JACC: CARDIOVASCULAR INTERVENTIONS
VOL. ■, NO. ■, 2015

ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER INC.
http://dx.doi.org/10.1016/j.jcin.2015.07.012

Acute Kidney Injury With the RenalGuard System in Patients Undergoing Transcatheter Aortic Valve Replacement

The PROTECT-TAVI (PROphylactic effecT of furosEmide-induCed diuresis with matched isotonic intravenous hydraTion in Transcatheter Aortic Valve Implantation) Trial

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ABSTRACT

OBJECTIVES The purpose of this study was to investigate the effect of the RenalGuard System (PLC Medical Systems, Milford, Massachusetts) on prevention of acute kidney injury (AKI) in patients undergoing transcatheter aortic valve replacement (TAVR).

BACKGROUND TAVR is associated with varying degrees of post-procedural AKI. The RenalGuard System is a dedicated device designed for contrast-induced AKI prevention. Whether this device is also effective in patients with severe aortic stenosis undergoing TAVR is unexplored.

METHODS The present is an investigator-driven, single-center, prospective, open-label, registry-based randomized study that used the TAVR institutional registry of the Ferrarotto Hospital in Catania, Italy, as the platform for randomization, data collection, and follow-up assessment. A total of 112 consecutive patients undergoing TAVR were randomly assigned to hydration with normal saline solution controlled by the RenalGuard system and furosemide (RenalGuard group) or normal saline solution (control group). The primary endpoint was the incidence of Valve Academic Research Consortium–defined AKI in the first 72 h after the procedure.

RESULTS The AKI rate was lower in the RenalGuard group than in the control group (n = 3 [5.4%] vs. n =14 [25.0%], respectively, p = 0.014]. The majority of patients (5.4% vs. 23.2%) developed a mild AKI (stage 1); severe damage (stage 3) occurred only in 1 patient in the control group (0.0% vs. 1.8%). No case of in-hospital renal failure requiring dialysis was reported. No significant differences in terms of mortality, cerebrovascular events, bleeding, and hospitalization for heart failure were noted in both groups at 30 days.

CONCLUSIONS Furosemide-induced diuresis with matched isotonic intravenous hydration using the RenalGuard system is an effective therapeutic tool to reduce the occurrence of AKI in patients undergoing TAVR. (J Am Coll Cardiol Intv 2015;■:■–■) © 2015 by the American College of Cardiology Foundation.

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Manuscript received May 25, 2015; revised manuscript received July 9, 2015, accepted July 16, 2015.

ABBREVIATIONS AND ACRONYMS

AKI = acute kidney injury

CI = confidence interval

eGFR = estimated glomerular filtration rate

TAVR = transcatheter aortic valve replacement

VARC = Valve Academic Research Consortium

Acute kidney injury (AKI) is a frequent complication of contrast-guided interventional procedures (1,2). Not surprisingly, transcatheter aortic valve replacement (TAVR) is also associated with varying degrees of post-procedural AKI, ranging from 12% to 57%, which carries a negative prognostic effect (3-8). Preventive intravenous hydration with isotonic saline solution is known to decrease the risk of AKI (9,10). However, in patients with impaired left ventricular function and left side valvular heart diseases, hydration is usually suboptimal due to the perceived risk of overhydration and pulmonary edema. In previous studies, diuretic agents have been combined with hydration to increase urine output and prevent overhydration (11-13).

The RenalGuard System (PLC Medical Systems, Milford, Massachusetts), a recently introduced device delivering intravenous fluids matched to the urine output, has emerged as an alternative strategy for AKI prevention. Studies conducted in patients undergoing percutaneous coronary intervention have recently demonstrated that furosemide-induced diuresis with matched isotonic intravenous hydration by the RenalGuard System significantly reduced AKI in high-risk patients undergoing coronary procedures (14-16). Whether these findings translate to patients undergoing TAVR is unexplored. To fill this gap, we performed a randomized study to assess the efficacy of the RenalGuard System to prevent AKI in patients with severe aortic stenosis undergoing TAVR.

METHODS

STUDY DESIGN. PROTECT-TAVI (PROphylactic effecT of furosEmide-induCed diuresis with matched isotonic intravenous hydraTion in Transcatheter Aortic Valve Implantation) was an investigator-driven, single-center, prospective, open-label, registry-based randomized study that used the TAVR institutional registry of the Ferrarotto Hospital in Catania, Italy (REPLACE [REgistry of Percutaneous aortic vaLve replacement]), as the platform for randomization, data collection, and follow-up assessment. All trial management activities including data management and statistical analyses were performed at the Ferrarotto Hospital, Catania. All subjects provided written informed consent before randomization. The study was conducted according to the principles of the Declaration of Helsinki and Good Clinical Practice. The authors wrote all drafts of the paper and vouch for the integrity of and completeness of the data and analyses.

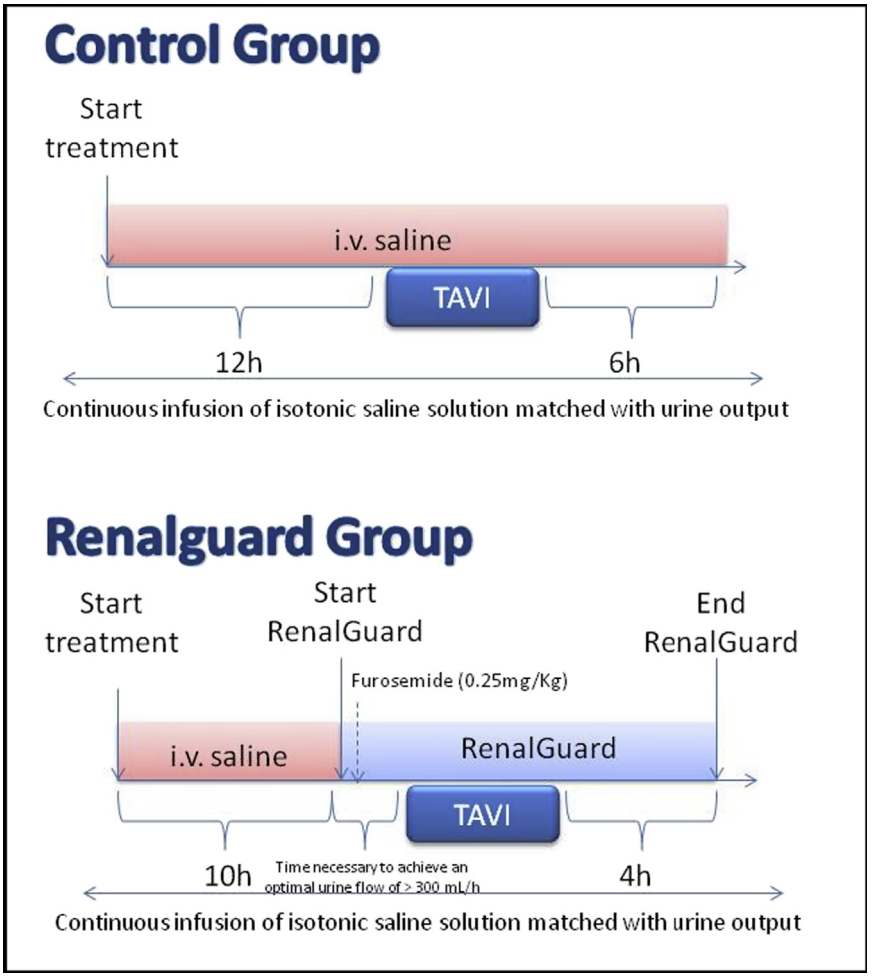
THE REPLACE REGISTRY. REPLACE is a spontaneous registry created to monitor the institutional procedural, acute, and long-term outcomes of TAVR. A stream of patient demographics, medical history, concomitant medications, procedure details, and in-hospital clinical outcomes is routinely entered in the registry's electronic data collection system using standardized case report forms. Follow-up data are obtained at serial time points by clinical visits and phone calls. Trial-specific information, including renal outcomes of interest not obtained as part of the registry, was collected using additional case report form pages.

STUDY POPULATION. All consecutive patients with symptomatic severe aortic stenosis undergoing TAVI were considered eligible for the trial. Exclusion criteria included chronic end-stage renal failure on dialysis, ≥1 episode of acute congestive heart failure with left ventricular ejection fraction <30% in the past 30 days before randomization, contraindications to placement of a Foley catheter, urgent TAVI, and unavailability of the RenalGuard system before randomization. All analyses were performed following the intention-to-treat principle.

RANDOMIZATION. Patients were 1:1 randomly assigned to either RenalGuard or standard management. Randomization was obtained with computer-generated codes, which were sealed in sequentially numbered envelopes.

STUDY PROCEDURES. Study procedures are detailed in the **Central Illustration**. The iodixanol (Visipaque, GE Healthcare, Little Chalfont, Buckinghamshire, UK), a nonionic, iso-osmolar (290 mOsm/1 kg water) contrast agent was used during TAVR in all patients. Patients randomized to RenalGuard received hydration with a normal saline solution. The RenalGuard system (**Figure 1**) includes a closed-loop fluid management system, a high-volume fluid pump, a high-accuracy dual weight measuring system, motion-detection artifact reduction, a single-use intravenous set and urine collection system that interfaces with a standard Foley catheter, real-time display of urine and replacement fluid volume, timely alerts to drain the urine bag or to replace the hydration fluid bag, and safety features such as automatic air and occlusion detection. An initial bolus (priming) of 250 ml was infused over 30 min (pre-procedural phase). In the presence of left ventricular dysfunction (ejection fraction <30% as assessed by 2-dimensional echocardiography), priming was reduced to 150 ml. After the

CENTRAL ILLUSTRATION **Study Protocol**



i.v. = intravenous; TAVI = transcatheter aortic valve implantation.

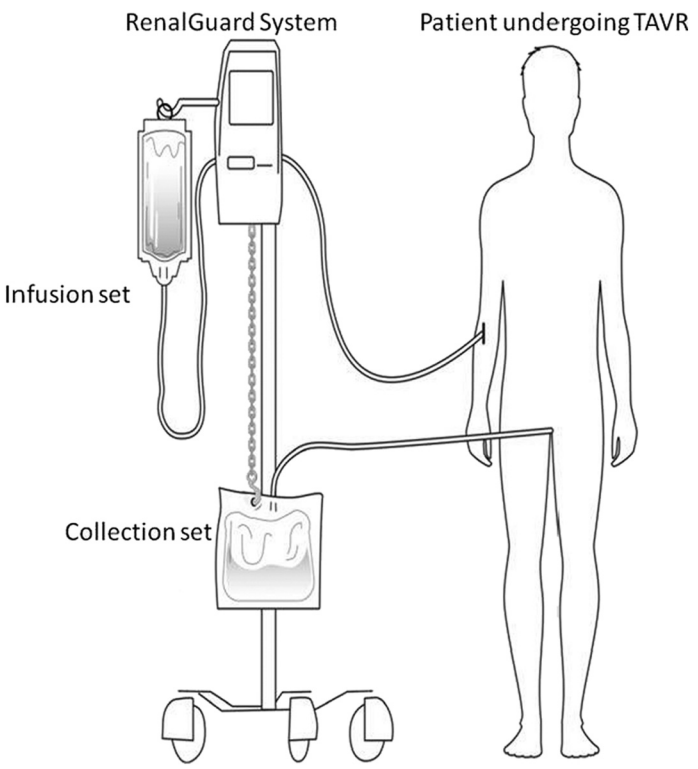
priming, furosemide (0.25 mg/kg) is administered intravenously to achieve an optimal urine flow of >300 ml/h. As soon as the urine flow reached the target value, the patient was moved into the catheterization laboratory and the TAVR procedure was started (procedural phase). Controlled hydration by the RenalGuard system continued during the procedure and for 4 h after the procedure (post-procedural phase). Urine flow was monitored and maintained at the target value throughout the procedure and during the following 4 h. Additional furosemide doses were allowed in instances when there was a decrease in urine flow below the target value.

Patients allocated to the control group received sodium normal saline solution at a rate of 1 ml/kg/h 12 h before TAVR, during contrast exposure, and for 6 h after the procedure. In the presence of left ventricular dysfunction (ejection fraction <30% as assessed by 2-dimensional echocardiography), the hydration's rate was reduced to 0.5 ml/kg.

ENDPOINTS AND DEFINITIONS. The primary endpoint was the incidence of AKI occurring within the first 72 h after the procedure. Secondary outcomes were defined according to the Valve Academic Research Consortium (VARC) (17).

AKI was defined as an absolute reduction in kidney function (≤72 h) and defined as: 1) stage 1: increase in serum creatinine to 150% to 200% (1.5 to 2.0× increase compared with baseline) or increase of ≥0.3 mg/dl (≥26.4 mmol/l); 2) stage 2: increase in serum creatinine

FIGURE 1 RenalGuard System



Schematic representation of the RenalGuard system (PLC Medical Systems, Milford, Massachusetts) connected to the patient. TAVR = transcatheter aortic valve replacement.

to 200% to 300% (2.0 to 3.0× increase compared with baseline); and 3) stage 3: increase in serum creatinine to ≥300% (>3× 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).

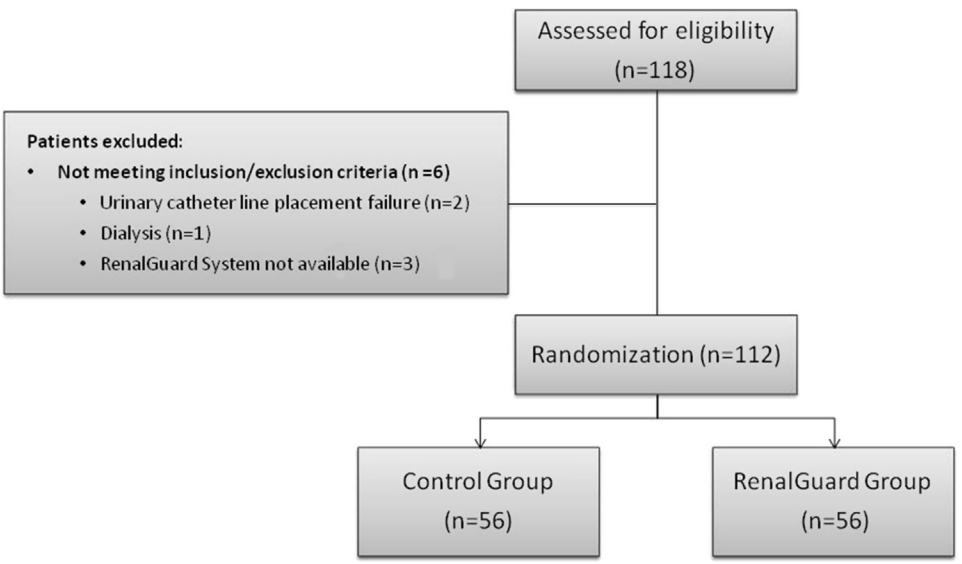
Estimates of glomerular filtration rate were calculated by applying both the Cockcroft-Gault and the Modification of Diet in Renal Disease formulas. A risk score for predicting contrast-induced AKI was calculated as previously described by Mehran et al. (18).

SERUM BIOMARKERS. Serum creatinine, blood urea nitrogen, sodium, and potassium were measured the day before the procedure; at 24, 48, and 72 h after administration of the contrast agent; and before discharge.

SAMPLE SIZE CALCULATION. Averaging the 12% and 57% AKI rates post-TAVR reported by the available published data (4,5,19,20) and the AKI rate in the REPLACE registry before trial initiation (30%), we anticipated that the overall rate of AKI in the control group would be 28%. Assuming an incidence of 8% of overall rate of AKI in the RenalGuard group, a sample size of 110 patients (55 patients per group) provided 80% power to detect statistically significant differences in AKI at a 2-sided alpha of 0.05.

STATISTICAL ANALYSIS. Continuous variables are presented as mean ± SD or medians with first (Q1) and third (Q3) quartiles in cases of skewed distributions.

FIGURE 2 Study Flow Chart



A total of 112 patients were randomized and assigned to either the RenalGuard group (n = 56) or the control group (n = 56) with no crossover.

Categorical variables are described by frequencies and percentages. Differences between independent groups were tested using the Wilcoxon rank sum test and Student *t* test for continuous variables. In cases in which the samples were paired, the Wilcoxon signed rank or paired Student *t* test were used. Categorical variables were compared with the chi-square test. Relative risks are reported with 95% confidence intervals (CIs). A Pearson correlation analysis was used for the evaluation of 2 continuous variables.

A multivariable analysis for the development of AKI was performed using a logistic regression, adjusting for the following variables: "no RenalGuard use" and AKI risk score 4. All tests were 2-tailed, and a p value of 0.05 was required for statistical significance. All data were processed using the Statistical Package for Social Sciences, version 20 (IBM, Armonk, New York).

RESULTS

POPULATION. The flow of the study is depicted in Figure 2. Between February 2014 and January 2015, 118 patients were screened for TAVR. Six patients met at least 1 exclusion criterion. A total of 112 patients with a mean age of 80.6 ± 5.1 years were randomized and assigned to either the RenalGuard group (n = 56) or the control group (n = 56). All patients received the allocated AKI prevention protocol with no crossovers. Follow-up data for the primary and secondary endpoints was available for all patients. Serum creatinine, sodium, and potassium values at baseline and post-procedure were available for all patients in each group.

Baseline demographic, clinical, and echocardiographic characteristics of 2 study groups are summarized in Table 1. An estimated glomerular filtration rate <60 ml/m calculated by the Cockcroft-Gault and the Modification of Diet in Renal Disease formulas was reported in 74 patients (66.1%) and 50 patients (44.6%), respectively. A total of 64 patients (57%) had moderate predicted risk to develop a contrast-induced AKI according to the Mehran risk score, with no differences between study groups (Figure 3).

PROCEDURAL OUTCOMES. Procedural data are shown in Table 2. VARC-defined device success was obtained in 107 patients (95.5%), with no differences between the 2 groups. Also, no differences in terms of contrast dye administered were observed.

PRIMARY ENDPOINT AND RENAL OUTCOMES. The incidence of AKI was lower in the RenalGuard group compared with the control group (n = 4, 5.4% vs. n = 13, 25.2%; relative risk: 0.21 [95% CI: 0.06 to 0.71]; p = 0.014). The majority of patients developed a mild AKI (stage 1), whereas severe AKI (stage 3) occurred in only 1 patient in the control group (Figure 4). No case of in-hospital renal failure requiring dialysis was reported. Key characteristics of patients who developed AKI are listed in Table 3. A significant increase in serum creatinine was noted in the control group compared with the RenalGuard group (Figure 5).

Figure 6 shows the relationship between the variation in creatinine value and the amount of contrast dye administered during the procedure in the 2 groups. This correlation was found to be significant in the control group (p = 0.028) but not in the RenalGuard group (p = 0.570).

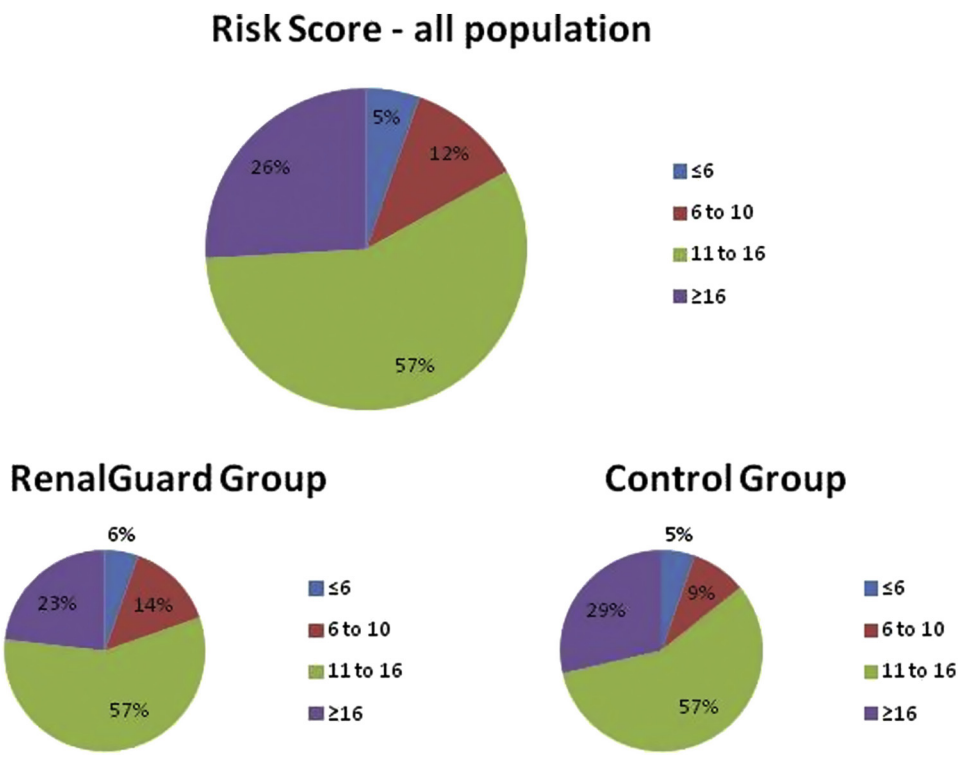
TABLE 1 Baseline Characteristics

	RenalGuard Group (n = 56)	Control Group (n = 56)	p Value
Clinical parameters			
Age, yrs	82 (78-83)	81 (78-84)	0.908
BMI, kg/m^2	26 ± 4.7	28 ± 4.6	0.143
Female	34 (60.7)	33 (58.9)	0.847
Hypertension	42 (75.0)	49 (87.5)	0.145
Diabetes mellitus	16 (28.6)	22 (39.3)	0.318
Dyslipidemia	27 (48.2)	30 (53.6)	0.706
Prior acute heart failure†	18 (32.1)	14 (25.0)	0.531
Prior myocardial infarction	4 (7.1)	6 (10.7)	0.742
Prior stroke/TIA	5 (8.9)	2 (3.6)	0.438
Prior bypass graft surgery	3 (5.4)	6 (10.7)	0.489
Prior PCI	9 (16.1)	9 (16.1)	0.603
Prior aortic valvuloplasty	2 (3.6)	1 (1.8)	0.569
Peripheral vascular disease	8 (14.3)	9 (16.1)	0.798
Chronic obstructive pulmonary disease	12 (21.4)	9 (16.1)	0.629
Prior pacemaker	5 (8.9)	7 (12.5)	0.761
Porcelain aorta	1 (1.8)	1 (1.8)	0.752
NYHA functional class III and IV	46 (82.1)	46 (82.1)	0.517
Serum creatinine, mg/dl	1.0 (0.85-1.15)	0.97 (0.83-1.16)	0.357
eGFR, mg/dl*	50.0 ± 20.7	53.0 ± 19.2	0.488
eGFR,† mg/dl	62.6 ± 25.6	63.5 ± 20.6	0.848
eGFR* ≤30 mg/dl	9 (16.1)	6 (10.7)	0.580
eGFR† ≤30 mg/dl	5 (8.9)	3 (5.4)	0.716
eGFR* between 30 and 60 mg/dl	29 (50)	30 (53.6)	0.850
eGFR† between 30 and 60 mg/dl	22 (39.3)	20 (35.7)	0.845
STS score	4.5 (4.0-5.0)	3.8 (2.8-4.8)	0.761
Medications at time of randomization			
Aspirin	30 (53.6)	25 (44.6)	0.848
ARB	23 (41.1)	23 (41.1)	0.935
ACE inhibitors	13 (23.2)	14 (25.0)	0.825
Furosemide	35 (62.5)	38 (67.8)	0.545
Baseline echocardiographic parameters			
LVEF, %	53.6 ± 13	55.5 ± 8.7	0.356
Peak pressure gradient, mm Hg	85.0 ± 21.5	80.4 ± 18	0.230
Mean pressure gradient, mm Hg	53.0 ± 15.4	48.0 ± 11.5	0.066
Aortic valve area, cm^2	0.6 ± 1.7	0.7 ± 1.7	0.084

Values are median (interquartile range), mean ± SD, or n (%). *Cockcroft-Gault formula. †Modification of Diet in Renal Disease formula.

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; BMI = body mass index; eGFR = estimated glomerular filtrate rate; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; STS = Society of Thoracic Surgery; TIA = transient ischemic attack.

FIGURE 3 AKI Risk Score



Predicted risk score to develop a contrast-induced acute kidney injury (AKI) according to Mehran et al. (18).

SECONDARY OUTCOMES. No significant hydration-associated complications were observed. A total of 41 patients (23 patients [41.1%] in the RenalGuard group vs. 18 patients [32.1%] in the control group; p = 0.432) developed asymptomatic hypokalemia that was corrected with potassium supplementation as per usual practice. No patients developed hypernatremia (Figure 5). No cases of pulmonary edema were reported.

Length of in-hospital stay (from TAVR to discharge) was similar in the 2 groups (RenalGuard group

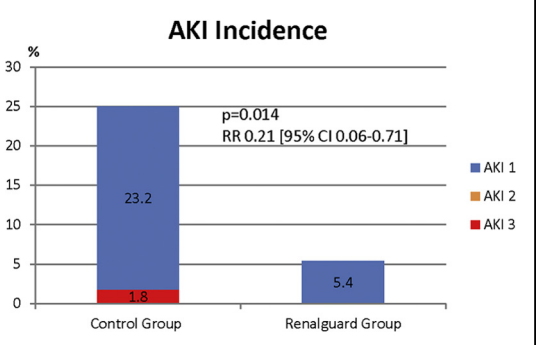
TABLE 2 Procedural data

	RenalGuard Group (n = 56)	Control Group (n = 56)	p Value
Device success	55 (98.2)	52 (92.8)	0.170
Device			
CoreValve, Medtronic	40 (71.4)	31 (55.3)	0.116
SAPIEN, Edwards	10 (17.8)	22 (39.3)	0.021
Portico, St. Jude	2 (3.6)	1 (1.8)	0.558
Lotus, Boston	2 (3.6)	1 (1.8)	0.558
Rapid pacing use	56 (100)	56 (100)	1.000
Concomitant PCI	6 (10.7)	5 (8.9)	0.751
Post-dilation	12 (21.4)	7 (12.5)	0.314
Valve-in-valve*	2 (3.6)	3 (5.3)	0.647
Valve-on-valve†	1 (1.8)	2 (3.6)	0.558
Contrast dye (ml)	180 (140–220)	170 (130–230)	0.633

Values are n (%) or median (interquartile range). *Valve-in-valve: implantation of a second prosthesis inside the first one to treat the first valve's malposition during the index procedure. †Valve-on-valve: implantation of a second valve in its anatomical position after embolization in ascending aorta of the first valve deployed.

PCI = percutaneous coronary intervention.

FIGURE 4 Study Primary Endpoint



Incidence of acute kidney injury (AKI) stages 1, 2, and 3 in the study population. CI = confidence interval; RR = relative risk.

TABLE 3 Characteristics of Patients Who Developed AKI

n	Group	Age (yrs)	Sex	LVEF (%)	CI-AKI Risk Score	Baseline eGFR (CG/MDRD)	Minimum eGFR (CG/MDRD)	Creatinine Peak (mg/dl)	Contrast Volume (ml)	AKI Stage
1	Control	84	F	60	12.1	52.2/77.1	19.3/22.9	2.06	310	1
2	Control	85	F	60	16	28.2/36.5	17.5/19.8	2.34	100	1
3	Control	83	M	50	16	61.0/94.0	38.7/52.3	1.31	100	1
4	Control	74	F	60	4.7	63.2/65.1	46.6/43.1	1.22	170	1
5	Control	81	F	69	18	23.9/32.3	18.1/22.1	2.15	200	1
6	Control	67	F	33	1	91.7/75.2	60.9/44.1	1.22	100	1
7	Control	84	M	57	7	53.6/63.8	10.4/9.1	5.97	300	3
8	Control	83	M	48	14.2	69.4/78.6	35.8/34.4	1.88	220	1
9	Control	85	F	60	13.2	41.7/49.1	27.8/29.0	1.68	120	1
10	Control	74	F	48	17	38.1/30.0	26.8/18.8	2.5	200	1
11	Control	74	F	50	8	45.5/50.2	28.4/27.4	1.81	200	1
12	RG	73	M	50	17.5	45.0/33.2	30.5/19.9	3.1	250	1
13	RG	84	F	45	20.8	23.0/24.6	14.4/13.5	3.27	180	1
14	Control	81	F	35	16.2	29.9/38.4	23.2/27.0	1.8	120	1
15	Control	83	M	68	19.6	31.5/33.7	25.6/24.9	1.92	60	1
16	Control	83	F	60	17.9	36.2/57.6	16.4/21.7	2.8	290	1
17	RG	84	F	62	14	39.7/56.3	30.1/38.4	1.32	200	1

CG = Cockcroft-Gault formula; CI-AKI = contrast induced acute kidney injury; MDRD = Modification of Diet in Renal Disease formula; RG = RenalGuard; other abbreviations as in Table 1.

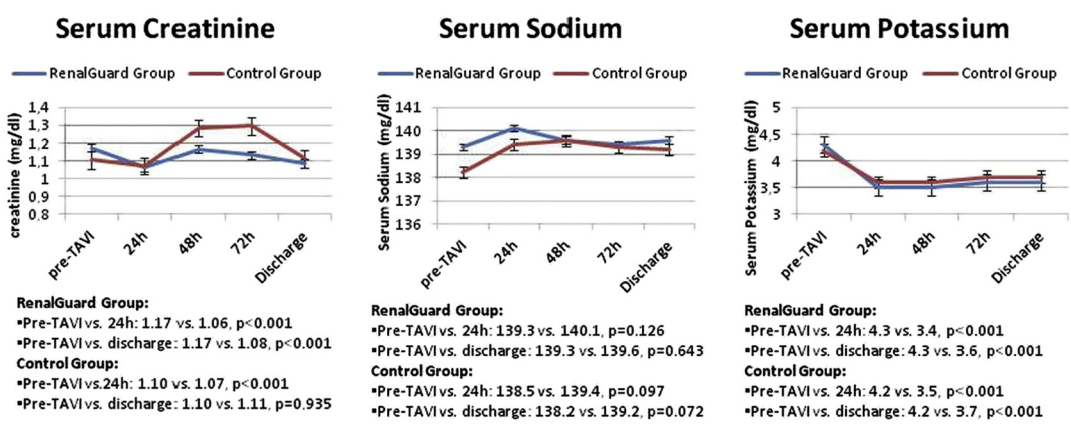
3.5 ± 4.1 days vs. control group 3.5 ± 3.5 days; p = 0.940). VARC-defined in-hospital outcomes and 30-day outcomes are listed in Table 4. No significant differences in terms of mortality, cerebrovascular events, bleeding, vascular complications, and re-hospitalization for heart failure were noted between groups.

PREDICTORS OF AKI. At the multivariable analysis, procedures performed without the RenalGuard System (adjusted odds ratio: 5.99, 95% CI: 1.56 to 23.04; p = 0.009) and AKI risk score 4 (adjusted odds ratio: 4.31, 95% CI: 1.39 to 13.37) were found to be independently associated with an increased risk of AKI.

DISCUSSION

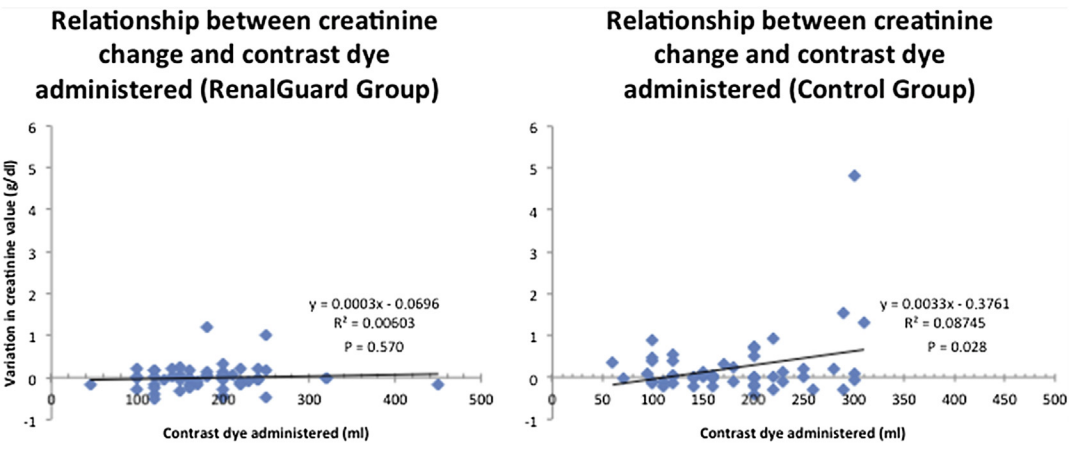
Baseline renal function should be kept in mind in elderly and sick patients, such as those with severe aortic stenosis, because post-operative AKI seems to significantly worsen the early and late prognosis of those undergoing TAVR (19,21). Despite the widespread utilization of this procedure, no standardized

FIGURE 5 Serum Biomarkers



Trends of serum creatinine **(right)**, sodium **(middle)**, and potassium **(left)** values. TAVI = transcatheter aortic valve implantation.

FIGURE 6 Renal Function and Contrast Dye



Variation in creatinine value in response to contrast dye administered in the 2 groups.

TABLE 4 Clinical Outcomes Up to 30 Days

	RenalGuard Group (n = 56)	Control Group (n = 56)	p Value
In-hospital			
Death	1 (1.8)	2 (3.6)	0.537
Cardiovascular death	0 (0)	1 (1.8)	0.306
Stroke/TIA	0 (0)	0 (0)	–
Permanent PM	6 (10.7)	5 (8.9)	0.799
Bleeding	5 (8.9)	6 (10.7)	0.354
Life threatening	2 (3.6)	0 (0.0)	0.558
Major	1 (1.8)	3 (5.4)	0.309
Minor	2 (3.6)	3 (5.4)	0.647
Major vascular complication	3 (5.4)	3 (5.4)	0.661
Minor vascular complication	13 (23.2)	6 (10.7)	0.078
Acute kidney injury	3 (5.4)	14 (25.0)	0.014
Stage 1	3 (5.4)	13 (23.2)	0.013
Stage 2	0 (0.0)	0 (0.0)	–
Stage 3	0 (0.0)	1 (1.8)	0.315
30 days			
Death	1 (1.8)	1 (1.8)	0.752
Cardiovascular death	1 (1.8)	1 (1.8)	0.752
Stroke/TIA	0 (0.0)	0 (0.0)	–
Disabling stroke	0 (0.0)	0 (0.0)	–
Nondisabling stroke	0 (0.0)	0 (0.0)	–
TIA	1 (1.8)	2 (3.6)	0.537
Permanent PM	6 (10.7)	5 (8.9)	0.799
Bleeding	5 (8.9)	6 (10.7)	0.354
Life threatening	2 (3.6)	0 (0.0)	0.558
Major	1 (1.8)	3 (5.4)	0.309
Minor	2 (3.6)	3 (5.4)	0.647
Hospitalization for heart failure	1 (1.8)	1 (1.8)	0.752

Values are n (%).
PM = pacemaker; TIA = transient ischemic attack.

protocol for AKI prevention has been proposed yet. The results of this single-center randomized study powered to detect differences in AKI within 72 h after TAVR demonstrate that prophylactic intravenous loading dose of 250-ml normal saline solution combined with furosemide-induced high-volume diuresis and maintenance of intravascular volume through automatic matched hydration (RenalGuard system) is safe and superior to standard infusion of normal saline solution at a high dose.

Hydration remains the cornerstone of AKI prevention in patients exposed to contrast media by producing plasma volume expansion with concomitant suppression of the renin-angiotensin-aldosterone system, down-regulation of tubuloglomerular feedback, dilution of contrast media, and thus, prevention of renal vasoconstriction and tubular obstruction (9,10). Furosemide administration may have some positive effects when associated with hydration because it enhances contrast dilution in the renal tubule through increased urine flow and prevents fluid overload and congestive heart failure. However, these positive actions may be thwarted by furosemide-induced reduction of the effective circulating volume, prostaglandin-mediated venodilation, and dehydration as a result of increased urine output (22). This explains why achieving a high urine flow rate is key. In the PRINCE (Prevention of Radiocontrast Induced Nephropathy Clinical Evaluation) study, a protective effect against contrast-induced AKI was observed when a mean urine flow rate >150 ml/h was achieved with a single dose of diuretic agent and

matched intravenous fluid replacement (23). Hence, there is a rationale for furosemide-induced high-volume diuresis with concurrent maintenance of intravascular volume through matched hydration as an alternative strategy for AKI prevention in high-risk patients.

The RenalGuard System is a device capable of delivering intravenous fluid in an amount exactly matched to the volume of urine produced by the patient and precisely weighed by the system. The RenalGuard, with its matched fluid replacement capability, enables the physician to achieve high urine output safely with a low furosemide dose by maintaining the intravascular volume and minimizing the risk of overhydration or underhydration. This feature is important particularly in patients with severe aortic stenosis, which usually are in labile hemodynamic compensation.

Two randomized trials (REMEDIAL [Renal Insufficiency After Contrast Media Administration Trial] and MYTHOS [Induced Diuresis With Matched Hydration Compared to Standard Hydration for Contrast Induced Nephropathy Prevention]) have demonstrated that the RenalGuard system protects patients undergoing percutaneous coronary intervention from AKI (14–16). In the present registry-based randomized study, we extended these findings to a more complex and aged population, where the benefits are expected to accrue. We showed that the approach of controlled, forced diuresis with RenalGuard is more effective than standard hydration protocols in preventing AKI in patients undergoing TAVR. Indeed, we observed a 79% relative risk reduction in the RenalGuard group as compared with the control group.

Despite a favorable effect of this strategy, we did not observe a significant reduction in major endpoints (death, bleeding, and so on) in the study group. This finding can be explained by the high prevalence of AKI stage 1, which has been already demonstrated to not be associated with poorer outcomes after TAVR (19). Putting these results into perspective, we can only speculate that a strategy of furosemide-induced diuresis with matched isotonic intravenous hydration also has the potential to reduce the risk of AKI stage 2 and 3. To test this hypothesis, adequately powered studies targeting patients with AKI stage 2 and 3 are warranted.

Finally, we found that the RenalGuard System may be well founded in almost all patients undergoing elective TAVR due to its safety profile and its simple use. In our population, it has been used without any consequences. Indeed, no hydration-associated complications were observed, with only few patients developing asymptomatic hypokalemia that was corrected with potassium supplementation as per usual practice.

STUDY LIMITATIONS. First, this was a single-center study, which may affect the generalizability of our findings. Second, the trial was open-label. Third, the hydration strategy in the control group did not include N-acetylcysteine coupled with normal saline solution. However, the data available on N-acetylcysteine before coronary angiography to prevent AKI in patients with impaired renal function neither are conclusive nor provide conclusive proofs to influence clinical practice and public policies (24).

CONCLUSIONS

Furosemide-induced diuresis with matched isotonic intravenous hydration using the RenalGuard system is an effective therapeutic tool to reduce the occurrence of AKI in patients undergoing TAVR. Larger studies are warranted to define the optimal AKI prevention strategy in TAVR patients.

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PERSPECTIVES

WHAT IS KNOWN? Studies conducted in patients undergoing percutaneous coronary intervention have recently demonstrated that furosemide-induced diuresis with matched isotonic intravenous hydration by the RenalGuard System significantly reduced AKI in high-risk patients undergoing coronary procedures. Whether these findings translate to patients undergoing TAVR is unexplored.

WHAT IS NEW? The results of this single-center randomized study powered to detect differences in AKI within 72 h after TAVR demonstrate that a prophylactic intravenous loading dose of 250 ml normal saline solution combined with furosemide-induced high-volume diuresis and maintenance of intravascular volume through automatic matched hydration (RenalGuard system) is safe and superior to standard infusion of normal saline solution at a high dose.

WHAT IS NEXT? Furosemide-induced diuresis with matched isotonic intravenous hydration using the RenalGuard system is an effective therapeutic tool to reduce the occurrence of AKI in patients undergoing TAVI.

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KEY WORDS AKI, RenalGuard, TAVR