

ORIGINAL ARTICLE

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EuroSCORE II and STS score as a predictor of acute kidney injury following transcatheter aortic valve replacement: Two birds with one stone?

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Abstract

Acute kidney injury (AKI) is a significant predictor of mortality in patients who underwent transcatheter aortic valve replacement (TAVR). Early identification and management of AKI can mitigate further complications and improve survival. The incidence and predictors of acute kidney injury in patients with TAVR were evaluated in different studies. Our aim is to evaluate EuroSCORE II and STS score in terms of predicting AKI following TAVR. One hundred and five patients who underwent TAVR procedure due to severe aortic stenosis in our clinic were retrospectively screened. Demographic, laboratory, echocardiographic and procedural data were collected retrospectively. AKI was defined according to the valve academic research consortium-2 (VARC-2). Sixty-five (61.9%) patients out of 105 were females with a mean age of 77.00 ± 4.88 years. AKI developed in 31.4% of all patients who underwent TAVR. The mean $\pm$ standard deviation (SD) STS score was 8.03 ± 2.30 while mean $\pm$ SD EuroSCORE II was 10.93 ± 7.53 . Mean $\pm$ SD STS score and EuroSCORE II were 14.35 ± 7.66 and 22.34 ± 6.07 in patients who developed AKI respectively and 5.26 ± 2.41 and 4.88 ± 3.07 respectively in those who did not develop AKI. Multivariate analysis revealed that STS (odds ratio: 1.30; 95% CI: 1.04 to 1.62; $p=0.02$) and EuroSCORE II (odds ratio: 1.26; 95% CI: 1.10 to 1.44; $p=0.001$) were independent predictors of AKI. A EuroSCORE cut-off value of 6.16 exhibited a 91% sensitivity and 68% specificity while STS score cut-off value of 6.30 showed 84% sensitivity and 75% specificity in predicting AKI following TAVR. STS score and EuroSCORE II which were developed for the prediction of postoperative mortality may be the predictors of AKI in patients following TAVR.

Keywords: Acute kidney injury, aortic stenosis, contrast media, renal dialysis, transcatheter aortic valve replacement

Introduction

Transcatheter aortic valve replacement (TAVR) has emerged as an attractive and alternative therapy not only in the treatment of high-risk or non-operable patients [1,2] but also in intermediate [3] and low-risk patients [4,5]. Numerous multicenter registries and randomized trials had shown effectiveness and safety of this procedure and demonstrated an improvement in functional capacity and survival [6-9].

Even though technology and physician experience has been improving, complications following TAVR still remain one of the primary concerns. Moreover, no dedicated score system exists to predict the long-term prognosis following TAVR. Logistic EuroSCORE failed to demonstrate the outcome after TAVR

in SOURCE registry [10]. In a two-center registry, STS score outperformed the logistic EuroSCORE in predicting adverse outcomes subsequent to TAVR [11].

The incidence of acute kidney injury (AKI) varies from 8.3% to 58% in different studies [12,13]. AKI has been demonstrated to be associated with increased 30-day and 3-year mortality rate following TAVR [14]. A recent meta-analysis reported that development of AKI was associated with 2-6 fold increase in post-TAVR mortality [15]. Hence, identifying patients at increased risk for AKI is crucial and once identified, the risk of development of AKI can be mitigated by the optimization of medical treatment along with periprocedural and intraoperative procedures.

Several predictors have been shown to predict AKI following TAVR previously. These predictors can be individual patient (hypertension, diabetes mellitus, chronic kidney disease, peripheral vascular disease, anemia), intraoperative (transapical route, general anesthesia, right ventricular pacing, prolonged hypotension), and postoperative risk factors (major bleeding, contrast media volume, hemoglobin drop, >3 units of packed

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erythrocyte transfusion) [13,16-18]. Although lots of predictors were demonstrated in previous studies, these results have not been replicated consistently.

As a result of these discrepancies, the effort for improving the prediction of AKI is still the subject of new studies. Establishing new or repurposing of existing scoring systems may help to predetermine such patients. To develop a new risk score requires more effort and big studies. Therefore, existing risk scores have been evaluating in prediction of AKI in patients after TAVR. Mehran risk score was developed and validated in patients with undergoing percutaneous coronary intervention and ST-elevation myocardial infarction [19,20]. This score predicted AKI weakly in patients following TAVR [21]. EuroSCORE II and STS score which was developed for the prediction of postoperative mortality in patients with planning cardiac surgery have not been evaluated in the prediction of AKI after TAVR so far. Therefore, this study aimed to determine the association between EuroSCORE II or STS score and AKI.

Materials and Methods

Patient population

One hundred and ten patients who underwent TAVR at our center were screened retrospectively. A total of five patients were excluded from the study. Of them, one patient was disqualified due to the transapical approach, two patients due to death during or immediately after the procedure and two patients on prior permanent hemodialysis. The rest of the patients enrolled in the study were underwent the transfemoral procedure. TAVR was indicated in all patients because of symptomatic severe aortic stenosis. Severe aortic stenosis was described as aortic valve effective orifice area (EOA) $<1.0 \text{ cm}^2$ or index EOA $\leq 0.6 \text{ cm}^2/\text{m}^2$ and, mean gradient $\geq 40 \text{ mmHg}$ as in echocardiography or combination of an EOA $\leq 1.0 \text{ cm}^2$ or $\leq 0.6 \text{ cm}^2/\text{m}^2$ when indexed for body surface area, a low mean transvalvular gradient (i.e., $<40 \text{ mmHg}$) and a low left ventricular ejection fraction (LVEF) ($\leq 40\%$), causing a low flow (LF) state. All the patients were evaluated and decided to be eligible for TAVR by a "Heart Team" including an interventional and non-interventional cardiologist, cardiovascular surgeon, radiologist, and an anesthesiologist. Indications for TAVR included high STS and EuroSCORE II, a high risk for reoperation, fragility/poor mobilization, severe pulmonary hypertension, serious pulmonary disease and the presence of a porcelain aorta. The patients with certain conditions [those who were not approved by the "Heart Team", patients estimated to have life expectation of less than one year, other serious organ dysfunctions, unsuitable annulus size ($<18 \text{ mm}$ and $>29 \text{ mm}$), left ventricular thrombus, active endocarditis, increased risk of coronary ostium obstruction (asymmetric valve calcification, short distance between annulus and coronary ostium, small aortic sinus), plaques with mobile thrombi in the ascending aorta or arch, bicuspid or non-calcified valve, hemodynamic instability and LVEF $<15\%$] were accepted ineligible for TAVR.

AKI was defined according to the valve academic research consortium-2 (VARC-2) [22] as an absolute (<7 days) reduction in kidney function in addition to (1) an absolute increase in the highest value of serum creatinine $\geq 0.3 \text{ mg/dL}$ ($\geq 26.4 \text{ } \mu\text{mol/L}$) or (2) a percent increase in the highest value of serum creatinine $\geq 50\%$

(1.5-fold from baseline) or (3) urine output of $<0.5 \text{ mL/kg/h}$ for $>6 \text{ h}$. Patients who developed AKI were classified according to the degree of severity of AKI as stage I [increase in serum creatinine to 150–199% or increase of $\geq 0.3 \text{ mg/dL}$ ($\geq 26.4 \text{ } \mu\text{mol/L}$) or urine output $<0.5 \text{ mL/kg/h}$ for $>6 \text{ h}$ but $<12 \text{ h}$], stage II [increase in serum creatinine to 200–299% (2.0–2.99 folds increase compared with the baseline) or urine output $<0.5 \text{ mL/kg/h}$ for >12 but $<24 \text{ h}$] and stage III [increase in serum creatinine to $\geq 300\%$ (3 folds increase compared with the baseline) or serum creatinine of $\geq 4.0 \text{ mg/dL}$ ($\geq 354 \text{ } \mu\text{mol/L}$) with an acute increase of at least $\geq 0.5 \text{ mg/dL}$ ($44 \text{ } \mu\text{mol/L}$) or urine output $<0.3 \text{ mL/kg/h}$ for $\geq 24 \text{ h}$ or anuria for $\geq 12 \text{ h}$]. Patients receiving renal replacement therapy were considered as Stage 3 criteria, irrespective of other criteria.

Pre-procedural assessment

Electrocardiography (ECG), transthoracic echocardiography (TTE), transesophageal echocardiography (TEE), coronary and peripheral angiography and MDCT (multi-detector computed tomography) were performed as required. Aortic annulus diameter was measured by either TEE or MDCT.

STS score and EuroSCORE II were calculated using the following calculators available online: <http://riskcalc.sts.org/stswebriskcalc/calculate> and <http://www.euroscore.org/calc.html>, respectively.

Valve implantation: The procedures for valve implantation were performed under monoplane fluoroscopy with the help of combined local and systemic analgesics. Clopidogrel 300 mg, acetylsalicylic acid 300 mg, and cefazolin 2 g were given to all patients prior to the procedure. Both balloon-expandable and self-expanding valves were used during procedures and the choice of which was at operator discretion. Rapid ventricular pacing was used only in some patients. Balloon pre-dilatation was used in a few patients, especially those who had severe calcifications. Balloon post-dilatation was performed if valve inadequately opened.

Laboratory Methods

Renal functions were monitored pre-procedurally and at 1 h, 12 h, 24 h, 48 h, 72 h after the procedure and pre-discharge. Estimated Glomerular Filtration Rate (eGFR) was calculated according to the simplified MDRD (Modification of Diet in Renal Disease Study Equation) formula. AKI was defined according to VARC-2. Electrocardiograms (ECG) were assessed retrospectively. Indication for the permanent pacemaker was made on the basis of the 2013 ESC guidelines on cardiac pacing and resynchronization therapy.

Statistical analysis

All statistical analyses were performed using SPSS 22.0 (IBM Inc. USA) software. Continuous variables were expressed as mean $\pm$ standard deviation (SD), while percentiles were given for categorical variables. Normality of data was tested with the one-way Kolmogorov-Smirnov test and visual inspection of histograms, and the equality of variances were checked with Levene test. Student's t-test was preferred for variables with normal distribution. When the dataset was homogenous for at least one group or less than ten subjects were present in a subgroup, the Mann-Whitney U test was preferred. For categorical variables, χ^2

or Fisher's test was used according to the expected cell count.

AKI was defined according to VARC-2. Predictors for AKI were assessed using univariate analysis, and parameters with a p-value of 0.1 or less were included in the binary logistic regression analysis. The forward likelihood method was used in binary logistic regression analysis. Hosmer-Lemeshow goodness-of-fit tests were performed to assess the fit of the model. A receiver operating characteristic (ROC) curve was constructed, and the sensitivity and specificity of EuroSCORE II and STS score values for predicting AKI were determined. Parameters with a p-value of less than 0.05 were accepted as independent predictors for renal damage following TAVI.

For all statistical analyses, a p-value (2-tailed significance) of <0.05 was accepted as a significant difference between groups, and 95% confidence intervals were considered for all relevant analyses.

Results

One hundred and five patients with severe aortic stenosis (mean age [SD] 77.00 [4.88] years, females 61.9%) were enrolled in the study. Of them, 22.9% patients had a history of previous cardiac surgery. Among these patients, 71.4% had hypertension, 37.1% had diabetes mellitus while 59% had previous coronary artery disease (Table 1). Laboratory parameters for both groups (with and without AKI) were shown in Table 1. Overall mean (SD) STS score was 8.03 (2.3) and mean (SD) EuroSCORE II was 10.93 (7.53).

In all patients, TAVR was performed transfemorally. Different types of valves were used during these procedures. The valve choice was at operator discretion.

AKI developed in 31.4% of the patients underwent TAVR. According to the AKIN classification, stage I AKI was seen in 18.1%, stage II in 5.7% and stage III in 7.6% of patients (Figure 1). Four patients needed temporary and two patients needed permanent renal replacement therapy. Baseline serum creatinine was higher in AKI group (1.33 (1.17) vs. 0.97 (0.34), $p=0.02$). However, multivariate analysis indicated that baseline serum creatinine was not a strong independent predictor of AKI (odds ratio: 1.04; 95% confidence interval: 0.30 to 3.59; $p=0.95$). Pre- and post-procedure hemoglobin or hematocrit levels were not associated with the development of AKI. The correlation with high pulmonary pressure, mitral regurgitation, aortic regurgitation (significant or insignificant), aortic valve area, aortic gradient (all of them were measured echocardiographically) and nephropathy were not statistically significant. However, the majority of patients who developed AKI had mitral stenosis ($p=0.01$). Patients who developed AKI had lower LVEF than patients without AKI (46.28 (13.39) vs. 53.30 (9.01), $p=0.007$). Despite the fact that LVEF was correlated well with AKI in univariate analysis (odds ratio: 0.94; 95% confidence interval: 0.91 to 0.98; $p=0.005$), multivariate analysis failed to show LVEF as an independent predictor of AKI (odds ratio: 0.98; 95% confidence interval: 0.91 to 1.05, $p=0.54$) (Table 2). Multivariate analysis revealed that STS (odds ratio: 1.30; 95% confidence interval: 1.04 to 1.62; $p=0.02$) and EuroSCORE II (odds ratio: 1.26; 95% confidence interval: 1.10 to

1.44; $p=0.001$) were independent predictors of AKI. The Hosmer-Lemeshow goodness-of-fit test was not statistically significant ($p=0.88$), suggesting an adequate model fit.

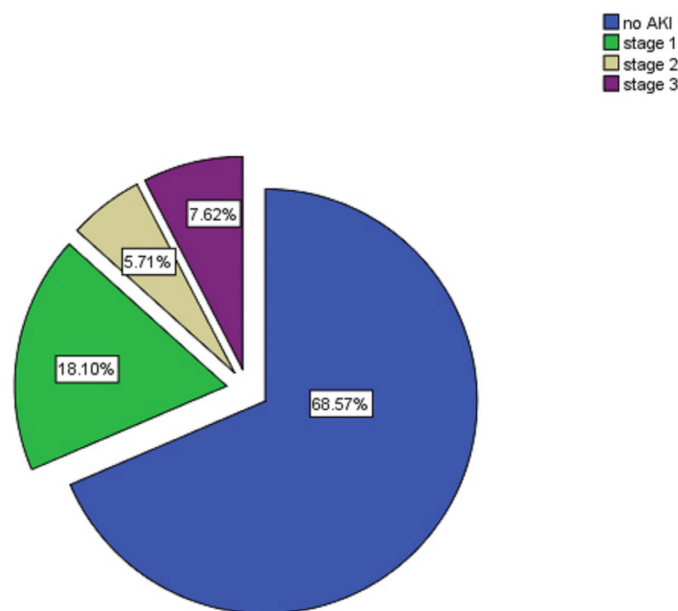


Figure 1. The distribution of AKI according to AKIN classification

ROC curve analysis was performed to assess the predictive power of STS and EuroSCORE II scores in relation to AKI. STS and EuroSCORE were significantly related to the development of AKI [STS score: AUC 0.86 (0.77–0.95), $p<0.001$; EuroSCORE II: AUC 0.86 (0.79–0.94), $p<0.001$] (Figure 2). A cut-off value of STS score ≥ 6.30 was associated with the development of AKI (84% sensitivity, 75% specificity). EuroSCORE II ≥ 6.16 predicted the development of AKI (91% sensitivity, 68% specificity).

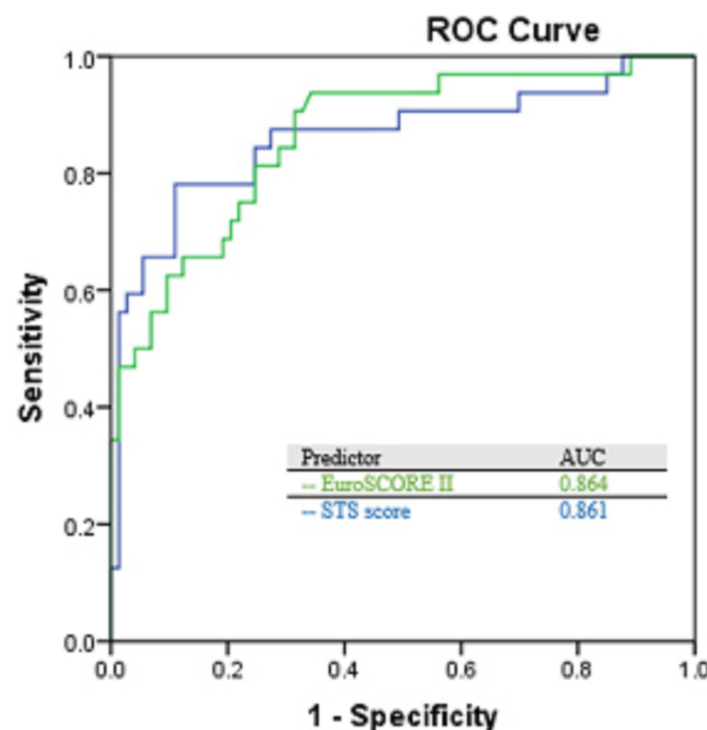


Figure 2. ROC characteristic showing the sensitivity and specificity of STS and EuroSCORE for predicting of acute kidney injury following

Table 1. Baseline and procedural features of the study population

Variables	Overall population	Acute Kidney Injury		P value
		Without (n=72)	With (n=33)	
Clinical Characteristics				
Age (yrs)	77.00±4.88	77.48±4.65	75.91±5.28	0.13
Female , n (%)	65 (61.9)	46 (63)	19 (59.4)	0.73
Hypertension, n (%)	75 (71.4)	49 (67.1)	26 (81.3)	0.17
Diabetes mellitus, n (%)	39 (37.1)	24 (32.9)	15 (46.9)	0.14
Smoking , n (%)	16 (15.2)	11 (15.1)	5 (15.6)	0.94
CAD , n (%)	62 (59.0)	39 (53.4)	23 (71.9)	0.08
Previous CABG , n (%)	24 (22.9)	13(17.8)	11(34.4)	0.06
COPD , n (%)	37 (35.2)	27(37)	10(31.3)	0.57
BMI	25.78±3.48	26.23±3.63	24.71±2.98	0.23
STS score	8.03±2.3	5.26±2.41	14.35±7.66	<0.001
EuroSCORE II	10.93±7.53	4.88±3.07	22.34±6.07	<0.001
Contrast volume, (ml)	206±30	202±25	215±36	0.07
Baseline Laboratories				
Serum Creatinine (mg/dL)	0.82±0.24	0.97±0.34	1.33±1.17	0.02
Hematocrit (%)	33.23±4.97	34.29±5.06	34.76±4.81	0.67
WBC , (x 10 ³ /uL), median (IQR)	6.63(5.46-8.30)	6.56(5.45-8.35)	6.75(6.08-8.28)	0.84
Platelet, (x10 ³ /μL)	201.08±63.72	217.53±69.04	224.27±78.42	0.67
Baseline Echocardiography				
Left Ventricular EF, %	51.16±10.96	53.30±9.01	46.28±13.39	0.007
AVA, cm ²	0.74±0.14	0.74±1.13	0.66±0.16	0.21
Mean Gradient, mmHg	48.95±12.77	49.02±13.33	48.69±10.89	0.94
Max Gradient, mmHg	80.16±18.06	79.86±17.53	81.31±20.66	0.89
AR, moderate-to severe, (%)	13.7	13.7	15.6	0.04
MR, moderate-to-severe, (%)	6.8	3.8	14.3	0.01
MS, (%)	4.8	1.4	12.5	0.01
SPAP, mmHg	44.87±13.22	44.30±13.47	36.82±12.95	0.65
Baseline Electrocardiography				
Atrial fibrillaion, %	22.9	24.2	18.8	0.51
LBBB, %	12.5	8.2	9.4	0.55
RBBB, %	8.6	8.2	6.2	0.67
Postprocedural features				
Serum creatinine, (md/dL)	1.11±0.43	1.00±0.34	2.45±2.07	<0.001
Hematocrit, (%)	28,45±4.94	29.04±5.14	27.12±4.37	0.29
RBC transfusion, n (%)	53 (50.5)	33(45.2)	20(62.5)	0.10
Prosthetic valve size, mm	25.73±2.49	25.18±2.11	25.19±2.09	0.98
AR, moderate -to-severe, (%)	6.7	6.9	6.1	0.77

Values in bold are statistically significant

AR- aortic regurgitation, AVA- aortic valve area, BMI- body mass index, CABG- coronary artery bypass grafting, CAD- coronary artery disease, COPD- chronic obstructive pulmonary disease, LBBB-left bundle branch block, MR- mitral regurgitation, MS- mitral stenosis, RBBB- right bundle branch block, RBC- red blood cell, SPAP- systolic pulmonary artery pressure, WBC- white blood cell

Table 2. Predictors of acute kidney injury : Univariate and Multivariate analysis

Parameters	Univariate analysis		Multivariate analysis	
	Odds ratio (95% Confidence Interval)	P value	Odds ratio (95% Confidence Interval)	P value
Female gender	0.86 (0.37- 2.01)	0.724		
Age	0.93(0.85-1.02)	0.13		
Hypertension	0.47(0.17-1.30)	0.15		
DM	0.56(0.24-1.30)	0.17		
Prior CABG	0.41(0.16-1.06)	0.067		
Contrast exposure in last 5 days	2.82(0.83-9.58)	0.96		
LVEF	0.94(0.91-0.98)	0.005	0.98(0.91-1.05)	0.54
Baseline serum creatinine	1.7(0.99-7.5)	0.051	1.04(0.30-3.59)	0.95
Contrast volume	1.01(1.00-1.03)	0.07	1.01(0.99-1.03)	0.35
STS score	1.62(1.32-1.98)	<0.001	1.30(1.04-1.62)	0.02
EuroSCORE	1.29(1.16-1.43)	<0.001	1.26(1.10-1.44)	0.001

Values in bold are statistically significant

CABG- coronary artery bypass grafting, DM-diabetes mellitus, LVEF- left ventricle ejection fraction

Discussion

AKI developed in 31.4% of all patients following TAVR in this study, which was similar to the results reported by Khawaja et al. [23]. Renal replacement therapy was required in 5.7% of patients.

Significant relationships between AKI and STS score and EuroSCORE II were observed in this study. These scores predicted the development of AKI in patients who underwent TAVR procedure. EuroSCORE and STS scores are a conglomerate of a number of patient-related variables and express the overall impact on kidney functions.

In previous studies, STS and EuroSCORE II were not evaluated as predictors of TAVR-induced nephropathy. However, in this study, STS and EuroSCORE II predicted the development of AKI. Multivariate analysis revealed that EuroSCORE II and STS were the independent predictors of AKI development. Similarly, Nuis et al. demonstrated the predictive value of logistic EuroSCORE (OR: 1.08; 95% CI: 1.01–1.14) [24].

It has previously been reported that baseline creatinine level, blood transfusion, use of the transapical route, peripheral vascular disease, diabetes, the amount of contrast and logistic EuroSCORE were predictors of AKI following TAVR [23–28]. In the present study, baseline serum creatinine level was higher in the AKI group, although it was not an independent predictor of AKI in multivariate analysis.

Despite the fact that in this study, LVEF was lower in the AKI group, multivariate analysis did not reveal LVEF as an independent predictor of AKI. Previous studies have also shown that LVEF was not an independent predictor of AKI [13].

AKI is an important predictor of mortality in patients underwent surgical AVR and TAVR. AKI is a frequent complication that may be seen in 30% of the patients undergoing cardiac surgery. However, kidney injury requiring hemodialysis was seen in nearly 2–15% of patients, and in these patients in-hospital mortality

was about 40% [29]. The incidence of AKI following TAVR was variable and varied from 8.3% to 57% [13]. The incidence of in-hospital mortality following TAVR was 15.2% in patients with AKI and 7.7% in patients without AKI [27].

Bagur and colleagues studied the rate of development of AKI in 213 patients undergoing TAVR procedure and observed that AKI developed in 11.7% of all patients and 1.7% of these patients required hemodialysis [26]. Arreger and colleagues observed that the incidence of AKI was 28% while permanent hemodialysis was 7.4% in their study [30]. In another study including 126 patients, Nuis et al. reported that the incidence of AKI was 19% and permanent hemodialysis was 2% [24]. The high incidence of nephropathy in the present study can be explained by the new definition of AKI described by VARC–2. In previous studies, AKI was considered if renal dysfunction occurred at 48–72 h after TAVR. Nevertheless, this time has been extended up to seven days by VARC–2 consensus [22].

The mechanism of AKI following TAVR and contrast administration have not yet been completely elucidated. However, the direct and indirect effects have been determined. Contrast agents caused ultrastructural changes in proximal tubules [31] and resulted in aggravated renal cortical and medullary hypoxic injury [32]. Enhanced metabolic demand makes it susceptible to contrast agents [33] and several predisposing factors exacerbated this process.

Even if mean arterial blood pressure was in the normal range, hypertension may cause AKI due to the alteration of auto-regulation in the kidneys [34]. Hsu et al. reported that hypertension increased the risk of AKI in patients with chronic renal diseases [35]. At the same time, hypertension is an independent predictor of AKI in patients undergoing cardiac surgery or percutaneous coronary intervention [36]. In the present study no relationship was demonstrated between AKI and hypertension ($p=0.15$). We linked it to the small sample size that increased the likelihood of type II error.

No relationship was observed between RBC transfusion and the development of AKI in our study. However, this link was well recognized in patients who underwent cardiac surgeries. Both Bagur et al. [26] and Arreger et al. [30] reported that red blood cell transfusion was associated with an increased risk of AKI. In stored packages, erythrocytes underwent structural and functional changes and in response, viability and functionality of red cells decreased. As a result, pro-inflammatory molecules, free iron, and hemoglobin, affecting the renal auto-regulation, were accumulated in the erythrocyte packages especially in older patients [37].

Study limitations

The most important limitation of this study was the small sample size, which weakened the power of the result. Being a single-centered study was another limitation. Our study was retrospective study and had all drawbacks which was valid for these trials.

All patients were given intravenous hydration due to risk of nephropathy and the hydration dose was at operator discretion. Records related to the amount of fluid were not entered to statistical analysis due to lots of missing values. Finally, no exact data existed regarding the right ventricular pacing during procedures.

Conclusion

EuroSCORE II and STS scores are calculated in all patients who planned on undergoing cardiac surgery. This study demonstrated the statistically significant association between EuroSCORE/STS score and the risk of developing AKI following TAVR. Taking additional measures can be helpful in decreasing the risk of AKI in patients who have high STS/EuroSCORE II. However, this data needs to be supported by larger studies.

Conflict of interests

The authors declare that they have no competing interests.

Financial Disclosure

All authors declare no financial support.

Ethical approval

Ethics approval was obtained before the study. (17/336 06.10.2020).

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