

	Univariate OR (95% CI)	p value	Multivariate OR (95% CI)	p value
AKI predictors				
Age	1.04 (1.01–1.07)	**0.007**		
Diabetes mellitus	1.26 (0.94–1.70)	0.117		
Anemia	1.16 (0.88–1.53)	0.299		
COPD	0.93 (0.68–1.28)	0.664		
PAD	1.56 (1.16–2.10)	**0.003**	1.40 (1.00-1.96)	0.050
CAD history	1.13 (0.83–1.56)	0.434		
Close to TAVI myocardial revascularization*	1.59 (1.12–2.25)	**0.009**	1.48 (1.02-2.17)	**0.041**
NYHA functional class III-IV	1.05 (0.63–1.75)	0.848		
Pre-TAVI CKD	1.79 (1.35–2.36)	**<0.001**	1.25 (0.89-1.75)	0.198
Chronic or persistent atrial fibrillation/flutter	1.44 (1.01–2.04)	**0.043**	1.52 (1.03-2.23)	**0.033**
LVEF ≤35%	1.53 (0.95–2.45)	0.079		
Pulmonary artery systolic pressure	1.02 (1.01–1.03)	**0.001**		
Logistic EuroSCORE	1.02 (1.01–1.03)	**0.001**		
EuroSCORE II	1.04 (1.02–1.06)	**<0.001**	1.01 (0.98-1.04)	0.361
STS-PROM	1.07 (1.03–1.11)	**<0.001**		
Non-transfemoral access route	1.15 (0.63–2.08)	0.649		
Orotracheal intubation	0.68 (0.44–1.06)	0.091		
Predilation	0.72 (0.54–0.95)	**0.022**	0.81 (0.59-1.10)	0.181
Self-expanding prosthesis	1.67 (1.25-2.23)	**<0.001**	1.50 (1.08-2.09)	**0.016**
Postdilation	1.39 (1.02–1.89)	**0.039**	1.08 (0.77-1.53)	0.644
LOCM	2.37 (1.62–3.48)	**<0.001**	2.30 (1.49-3.57)	**<0.001**
CM volume	1.00 (1.00–1.00)	0.957		
CM volume x SCr/BW	1.20 (1.10–1.32)	**<0.001**		
CM volume/CrCl	1.15 (1.08–1.22)	**<0.001**	1.15 (1.06-1.25)	**0.001**
CM volume/eGFR	1.20 (1.11–1.30)	**<0.001**		
Mehran score	1.08 (1.03–1.12)	**<0.001**		
WBH score	1.32 (1.18–1.47)	**<0.001**		
$CR_4EATME_3AD_3$ score	1.10 (1.06-1.15)	**<0.001**		
ACEF score	1.37 (1.08-1.74)	**0.010**		
Any bleeding	2.00 (1.50-2.66)	**<0.001**	1.27 (0.83-1.92)	0.266
Any transfusion	2.57 (1.84-3.58)	**<0.001**	1.77 (1.09-2.31)	**0.019**
Any vascular complication	1.98 (1.42-2.77)	**<0.001**	1.59 (1.09-2.31)	**0.015**
Moderate-to-severe residual aortic regurgitation	1.09 (0.64-1.85)	0.739		
New-onset atrial fibrillation/flutter	1.46 (0.92–2.34)	0.109		

AKI = acute kidney injury; OR = odds ratio; COPD = chronic obstructive pulmonary disease; PAD = peripheral arterial disease; CAD = coronary artery disease; TAVI = transcatheter aortic valve implantation; NYHA = New York Heart Association; CKD = chronic kidney disease; LVEF = left ventricular ejection fraction; EuroSCORE = european system for cardiac operative risk evaluation; STS-PROM = Society of Thoracic Surgery predictive risk of mortality; LOCM = low-osmolar contrast media; SCr = serum creatinine; BW = body weight; CrCl = creatinine clearance; eGFR = estimated glomerular filtration ratio; WBH = William Beaumont Hospital; $CR_4EATME_3AD_3$ = contrast medium volume, eGFR, emergency procedure, age, hypotension, myocardial infarction, LVEF, anemia, and diabetes; ACEF = age, SCr, and LVEF.
* Percutaneous and/or surgical myocardial revascularization performed no more than 1 month before TAVI.

In addition, we found a significant association between AKI and all major mortality risk scores[27]. This association was also confirmed by the fact that patients in our AKI population had worse outcomes, including higher bleeding rates, transfusions, vascular complications, longer hospital stays, lower early safety, and higher periprocedural mortality. Therefore, it is critical to identify what elements may help predict and prevent this complication.

4.2. AKI risk scores

Consistent with its main aim, this is the first study comparing the predictive powers of four AKI risk scores in a large TAVI population. The WBH score has never been tested in any TAVI patient. In contrast, the largest sample in which the Mehran, CR_4EA-TME_3AD_3, and ACEF scores were tested had 559 patients: according to this study, they showed an AUC of 0.55, 0.55, and 0.51, respectively, in predicting any stage of AKI[11].

Having detected only slightly higher AUC values, our receiver-operating characteristic analysis (Fig. 2) confirmed the limited diagnostic accuracy of these scores, which were developed and validated in a different setting. Therefore, in current clinical practice, they are less useful in predicting these complications in a precise and detailed manner.

Further clinical investigations should focus on developing a new score also based on some "TAVI-specific" AKI risk factors, such as the transapical approach[32], the systematic occurrence of short periods of extreme hypotension (during rapid pacing balloon valvuloplasty and valve implantation), cholesterol embolization because of manipulation of large catheters in the suprarenal atherosclerotic aorta[33,34], or the occurrence of significant paravalvular aortic regurgitation resulting in reduced diastolic renal blood flow.

4.3. Study limitations

Although it was obtained from a prospectively collected database, this is an unspecified *post hoc* analysis. Therefore, we cannot exclude that potential confounding factors not considered in the model may have influenced the results. The effect of a learning curve and changes in treatment strategy is also heterogeneous as the study spanned more than a decade. We believe that aspects of management not controlled or specified may have been a source of bias.

In addition, the precise degree of hemodynamic instability during TAVI is difficult to assess retrospectively. Furthermore, intra-aortic balloon pump use, one of the parameters considered in the Mehran and WBH scores, may be very rarely used in the valvular catheterization setting than in the coronary one.

Moreover, despite the pivotal role of new and emerging biomarkers in the assessment of renal function, the AKI definition from the Valve Academic Research Consortium-2 consensus document[13] was still SCr and UO based; this single definition has the further limitation of probably excluding a large number of patients who suffered from AKI at 3 days or later. Finally, all clinical events, including AKI, were not adjudicated by an independent committee and were site-referred.

5. Conclusions

Consequently to the extension of the indication for TAVI to patients with lower surgical risk, these ones will tend to be less and less aged and with less comorbidities that could increase the risk of AKI; identifying which patients are mostly exposed to this widespread complication could be crucial. Unfortunately, currently available AKI risk scores have not demonstrated sufficient diagnostic accuracy to predict TAVI-related AKI; this is probably because these coronary-specific scores do not include some parameters, such as prosthesis type and CM osmolality, whose role in its multifactorial pathophysiology is not yet well understood. Further studies are needed so that a TAVI-dedicated AKI risk score may be created; this may contribute to the prevention of a frequent and ominous complication.

Declarations of interest

Gaetano Contegiacomo serves as transcatheter heart valve proctor for Abbott Vascular Devices, Redwood City, CA, USA; Fortunato Iacovelli directly received speaker fees from GE Healthcare Srl, Milan, Italy; the remaining authors have no conflicts of interest to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.hjc.2022.12.007.

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